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for all that matters in pharmacy

SNOWED UNDER

DR DES CORRIGAN ON THE RESURGENCE OF IRELAND'S COCAINE EPIDEMIC

CLINICAL CONTENT

- RHEUMATOID ARTHRITIS
- CARDIAC CARE
- IBD/IBS

GOING VIRAL

ADVICE FOR PHARMACISTS ON HOW TO DEAL WITH COVID-19

TRELEGY▼ELLIPTA

(fluticasone furoate/umeclidinium/vilanterol)

The only COPD Triple Therapy delivered in a single daily inhalation.[1]
Improvement in quality of life vs. ICS/LABA.[2,3]

LESS TO TAKE. **MORE TO TAKE IN.**

A combination of ICS/LAMA/LABA (FF/UMEC/VI) administered through a single daily inhalation from the Ellipta inhaler, which is easy to use[1-5]

TRELEGY▼ELLIPTA
fluticasone furoate/umeclidinium/vilanterol

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions.

TRELEGY Ellipta FF/UMEC/VI 92/55/22 mcg OD is indicated for Maintenance treatment in adult patients with moderate to severe COPD who are not adequately treated by a combination of an inhaled corticosteroid (ICS) and a long-acting β_2-agonist (LABA) or a combination of a LABA and a long acting muscarinic antagonist.

COPD, chronic obstructive pulmonary disease; FF, fluticasone furoate; ICS, inhaled corticosteroids; LABA, long-acting β_2-agonist; LAMA, long-acting muscarinic antagonist; OD, once-daily; UMEC, umeclidinium, VI, vilanterol.

References: 1. TRELEGY Ellipta SmPC, available at www.medicines.ie, last accessed October 2019. **2.** Lipson DA *et al. Am J Respir Crit Care Med* 2017; 196:438–446. **3.** Lipson DA, *et al.* N Engl J Med. May 3 2018;378(18):1671-1680. **4.** Svedsater H *et al. BMC Pulm Med* 2013; 13:72–86. **5.** van der Palen J *et al. NPJ Prim Care Respir Med* 2016; 26:16079.

Trelegy▼ Ellipta (fluticasone furoate/umeclidinium/vilanterol [as trifenatate]) Prescribing information.
Please consult the full Summary of Product Characteristics (SmPC) before prescribing.

Trelegy Ellipta (fluticasone furoate/umeclidinium/vilanterol [as trifenatate]) inhalation powder. Each single inhalation of fluticasone furoate (FF) 100 micrograms (mcg), umeclidinium bromide (UMEC) 62.5 micrograms and vilanterol as trifenatate (VI) 25 mcg provides a delivered dose of 92 mcg FF, 55 mcg UMEC and 22 mcg VI. **Indications:** Maintenance treatment in adult patients with moderate to severe COPD who are not adequately treated by a combination of an inhaled corticosteroid (ICS) and a long-acting β_2-agonist (LABA) or a combination of a LABA and a long acting muscarinic antagonist. **Dosage and administration:** One inhalation once daily at the same time each day. **Contraindications:** Hypersensitivity to the active substances or to any of the excipients (lactose monohydrate & magnesium stearate). **Precautions:** Paradoxical bronchospasm, unstable or life-threatening cardiovascular disease or heart rhythm abnormalities, convulsive disorders or thyrotoxicosis, pulmonary tuberculosis or patients with chronic or untreated infections, narrow-angle glaucoma, urinary retention, hypokalaemia, patients predisposed to low levels of serum potassium, diabetes mellitus. In patients with moderate to severe hepatic impairment patients should be monitored for systemic corticosteroid-related adverse reactions. Eye symptoms such as blurred vision may be due to underlying serious conditions such as cataract, glaucoma or central serous chorioretinopathy (CSCR); consider referral to ophthalmologist. Increased incidence of pneumonia has been observed in patients with COPD receiving inhaled corticosteroids. *Risk factors for pneumonia include:* current smokers, old age, patients with a history of prior pneumonia, patients with a low body mass index and severe COPD. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take Trelegy. *Acute symptoms:* Not for acute symptoms, use short-acting inhaled bronchodilator. Warn patients to seek medical advice if short-acting inhaled bronchodilator use increases. Therapy should not be abruptly stopped without physician supervision due to risk of symptom recurrence. *Systemic effects:* Systemic effects of ICSs may occur, particularly at high doses for long periods, but much less likely than with oral corticosteroids. **Interactions with other medicinal products:** Caution should be exercised with concurrent use of β-blockers. Caution is advised when co-administering with strong CYP3A4 inhibitors (e.g. ketoconazole, ritonavir, cobicistat-containing products), hypokalaemic treatments or non-potassium-sparing diuretics. Co-administration with other long-acting muscarinic antagonists or long acting β_2-adrenergic agonists is not recommended. **Pregnancy and breast-feeding:** Experience limited. Balance risks against benefits. **Side effects:** *Common (≥1/100 to <1/10):* pneumonia, upper respiratory tract infection, bronchitis, pharyngitis, rhinitis, sinusitis, influenza, nasopharyngitis, candidiasis of mouth and throat, urinary tract infection, headache, cough, oropharyngeal pain, arthralgia, back pain. *Uncommon (≥1/1,000 to <1/100):* viral respiratory tract infection, supraventricular tachyarrhythmia, tachycardia, atrial fibrillation, dysphonia, dry mouth, fractures; *Not known (cannot be estimated from the available data):* vision blurred. **Marketing Authorisation (MA) Holder:** GlaxoSmithKline Trading Services Limited, Curabinny, Co. Cork, Ireland. **MA No. [EU/1/17/1236/002]. Legal category:** POM B. **Last date of revision:** June 2019. **Code:** PI-2093. Further information available on request from GlaxoSmithKline, 12 Riverwalk, Citywest Business Campus, Dublin 24. Tel: 01-4955000.

Adverse events should be reported to the Health Products Regulatory Authority (HPRA) using an Adverse Reaction Report Form obtained either from the HPRA or electronically via the website at www.hpra.ie. Adverse reactions can also be reported to the HPRA by calling: (01) 6764971. Adverse events should also be reported to GlaxoSmithKline on 1800 244 255.

A full list of adverse reactions can be found in the Summary of Product Characteristics.
In common with other corticosteroid-containing medicines, there is an increased risk of pneumonia in patients with COPD treated with TRELEGY Ellipta.[1] Trelegy Ellipta should be used with caution in patients with unstable life-threatening cardiovascular disease.[1]

Please see www.trelegy.ie to find out more

TRELEGY Ellipta was developed in collaboration with INNOVIVA

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MEDICINES SUPPLY

IPHA urges progress on access to new medicines following general election

Biopharmaceutical innovators have urged politicians to make faster access to innovative new medicines a Programme for Government priority when it is negotiated after the General Election. The Irish Pharmaceutical Healthcare Association (IPHA), which represents the originator biopharmaceutical industry, said the political leaders who form a new Government should adopt an explicit policy on how to allocate funding to new medicines, relying on both the State and industry contributions. Ireland is among the slowest in Western Europe to provide new medicines to patients. Patients in Ireland are waiting three times as long to get the same medicines, including cancer drugs, as patients in other comparable European countries.

Updated IPHA analysis has found that 13 medicines, eight of which are for cancer, have been waiting for more than 926 days to be reimbursed and made available to patients. Even though all the medicines have completed the full pharmacoeconomic process and some have received reimbursement approval, funding has not been made available, preventing access by patients. This compares to an average of 289 days from date of EMA licensing in 10 other European countries in which the medicines are available, said IPHA.

IPHA has called on all parties to pledge to improve patients' access to new medicines through policy.

Mr Oliver O'Connor, Chief Executive of IPHA, said: "... We are urging politicians and policymakers to work with the industry to solve the funding and access problem so that patients and their clinicians can get the same range of new medicines, including cancer drugs, as their peers in other Western European countries. The new Programme for Government, whatever parties agree it, should adopt an explicit policy on how to allocate funding to new medicines, relying on both the State and industry contributions."

The statement was released recently on World Cancer Day and according to the National Cancer Registry of Ireland, every three minutes, someone gets a cancer diagnosis. Every hour, someone dies from the disease. Cancer has overtaken heart disease as the most common cause of death in Ireland. The National Cancer Strategy aims to place Ireland in the top quartile of European countries for cancer survival in the next decade.

Mr Oliver O'Connor, IPHA

"That will mean improving access to new medicines, including cancer medicines," said Mr O'Connor. "Innovation is intensifying. Cell therapies are in development that can treat deadly blood cancers by reinfusing patients with their own engineered immune cells to tackle the illness. At the same time, scientists are making progress on gene therapy to cure genetic diseases. And, after a slow start, cancer immunotherapy is making big gains.

"But it remains the case that many of the new cancer medicines our industry discovers are beyond the reach of patients here. We must ensure there is political will behind the effort to correct that anomaly."

PHARMACY EDUCATION

Expressions of interest sought for learning placements

APPEL (Affiliation for Pharmacy Practice Experiential Learning) has said it is now seeking expressions of interest from pharmacists in community and hospital pharmacy settings who would like to facilitate an experiential learning placement for a final-year pharmacy student next year.

Pharmacy students in Ireland now undertake a five-year integrated masters programme to become qualified pharmacists. Key to this new programme are the experiential learning placements that students undertake throughout the course. In the fifth year of their studies, students solidify their learning by completing an eight-month placement in a patient-facing setting before becoming eligible to sit the Professional Registration Examination (PRE) and enter the PSI register. Pharmacists who have previously facilitated APPEL placements have found the experience enjoyable and rewarding, said APPEL. In surveys, 90 per cent of pharmacists said they would recommend facilitating a placement to other pharmacists. The advantages of facilitating an APPEL placement include:

Continuing professional development: APPEL Trainer Training can contribute to pharmacists' CPD, as can the experience of facilitating a placement.

Development of your talent pipeline: Many students will look to start their career in the organisations or practice settings where they undertook their placements.

Engagement: Participating in the APPEL programme provides you with the opportunity to increase awareness of your pharmacy/organisation. APPEL training and events provide valuable networking opportunities.

The next fifth-year placements will run from 4 January to 27 August 2021. The deadline to confirm interest in offering placements is **9 March 2020**. This can be done by visiting https://forms.gle/GT7AsjjA6ZbKRrwx8. For queries or further information, call 01-4025129 or email ops@appel.ie.

Pictured at the official opening of ARC Cancer Support Centres' newest centre, located at Lowell House, 23 Herbert Avenue, Dublin 4, were (L-R) Dr Vincent Carroll, Chairman, ARC Cancer Support Centres; Christy Dignam, Aslan lead singer; Ciara Griffin, Chief II Med Safety and Quality Pharmacist, St Vincent's Private Hospital; Mairead Ronan, TV and radio presenter; and Brian Fenton, Dublin GAA footballer. The drop-in centre, which joins the ARC family of centres already located in Eccles Street, Dublin 7, and South Circular Road, Dublin 8, is in response to the needs of the increasing numbers of people being diagnosed with cancer. The centre will initially be open on Tuesdays, Wednesdays and Thursdays from 10am to 4pm. It will offer a range of services to people with cancer and their loved ones, including counselling and complementary therapies, all entirely free of charge. For more information, visit www.arccancersupport.ie.

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LAMA

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LAMA + LABA

Brimica® Genuair®▼

aclidinium bromide + formoterol

Abbreviated Prescribing Information

Eklira® Genuair®▼ 322 micrograms inhalation powder. Please consult the Summary of Product Characteristics (SPC) for the full prescribing information. **Presentation:** Inhalation powder in a white inhaler with an integral dose indicator and a green dosage button. Each delivered dose contains 375 µg aclidinium bromide equivalent to 322 µg of aclidinium. Also, contains lactose. **Use:** Maintenance bronchodilator treatment to relieve symptoms in adult patients with chronic obstructive pulmonary disease (COPD). **Dosage:** For inhalation use. Recommended dose is one inhalation of 322 micrograms aclidinium twice daily. Patients should be instructed on how to administer the product correctly as the Genuair inhaler may work differently from inhalers used previously. It is important to instruct the patients to read the Instructions for Use in the pack. No dose adjustments are required for elderly patients, or those with renal or hepatic impairment. No relevant use in children and adolescents. **Contraindications:** Hypersensitivity to aclidinium bromide or to any of the excipients. **Warnings and Precautions:** Stop use if paradoxical bronchospasm occurs and consider other treatments. Do not use for the relief of acute episodes of bronchospasm. Use with caution in patients with myocardial infarction in the previous 6 months, unstable angina, newly diagnosed arrhythmia within the previous 3 months, or hospitalisation within the previous 12 months for heart failure functional classes III and IV. Dry mouth, observed with anticholinergic treatment, may be associated with dental caries in the long term. Use with caution in patients with symptomatic prostatic hyperplasia or bladder-neck obstruction or with narrow-angle glaucoma. Do not use in patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption. **Interactions:** Do not administer with other anticholinergic-containing medicinal products. No other interactions expected. Please consult the SPC for more details. **Fertility, pregnancy and lactation:** No data on use in pregnancy. Risk to newborns/infants cannot be excluded. Consider risk-benefit before using during lactation. Unlikely to affect fertility at the recommended dose. **Side-effects:** Common (1-10%): Sinusitis, nasopharyngitis, headache, cough, diarrhoea, nausea. Uncommon (0.1- 1%): Dizziness, blurred vision, tachycardia, palpitations, dysphonia, dry mouth, stomatitis, rash, pruritus, urinary retention. Rare (0.01-0.1%): hypersensitivity. Not known: angioedema, anaphylactic reaction. **Pack sizes:** Carton containing 1 inhaler with 60 unit doses. **Legal category:** POM **Marketing Authorisation Number:** EU/1/12/778/002 **Marketing Authorisation holder:** AstraZeneca AB, SE-151 85 Södertälje, Sweden. **Marketed by:** A. Menarini Pharmaceuticals Ireland Ltd., Castlecourt, Monkstown Farm, Monkstown, Glenageary, Co. Dublin A96 T924. Further information is available on request to A. Menarini Pharmaceuticals Ireland Ltd. or may be found in the SPC. **Last updated:** May 2018

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions to: HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2, Tel: +353 1 6764971, Fax: +353 1 6762517, Website: www.hpra.ie, e-mail: medsafety@hpra.ie. Adverse events should also be reported to A. Menarini Pharmaceuticals Ireland Ltd. Phone no: 01 284 6744.

Date of item: October 2019. IR-BRI-16-2019

Abbreviated Prescribing Information

Brimica® Genuair®▼ 340 micrograms/12 micrograms inhalation powder. Please consult the Summary of Product Characteristics (SPC) for the full prescribing information. **Presentation:** Inhalation powder in a white inhaler with an integral dose indicator and an orange dosage button. Each delivered dose contains 396 µg aclidinium bromide (equivalent to 340 µg of aclidinium) and 11.8 micrograms of formoterol fumarate dihydrate. Also, contains lactose. **Use:** Maintenance bronchodilator treatment to relieve symptoms in adult patients with chronic obstructive pulmonary disease (COPD). **Dosage:** For inhalation use. Recommended dose is one inhalation of 340 µg/12 µg twice daily. Patients should be instructed on how to administer the product correctly as the Genuair inhaler may work differently from inhalers used previously. It is important to instruct the patients to read the Instructions for Use in the pack. No dose adjustments are required for elderly patients, or those with renal or hepatic impairment. No relevant use in children and adolescents. **Contraindications:** Hypersensitivity to the active substances or to any of the excipients. **Warnings and Precautions:** Do not use in asthma. Stop use if paradoxical bronchospasm occurs and consider other treatments. Do not use for the relief of acute episodes of bronchospasm. Use with caution in patients with myocardial infarction in the previous 6 months, unstable angina, newly diagnosed arrhythmia within the previous 3 months, or hospitalisation within the previous 12 months for heart failure functional classes III and IV. Discontinue if increases in pulse rate, blood pressure or changes in ECG occur. Use with caution in patients with a history of or known prolongation of the QTc interval or treated with products affecting the QTc interval. Use with caution in patients with severe cardiovascular disorders, convulsive disorders, thyrotoxicosis and phaeochromocytoma. Hypokalaemia may occur, is usually transient and supplementation not needed. In patients with severe COPD, hypokalaemia may be potentiated by hypoxia and concomitant treatment. Use with caution in patients with symptomatic prostatic hyperplasia, urinary retention or with narrow-angle glaucoma. Dry mouth, observed with anticholinergic treatment, may be associated with dental caries in the long term. Do not use in patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption. **Interactions:** Do not administer with other anticholinergic and/or long-acting β2-adrenergic agonist containing medicinal products. Caution in use with methylxanthine derivatives, steroids, non-potassium-sparing diuretics, β-adrenergic blockers or medicinal products known to prolong the QTc interval. Please consult the SPC for more details. **Fertility, pregnancy and lactation:** No data on use in pregnancy. Consider risk-benefit before using during lactation. Unlikely to affect fertility at the recommended dose. **Side-effects:** Common (1-10%): Nasopharyngitis, urinary tract infection, sinusitis tooth abscess, insomnia, anxiety, headache, dizziness, tremor, cough, diarrhoea, nausea, dry mouth, myalgia, muscle spasms, peripheral oedema, increased blood creatine phosphokinase. Uncommon (0.1- 1%): Hypokalaemia, hyperglycaemia, agitation, dysgeusia, blurred vision, tachycardia, electrocardiogram QTc prolonged, palpitations, angina pectoris, dysphonia, throat irritation, stomatitis, rash, pruritus, urinary retention, increased blood pressure. Rare (0.01-0.1%): Hypersensitivity, bronchospasm, including paradoxical. Not known: anaphylactic reaction, angioedema. **Pack sizes:** Carton containing 1 inhaler with 60 unit doses. **Legal category:** POM **Marketing Authorisation Number:** EU/1/14/963/001 **Marketing Authorisation holder:** AstraZeneca AB, SE-151 85 Södertälje, Sweden. **Marketed by:** A. Menarini Pharmaceuticals Ireland Ltd., Castlecourt, Monkstown Farm, Monkstown, Glenageary, Co. Dublin A96 T924. Further information is available on request to A. Menarini Pharmaceuticals Ireland Ltd. or may be found in the SPC. **Last updated:** October 2019

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie. Adverse events should also be reported to A. Menarini Pharmaceuticals Ireland Ltd. Phone no: 01 284 6744.

A. MENARINI PHARMACEUTICALS IRELAND LTD

Healthcare for Life

References:

1. MIMS Ireland October 2019
2. Eklira Genuair Summary of Product Characteristics, last updated February 2018
3. Brimica Summary of Product Characteristics, last updated August 2019
4. Magnussen, H et al. COPD. 2019 Apr;16(2):196-205

FALSIFIED MEDICINES

Council of Europe study highlights inadequacy of legislation on pharmaceutical crime

A recent study, 'Medicrime vs Volcano: A practical case study on how the Council of Europe Convention could improve the fight against pharmaceutical crime', carried out within the framework of the Council of Europe MEDICRIME Convention, has highlighted shortcomings of current legislative approaches in relation to the protection of patients against falsified medicines in Europe.

The study, authored by Domenico Di Giorgio of the Italian Medicines Agency (AIFA), and Diana Russo, Public Prosecutor of Naples, Italy, with the support of the European Directorate for the Quality of Medicines and HealthCare (EDQM), focused on a real case from the 2014 'Operation Volcano', which saw anti-cancer medicines stolen from Italian hospitals and reintroduced in distribution chains to be sold throughout Europe.

The study shows how the MEDICRIME Convention would have supported the prosecution of the case and led to effective sanctions against perpetrators, making a case for the appropriate implementation of the convention.

Based on a survey of regulators and prosecutors in participating countries (Armenia, Belgium, Germany, Italy, Serbia and the UK), the study outcome highlighted the inadequacy of existing legislation on pharmaceutical crimes in light of their serious potential repercussions on public health. The study highlighted in particular shortcomings in traceability systems, the fragmentation of proceedings related to pharmaceutical crimes, and insufficient options for accessory sanctions.

The survey showed that applicable criminal charges remained mostly generic and were not fit for the specific implications for public health that derive from falsifying medicines. From theft of goods or handling of stolen goods, to criminal association — which can currently only be punished under provisions for mafia associations (Italy) or for conspiracy (UK) — most regulatory frameworks do not take into consideration the fact that reintroducing stolen medicines to markets represents a far greater risk for patients than ordinary thefts.

Medicines that are not stored correctly or are tampered with may deprive unwitting patients of the care needed and negatively affect their health. Similarly, sanctions for manufacturing illegal medicinal products or for manipulating authentic medicines, although covered in most criminal codes, are often subordinate to proof of damage to patients or considered as a breach of trademark, contrary to the provisions in the MEDICRIME Convention, which foresees direct charges thanks to its focus on the potential risk for patients.

The study concluded that overall, applicable sanctions were not a sufficiently strong deterrent when weighed against the potential profits of falsifying medicines. Co-ordination and information were also seen as important aspects in need of improvement, due to the involvement of many different judicial authorities in cross-border investigations and often also within the same country.

The study also pointed out that raising awareness of pharmaceutical crime within the judicial sector would pave the way for implementing good practices related to information-sharing between prosecution officers.

FGM

FGM 'continues to rise in Ireland' — World Vision Ireland

World Vision Ireland, an international aid charity, recently warned about the dangers of female genital mutilation (FGM) on International Day of Zero Tolerance for Female Genital Mutilation 2020.

On 27 January, a married couple were convicted of the FGM of their own daughter, the first conviction of FGM recorded in Ireland. The child was just one year old at the time when the FGM was carried out, in 2016. Judge Elma Sheahan sentenced the male accused to five-and-a-half years' imprisonment, and the female accused to four years and nine months.

According to World Vision Ireland, 200 million women and girls worldwide have undergone FGM. The charity said that FGM is an act of violence against women and girls and has no health benefits whatsoever. FGM is defined as the partial or total removal of the external female genitalia, or any practice that deliberately changes or injures the female genital organs for non-medical reasons.

"The recent judgement is one that World Vision Ireland welcomes — it sends a very clear and vital message that FGM is not tolerated in Ireland," Ms Fiona O'Malley, Director of Communications at World Vision Ireland, said. "The estimation of the number of girls at risk of FGM in EU Member States is quite complex, because of the intimate nature of the crime, the stigma and secrecy around it, and because of the lack of data that allows for accurate measurement. Whilst we do not have conclusive or recent data, the European Institute for Gender Equality (EIGE) estimates that the level of FGM continues to increase in Ireland. A 2015 EIGE report suggests that the number of girls at risk of FGM in Ireland is between 158 and 1,632... it is important to emphasise that the procedure has absolutely no health benefits whatsoever for women or girls. It is a reversal of the natural order for a parent, instead of shielding and protecting their child, to subject them to such horror."

Procedures can cause severe bleeding and problems urinating, cysts, infections, as well as complications in childbirth and increased risk of new-born deaths.

World Vision has set up protection committees to address issues of gender-based violence in Somalia, where 98 per cent of women have been subjected to FGM.

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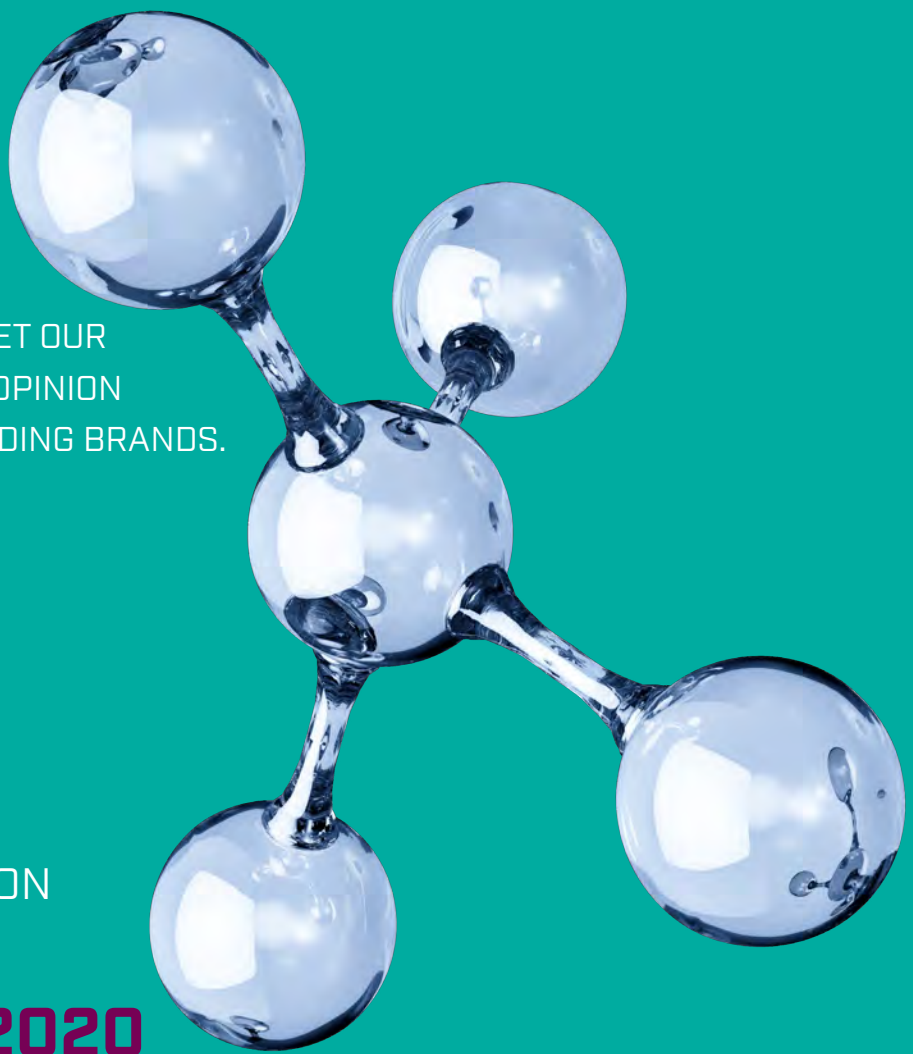

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SMOKING CESSATION

Smokers 'being deprived of much-needed help to quit'

The health system needs to do more to help smokers quit, otherwise smoking rates will not fall fast enough, the Irish Pharmacy Union (IPU) warned on National No Smoking Day as it criticised the lack of action and innovation in how smoking cessation supports are offered.

"The rate of smoking in Ireland has fallen steadily over the last five years," stated Mr Tomás Conefrey, a community pharmacist and member of the IPU, citing the Healthy Ireland 2019 Survey. "This is a huge achievement and all those responsible should be commended, most notably the quitters themselves. However, 17 per cent of people over the age of 15 still smoke every single day, and that is far too many.

"The welcome reduction over the last five years will not be sustained into the future unless access to support is improved. In particular, we need to offer greater support to medical card patients, as the research shows smoking in deprived areas is far higher than the national average (24 per cent) and higher still for those unemployed (40 per cent).

"Nicotine replacement therapy is proven to work and can significantly improve the chances that an attempt to quit will be successful. NRT has been successfully available in pharmacies for many years but unfortunately, medical card patients still must go through their GP. This reduces the convenience and creates an unnecessary barrier for would-be quitters. There is no reason why this artificial barrier should remain in place and it will limit Ireland's ability to lower smoking rates."

LYME DISEASE

Ethnobotanical medicine 'effective against the bacterium causing Lyme disease'

A recent preclinical study in test tubes has shown that selected plant-based herbal medicines, especially Ghanaian quinine and Japanese knotweed, work better than antibiotics in Lyme disease.

Lyme disease, also called borreliosis, is the most common vector-borne disease in the Northern hemisphere. It is caused by the spirochete (corkscrew-shaped) bacterium *Borrelia burgdorferi* and close relatives and is mainly spread through the bite of infected ticks.

Currently, more than 300,000 new cases are reported in the US each year, compared to 65,000 in Europe, and these numbers are rising due to climate change and urban sprawl.

The standard of care for Lyme disease, a course of antibiotics over two-to-four weeks, is not always effective: At least 10-to-20 per cent of treated patients continue to experience symptoms after treatment. Late-stage Lyme disease patients may experience many different symptoms, including fatigue, joint pains, memory problems, facial paralysis, aches, stiffness in the neck, heart palpitations, and severe headaches.

In a recent study published in *Frontiers in Medicine*, researchers from the Johns Hopkins Bloomberg School of Public Health, with colleagues at the California Centre for Functional Medicine and Focus Health, surveyed the power of 14 plant-based extracts to kill *Borrelia burgdorferi*, compared to the currently-used Lyme antibiotics doxycycline and cefuroxime.

The researchers tested these extracts' effectiveness *in vitro* on the free-swimming 'planktonic' form of the bacterium, as well as against microcolonies.

Microcolonies are aggregates of bacteria, the first stage in the development of biofilms.

The researchers showed that plant extracts from black walnut, cat's claw, sweet wormwood, Mediterranean rockrose, and Chinese skullcap had strong activity against *B.burgdorferi*, outperforming both tested antibiotics.

But by far the strongest performers were Ghanaian quinine (*Cryptolepis sanguinolenta*, also known as yellow-dye root, nibima, or kadze) and Japanese knotweed (*Polygonum cuspidatum*).

Ghanaian quinine is a shrub from West Africa containing the antimicrobial alkaloid cryptolepine and is used in ethnomedicine to treat malaria, hepatitis, septicaemia and tuberculosis. Japanese knotweed is a traditional medicine in India and China that contains the polyphenol resveratrol. In other preclinical studies, it has been found to have anti-tumour and anti-inflammatory effects and protect the nervous system and heart. Extracts from both plants were found to kill microcolonies of *Borrelia burgdorferi* and inhibit division of the planktonic form, even at low concentrations (0.03-0.5%). Remarkably, a single seven-day treatment with 1% Ghanaian quinine could completely eradicate the bacterium — it did not regrow, even under optimal conditions in the drug's absence.

"This study provides the first convincing evidence that some of the herbs used by patients, such as *Cryptolepis*, black walnut, sweet wormwood, cat's claw, and Japanese knotweed have potent activity against Lyme disease bacteria, especially the dormant persister forms, which are not killed by the current Lyme antibiotics," said Dr Ying Zhang from the Johns Hopkins Bloomberg School of Public Health.

"These findings are exciting, as they offer opportunities for improved treatment of persistent Lyme disease, which is not helped by the current standard treatment."

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CLONMEL HEALTHCARE
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PRE-ECLAMPSIA

Natural antioxidant found in mushrooms may alleviate features of pre-eclampsia

New research has revealed that a substance, L-ergothioneine, most commonly found in mushrooms, could help alleviate some features of pre-eclampsia.

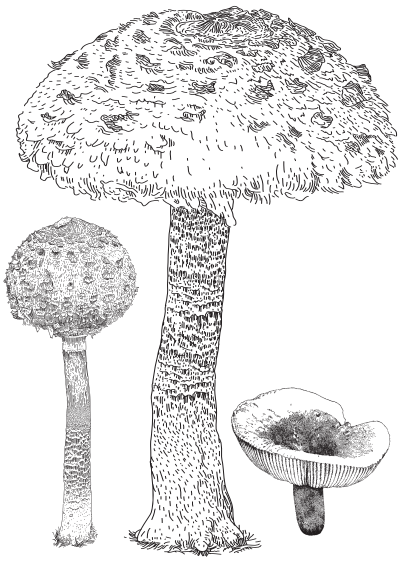
There is currently is no cure for pre-eclampsia other than delivery, which can present a major medical problem if the condition results in an extremely premature birth.

Now researchers in the Department of Pharmacology and Therapeutics at University College Cork (UCC), the INFANT Research Centre at UCC and the University of Liverpool, have shown that a natural diet-derived substance, L-ergothioneine, can alleviate some of the features of this condition.

Significant research suggests that pre-eclampsia may be caused by substances released from the placenta that disrupt normal biological processes in the mother. In particular, disruption of mitochondrial function can lead to exaggerated oxidative stress. Ergothioneine is a potent and effective mitochondrial antioxidant. Ergothioneine can be found in a wide variety of foods, but the chief source of ergothioneine in the human diet is mushrooms.

"We wanted to see if this natural antioxidant could ameliorate some of the biological features of pre-eclampsia using our model of disease," said Dr Cathal McCarthy at UCC, leader of this research. "Our research shows that treating rats with pre-eclampsia with the natural antioxidant L-ergothioneine reduced blood pressure, prevented foetal growth restriction and dampened production of the damaging substances released from the placenta during pre-eclampsia. Furthermore, using an exciting new approach, we identified that treatment with ergothioneine diminished mitochondrial-derived oxidative stress."

The new research opens up a new avenue for therapeutic investigation in the elusive search for a treatment for pre-eclampsia. Ergothioneine appears to be a safe, natural, diet-derived antioxidant whose therapeutic potential looks promising but remains to be validated by the gold standard of sufficiently-powered human clinical trials.



The study has been published in the leading journal *Hypertension*. This research was supported by a Health Research Board Health Research Award.

BLOOD PRESSURE

New NUI Galway study challenges blood pressure guidelines

A major research study from NUI Galway has interrogated the implications for patients of new, lower blood pressure thresholds recommended in recently-released American and European medical guidelines for the treatment of high blood pressure.

The findings from the study indicate that up to 150,000 Irish adults who are newly eligible for treatment to a lower than previously-recommended blood pressure target, may in fact not benefit from increases in their doses or number of blood pressure medications. This may have knock-on implications for the national drugs bill. The NUI Galway investigation, led by Prof Bill McEvoy, was conducted in collaboration with US investigators and is now published in the *Journal of the American Medical Association* (*JAMA*). The investigators looked specifically at the new American diastolic blood pressure threshold of 80 for the diagnosis of hypertension. This new diastolic blood pressure threshold of 80 was a reduction from prior guideline recommendations that advised doctors to use a diastolic blood pressure of 90 or more to make a diagnosis.

Diastolic blood pressure is the lower of two readings reported when describing blood pressure values; the other, top number is called systolic blood pressure. High blood pressure can be diagnosed when either the systolic or diastolic (or in some cases both) numbers are above the threshold value. The NUI Galway investigation looked at a type of high blood pressure or hypertension, termed isolated diastolic hypertension. This occurs when the systolic (top) number is normal (ie, below 130, according to new guidelines) but in contrast, the diastolic (bottom) number is high (ie, greater than or equal to 80, according to new guidelines). Prof McEvoy and co-authors report that, when applying the new guidelines, approximately 5 per cent of the US adult population will be newly-diagnosed with high blood pressure (or hypertension) based on this pattern of isolated diastolic hypertension. That translates into approximately 12 million adults in the US being newly-diagnosed with this condition.

The corresponding Irish figure would be 100,000 new cases. Prof McEvoy said: "Guidelines in both America and Europe advise that doctors treat blood pressure down to a level of 130/80 in the majority of patients. There is little doubt that treating the systolic (or top) blood pressure value down to 130 is beneficial and reduces heart disease and stroke. This is important to stress. However, the recommendation to also treat the diastolic (lower) value down to 80 is more controversial and our results would suggest that the more traditional target for diastolic blood pressure of 90 is also safe, as long as the top number is controlled below 130.

"By focusing on good control of the top number and by relaxing drug treatment goals for adults with isolated increases in the bottom diastolic blood pressure number, we may be able to avoid potential over-treatment of a lot of people and instead focus on healthy diet and lifestyle."

NEW*

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***New to Nytol range in Ireland.** **Nytol One-A-Night 50 mg Tablets** contains diphenhydramine hydrochloride. A symptomatic aid to the relief of temporary sleep disturbance in adults. **Adults:** One tablet to be taken 20 minutes before going to bed, or as directed by a physician. Do not exceed the maximum dose of one tablet in 24 hours. Elderly patients or patients with liver or kidney problems should consult their doctor before taking this medicine. **Children under 18 years:** Not recommended. The product should not be taken for more than 7 days without consulting a doctor. **Contraindications:** hypersensitivity to the active substance or to any of the excipients, stenosing peptic ulcer, pyloroduodenal obstruction, phaeochromocytoma, known acquired or congenital QT interval prolongation, known risk factors for QT interval prolongation. **Special warnings and precautions:** pregnancy/lactation, renal and hepatic impairment, myasthenia gravis, epilepsy or seizure disorders, narrow-angle glaucoma, prostatic hypertrophy, urinary retention, asthma, bronchitis, COPD. Patients should be advised to promptly report any cardiac symptoms. Do not take for more than 7 consecutive nights without consulting a doctor. Use in the elderly should be avoided. Avoid concomitant use of alcohol or other antihistamine-containing preparations. Do not drive or operate machines. **Interactions:** CNS depressants, MAO inhibitors, anticholinergic drugs (e.g. atropine, tricyclic antidepressants), metoprolol and venlafaxine, CYP2D6 inhibitors, Class Ia and Class III anti-arrhythmics. **Side effects:** thrombocytopenia, hypersensitivity reactions, confusion, paradoxical excitation, sedation, drowsiness, disturbance in attention, unsteadiness, dizziness, convulsions, headache, paraesthesia, dyskinesias, blurred vision, tachycardia, palpitations, thickening of bronchial secretions, dry mouth, gastrointestinal disturbance, muscle twitching, urinary difficulty, urinary retention, fatigue. **Legal classification:** P: PA1186/016/001. **MAH:** Chefaro Ireland DAC. The Sharp Building. Hogan Place. Dublin 2. Ireland. **RRP** (ex. VAT)**:** 20s €7.99. **SPC:** https://www.medicines.ie/medicines/nytol-one-a-night-50-mg-tablets-34889/smpc

IRE-NYT-2019-013

NUTRITION

New safefood research reveals gluten-free snack foods 'not as healthy as people think'

A new research report launched recently by *safe*food found that while more than one-in-five people (23 per cent) surveyed buy gluten-free foods, 92 per cent of those people did not have a gluten-related disorder or had not been medically diagnosed with coeliac disease.

Among those people surveyed, there was a misperception of the health benefits of gluten-free products; more than one-in-five people (23 per cent) thought that gluten-free products were lower in fat, 21 per cent thought they were lower in sugar, and 19 per cent considered a gluten-free diet was a healthy way to lose weight.

The research also included a snapshot survey that looked at the nutritional content of 67 gluten-free snack foods. These snack foods included nut products and savoury snacks, cereal and baked products, and confectionery. Of all the gluten-free snack products surveyed, 75 per cent were high in fat and 69 per cent were high in sugar, with calorie levels similar to that of a standard chocolate bar.

Introducing the research, Dr Catherine Conlon, Director of Human Health and Nutrition, *safe*food, said: "For those people who have a diagnosis of coeliac disease or those with a gluten-related disorder, avoiding gluten in their daily diet is an absolute must. However, we would have a concern that some of these snack foods have an unhealthy nutritional profile for everyone, whether or not they have a gluten-related disorder. Snacking on foods such as fruit and vegetables, unsalted plain nuts and gluten-free rice cakes and cheese are healthier options for us all.

"We know from our survey that 92 per cent of people buying these products do not have a gluten-related disorder or have not been diagnosed with coeliac disease and therefore have no medical reason to avoid gluten in their diet. There is no consistent evidence that a gluten-free diet will improve your health if you aren't sensitive to gluten. Many of the gluten-free snacks we surveyed are high in fat and sugar, like other treat foods."

According to industry estimates, the gluten-free food market in Ireland was worth €66 million in 2017, an increase of 33 per cent on the previous year. Many gluten-free food products are promoted by media personalities and sports stars as part of a trend for 'clean labels', including 'free-from' food products.

The report, ***Cutting out gluten – the nutrient profile of gluten-free snack foods on the island of Ireland***, is available to download at **www.safefood.eu**.

DRUG INNOVATION

How astronauts will make their own drugs in space

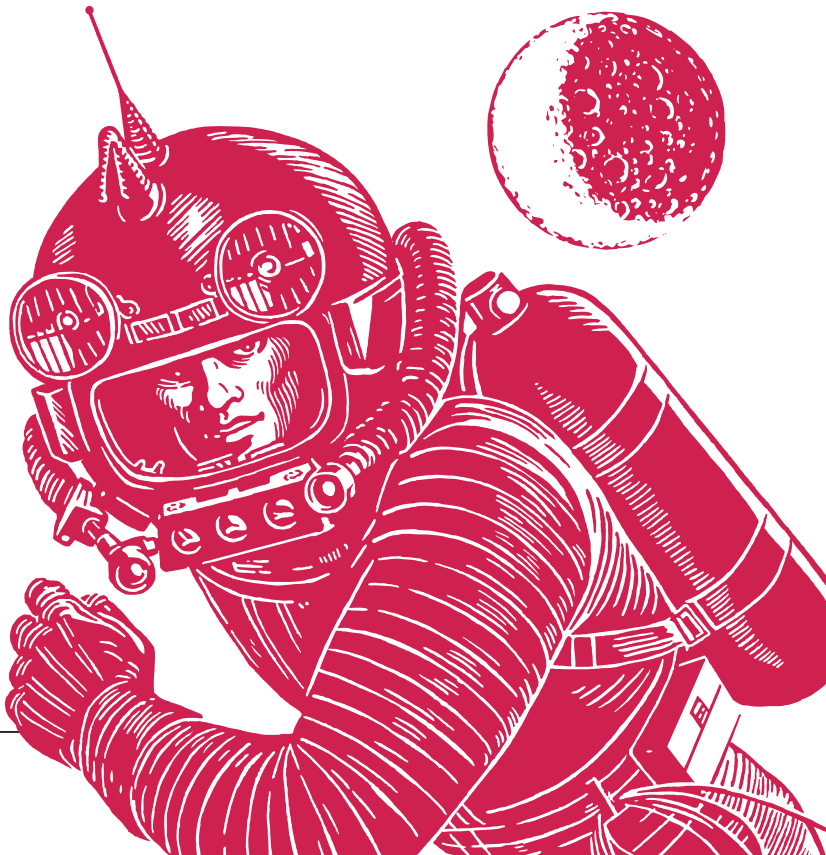
NASA's Translational Research Institute for Space Health (TRISH) has funded innovative projects seeking to better protect astronauts' health during deep space missions of three years or more. Two of the six projects focus on 'just-in-time' medications, which allow drugs to be manufactured on-demand and on-board the spacecraft.

Two of these on-demand medications projects recently received two-year funding from TRISH. The first is from the Massachusetts Institute of Technology (MIT) and creates just-in-time medications from gastric resident microbial systems, and the second, from the University of California, Davis (UC Davis), involves genetically modifying and growing lettuces to produce associated drugs.

The drug delivery device is ingested by astronauts in the same manner as an oral drug. It then resides in their stomach for a specific period and gradually releases the drug it manufactures into their body.

The proof of concept will involve using bacterium, such as *E.Coli*, to produce three medications — caffeine, melatonin and acetaminophen — within the device. It is hoped that this device's capacity would be expanded to a broader range of conditions in the future.

"The synthetic biology project is based around genetically modifying lettuce so the plants can produce certain medications. Astronauts would grow the lettuce on the spacecraft, as is currently done on the International Space Station," said David H Koch, study lead. "The general concept is that if you need a medicine, the next time you grow a lettuce, you will grow it from seeds containing one of three genes — granulocyte-colony stimulating factor (GCSF), granulocyte macrophage colony stimulating factor (GMCSF), and parathyroid hormone (PTH), and the lettuce will produce the medications needed."



Coming up short on MEDICATIONS

The most recent PGEU Medicine Shortages Survey showed a continuing crisis that is causing patients to lose trust in their pharmacist and damaging staff satisfaction

Each year, the Pharmaceutical Group of the European Union (PGEU) conducts a survey among its membership to map the impact of medicine shortages across Europe from community pharmacists' perspective.

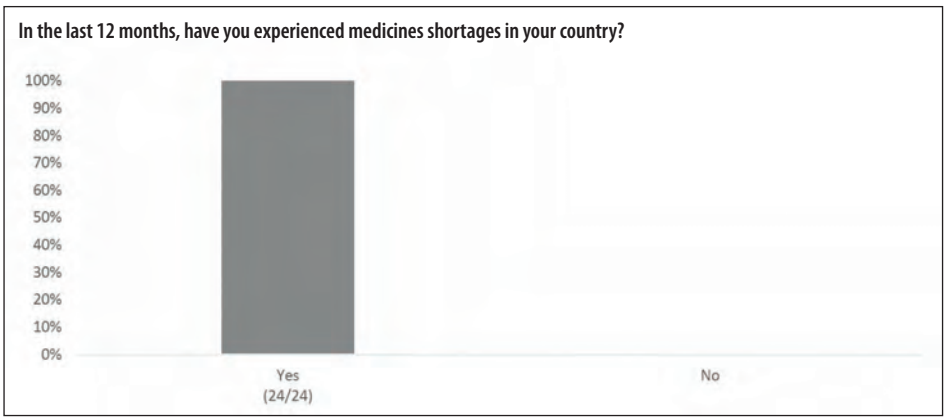
The 2019 Survey was open to all PGEU member organisations and was conducted between 4 November-16 December 2019.

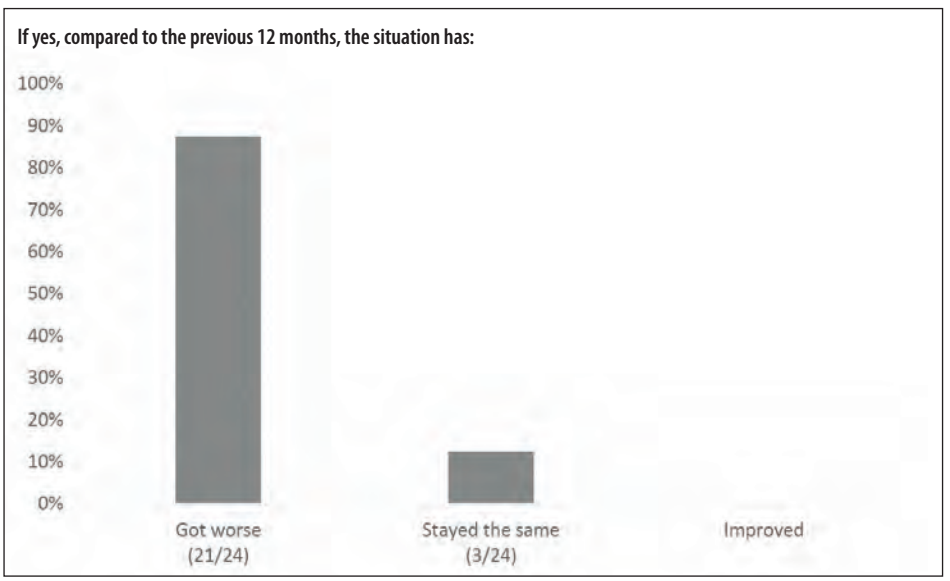
For the purpose of the survey, the term 'medicine shortage' was defined as every (temporally) inability for a community or hospital pharmacy to supply patients with the medicinal product requested as a result of factors beyond their control, requiring the dispensing of an alternative agent or even discontinuation of an ongoing medical therapy. In terms of reporting/notification of medicine shortages, respondents were asked to apply their national definition if available.

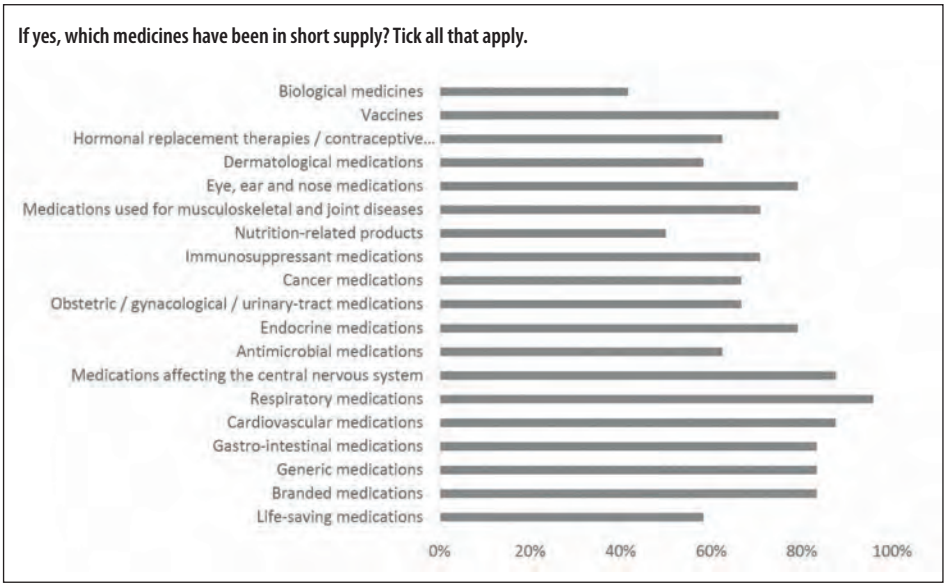
Among the key findings of the survey are:

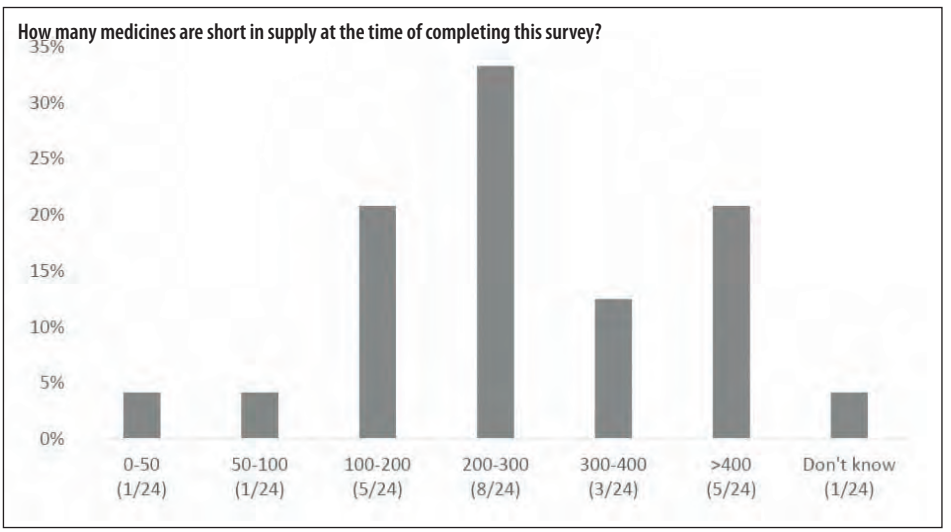
- The high incidence and ongoing rise of the number of medicine shortages in most European countries;
- The daily and burdensome impact of medicine shortages on patients and pharmacy practice across Europe; and
- The existing gap in needed information, tools and legal solutions available to community pharmacists in many European countries for providing solutions to patients in case of a shortage.

The respondents were also asked, on average, per week, how much time pharmacy staff spend dealing with medicine shortages. While answers ranged from two hours to 15 hours per week, the average amount of time spent by pharmacy staff dealing with medicines shortages is 6.6 hours per week.









Other main findings from the survey include:

- All responding countries experienced medicine shortages in community pharmacies in the past 12 months, and in the vast majority (87 per cent) of countries, respondents indicated that the situation had gotten worse compared to 2018.
- All classes of medicines are affected by medicine shortages in community pharmacies across the different responding European countries. Respiratory medications have been short in supply in the highest percentage of countries (87 per cent), while biological medicines have been short in supply in the lowest percentage of countries (42 per cent).
- In the majority of responding countries (67 per cent), over 200 medicines were listed as in short supply at the time of completing the survey, with five countries indicating that there were more than 400 medicines short in supply.
- All responding countries indicated that they believe medicine shortages cause distress and inconvenience to patients. Interruption of treatments (75 per cent of countries), increased co-payments as a result of more expensive/non-reimbursed alternatives (58 per cent), and suboptimal treatment/inferior efficacy (42 per cent) are also perceived as negative consequences of medicine shortages on patients.
- Medicine shortages are believed to affect community pharmacy businesses in most countries by reduced patient trust (92 per cent of countries), financial loss due to time invested in mitigating shortages (82 per cent), and reduced employee satisfaction (79 per cent).
- Across European countries, strong differences exist in terms of legal solutions community pharmacists can offer in case of a shortage. Generic substitution (79 per cent of countries), sourcing the same medicine from alternative authorised sources (such as other pharmacies) (63 per cent), and importing the medicine from a country where it is available (46 per cent) are the solutions which can be provided in most of the European countries. However, some of these solutions are subject to restrictions (ie, new prescription is needed) and can be cumbersome and time-consuming for the patient and the pharmacist.
- 25 per cent of responding countries indicated that there is still no reporting system for shortages in place which can be used by community pharmacists in their country, despite that pharmacists often experience or foresee supply difficulties before the industry or wholesalers are aware that there is, or will be, a problem.
- Community pharmacists receive their needed information on shortages in most countries from wholesalers (71 per cent), medicines agencies (67 per cent) and pharmacy organisations (42 per cent).

Mr Darragh O'Loughlin, General Secretary of the Irish Pharmacy Union, commented on the survey results: "The release of this survey underlines that medicine shortages are an increasing challenge, not just in Ireland, but across Europe.

"In Ireland, we have experienced significant shortages of medicines in the last year and the situation continues to get worse. Patients can sometimes wait for weeks to get a new supply of a common drug. Not only is this putting their health at risk, but it is causing undue stress, fear and anxiety for patients. Instead of directing their efforts and professional expertise towards the needs of patients, pharmacists are spending nearly seven hours a week resolving medicines shortages and firefighting on behalf of our patients."

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Abbreviated Prescribing Information

Please refer to the Summary of Product Characteristics (SmPC) before prescribing **Pelgraz▼** (pegfilgrastim) **6 mg solution for injection in pre-filled syringe or pre-filled injector. Presentation: Pelgraz 6 mg solution for injection in pre-filled syringe:** Each pre-filled syringe contains 6 mg of pegfilgrastim* in 0.6 mL solution for injection. The concentration is 10 mg/mL based on protein only**. **Pelgraz 6 mg solution for injection in pre-filled injector:** Each pre-filled injector contains 6 mg of pegfilgrastim* in 0.6 mL solution for injection. The concentration is 10 mg/mL based on protein only**. *Produced in *Escherichia coli* cells by recombinant DNA technology followed by conjugation with polyethylene glycol (PEG). ** The concentration is 20 mg/mL if the PEG moiety is included. **Indications**: Reduction in the duration of neutropenia and the incidence of febrile neutropenia in adult patients treated with cytotoxic chemotherapy for malignancy (with the exception of chronic myeloid leukaemia and myelodysplastic syndromes). **Dosage and Administration**: Pelgraz therapy should be initiated and supervised by physicians experienced in oncology and/or haematology. Posology: One 6 mg dose (a single pre-filled syringe or pre-filled injector) of Pelgraz is recommended for each chemotherapy cycle, given at least 24 hours after cytotoxic chemotherapy. Safety and efficacy of Pelgraz in children and adolescents has not yet been established. No dose change is recommended in patients with renal impairment, including those with end-stage renal disease. **Method of administration:** Pelgraz is for subcutaneous use. The injections should be given subcutaneously into the thigh, abdomen or upper arm. See SPC for instructions on handling of the medicinal product before administration. **Contraindications**: Hypersensitivity to pegfilgrastim or any of the excipients in Pelgraz. **Warnings and precautions**: In order to improve the traceability of biological medicinal products, the trade name of the administered product should be clearly recorded. The long-term effects of pegfilgrastim have not been established in acute myeloid leukaemia (AML); therefore, it should be used with caution in this patient population. Granulocyte-colony stimulating factor can promote growth of myeloid cells *in vitro* and similar effects may be seen on some non-myeloid cells *in vitro*. The safety and efficacy of pegfilgrastim have not been investigated in patients with myelodysplastic syndrome, chronic myelogenous leukaemia, and in patients with secondary AML; therefore, it should not be used in such patients. Particular care should be taken to distinguish the diagnosis of blast transformation of chronic myeloid leukaemia from AML. The safety and efficacy of pegfilgrastim administration in *de novo* AML patients aged < 55 years with cytogenetics t(15;17) have not been established. The safety and efficacy of pegfilgrastim have not been investigated in patients receiving high dose chemotherapy. This medicinal product should not be used to increase the dose of cytotoxic chemotherapy beyond established dose regimens. Pulmonary adverse reactions, in particular interstitial pneumonia, have been reported after G-CSF administration. Patients with a recent history of pulmonary infiltrates or pneumonia may be at higher risk. The onset of pulmonary signs such as cough, fever, and dyspnoea in association with radiological signs of pulmonary infiltrates, and deterioration in pulmonary function along with increased neutrophil count may be preliminary signs of Adult Respiratory Distress Syndrome (ARDS). In such circumstances pegfilgrastim should be discontinued at the discretion of the physician and the appropriate treatment given. Glomerulonephritis has been reported in patients receiving filgrastim and pegfilgrastim. Generally, events of glomerulonephritis resolved after dose reduction or withdrawal of filgrastim and pegfilgrastim. Urinalysis monitoring is recommended. Capillary leak syndrome has been reported after granulocyte-colony stimulating factor administration and is characterised by hypotension, hypoalbuminaemia, oedema and haemoconcentration. Patients who develop symptoms of capillary leak syndrome should be closely monitored and receive standard symptomatic treatment, which may include a need for intensive care. Generally asymptomatic cases of splenomegaly and cases of splenic rupture, including some fatal cases, have been reported following administration of pegfilgrastim. Therefore, spleen size should be carefully monitored (e.g. clinical examination, ultrasound). A diagnosis of splenic rupture should be considered in patients reporting left upper abdominal pain or shoulder tip pain. Treatment with pegfilgrastim alone does not preclude thrombocytopenia and anaemia because full dose myelosuppressive chemotherapy is maintained on the prescribed schedule. Regular monitoring of platelet count and haematocrit is recommended. Special care should be taken when administering single or combination chemotherapeutic medicinal products which are known to cause severe thrombocytopenia. Sickle cell crises have been associated with the use of pegfilgrastim in patients with sickle cell trait or sickle cell disease. Therefore, physicians should use caution when prescribing pegfilgrastim in patients with sickle cell trait or sickle cell disease, should monitor appropriate clinical parameters and laboratory status and be attentive to the possible association of this medicinal product with splenic enlargement and vasoocclusive crisis. White blood cell (WBC) counts of 100 x 10^9/L or greater have been observed in less than 1% of patients receiving pegfilgrastim. No adverse reactions directly attributable to this degree of leukocytosis have been reported. Such elevation in WBCs is transient, typically seen 24 to 48 hours after administration and is consistent with the pharmacodynamic effects of this medicinal product. Consistent with the clinical effects and the potential for leukocytosis, a WBC count should be performed at regular intervals during therapy. If leukocyte counts exceed 50 x 10^9/L after the expected nadir, this medicinal product should be discontinued immediately. Hypersensitivity, including anaphylactic reactions, occurring on initial or subsequent treatment have been reported in patients treated with pegfilgrastim. Permanently discontinue pegfilgrastim in patients with clinically significant hypersensitivity. Do not administer pegfilgrastim to patients with a history of hypersensitivity to pegfilgrastim or filgrastim. If a serious allergic reaction occurs, appropriate therapy should be administered, with close patient follow-up over several days. As with all therapeutic proteins, there is a potential for immunogenicity. Rates of generation of antibodies against pegfilgrastim is generally low. Binding antibodies do occur as expected with all biologics; however, they have not been associated with neutralising activity at present. Aortitis has been reported after filgrastim or pegfilgrastim administration in healthy subjects and in cancer patients. The symptoms experienced included fever, abdominal pain, malaise, back pain and increased inflammatory markers (e.g. C-reactive protein and WBC count). In most cases aortitis was diagnosed by CT scan and generally resolved after withdrawal of filgrastim or pegfilgrastim. The safety and efficacy of Pelgraz for the mobilisation of blood progenitor cells in patients or healthy donors has not been adequately evaluated. Increased haematopoietic activity of the bone marrow in response to growth factor therapy has been associated with transient positive bone-imaging findings. This should be considered when interpreting bone-imaging results. This medicinal product contains 50 mg sorbitol in each unit volume, which is equivalent to 30 mg per 6 mg dose. Pelgraz contains less than 1 mmol (23 mg) sodium per 6 mg dose, that is to say essentially 'sodium-free'. The needle cover contains dry natural rubber (a derivative of latex), which may cause allergic reactions. **Pregnancy and Lactation**: Pegfilgrastim is not recommended during pregnancy and in women of childbearing potential not using contraception. A decision must be made whether to discontinue breastfeeding or to discontinue/abstain from pegfilgrastim therapy taking into account the benefit of breastfeeding for the child and the benefit of therapy for the woman. **Adverse Events include: Adverse events which could be considered serious include: Common:** Thrombocytopenia. **Uncommon:** Sickle cell crisis, capillary leak syndrome, glomerulonephritis, hypersensitivity reactions (including angioedema, dyspnoea, anaphylaxis), splenic rupture (including some fatal cases), Sweet's syndrome (acute febrile dermatosis), pulmonary adverse reactions including interstitial pneumonia, pulmonary oedema and pulmonary fibrosis have been reported. Uncommonly cases have resulted in respiratory failure or ARDS which may be fatal. **Rare:** Aortitis, pulmonary haemorrhage. **Other Very Common adverse events:** Headache, nausea, bone pain. **Other Common adverse events:** Leukocytosis, musculoskeletal pain (myalgia, arthralgia, pain in extremity, back pain, musculoskeletal pain, neck pain), injection site pain, non-cardiac chest pain. See SPC for details of other adverse events. **Shelf Life:** 3 years. Store in a refrigerator (2°C – 8°C). Pelgraz may be exposed to room temperature (not above 25°C ± 2°C) for a maximum single period of up to 72 hours. Pelgraz left at room temperature for more than 72 hours should be discarded. Do not freeze. Accidental exposure to freezing temperatures for a single period of less than 24 hours does not adversely affect the stability of Pelgraz. Keep the container in the outer carton in order to protect from light. **Pack Size: Pelgraz 6 mg solution for injection in pre-filled syringe:** Each prefilled syringe contains 0.6 mL of solution for injection. Pack size of one prefilled syringe with one alcohol swab, in a blistered packaging. **Pelgraz 6 mg solution for injection in pre-filled injector:** Each prefilled syringe injector contains 0.6 mL of solution for injection. Pack size of one prefilled injector with one alcohol swab, in a blistered packaging. **Marketing Authorisation Numbers: Pre-filled syringe:** EU/1/18/1313/001, **Pre-filled injector:** EU/1/18/1313/002. **Marketing Authorisation Holder (MAH):** Accord Healthcare S.L.U, World Trade Center, Moll de Barcelona, s/n, Edifici Est, 6a planta, Barcelona, 08039 Spain. **Legal Category:** POM. Full prescribing information including the SPC is available on request from Accord Healthcare Ireland Ltd, Euro House, Little Island, Co. Cork, Tel: 021-4619040 or www.accord-healthcare.ie/products. **Adverse reactions can be reported to Medical Information at Accord Healthcare Ltd. via E-mail:** medinfo@accord-healthcare.com **or Tel:** +44(0)1271385257. **Date of Generation of API:** August 2019. IE-01426

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Adverse events should be reported. Reporting forms and information can be found on the HPRA website (www.hpra.ie), or by e-mailing medsafety@hpra.ie. Adverse events should also be reported to Medical Information via email; medinfo@accord-healthcare.com or tel:0044 (0) 1271 385257

October 2019. IE-01429

Getting to grips with over-reliance on RELIEVER MEDICATION

The Asthma Society of Ireland has warned of the dangers of over-reliance on reliever medication by using a reliever more than twice a week, according to the Global Initiative for Asthma

The Asthma Society of Ireland has released research carried out by hmR Ireland, which looks at the over-reliance on reliever inhaler medication by people with asthma in Ireland. Reliever inhalers, which most people will recognise as the blue inhalers, if over-used, are strongly linked with severe asthma exacerbations and asthma-related deaths. An asthma exacerbation is an episode of progressive worsening of symptoms of asthma, including shortness of breath, wheezing, cough, and chest tightness and it can progress to a severe asthma attack.

Using three or more reliever inhalers a year indicates a person is at risk of an severe asthma exacerbation, while the use of 12 or more a year is an indication someone is at risk of an asthma-related death, according to the Global Initiative for Asthma (GINA), a body tasked with evidence-based strategy for asthma management working to improve the lives of people with asthma in every corner of the globe.

hmR Ireland worked with 70 per cent of Irish pharmacies in 2019, conducting research on asthma medication usage trends, using anonymised patient transactional dispensing data.

The research results found:

- Three-in-10 use more than 12 reliever inhalers a year, putting them at risk of an asthma-related death.
- Seven-in-ten are using more than three reliever inhalers a year, putting them at risk of an asthma attack (or some form of asthma exacerbation).
- Within five years of diagnosis, half the asthma population are over-reliant on their reliever inhaler.
- In the year after diagnosis, 30 per cent of children aged 0-17 are overusing their reliever inhaler.
- In the year after diagnosis, 60 per cent people aged 50 or over are overusing their reliever inhaler.

Ms Sarah O'Connor, CEO of the Asthma Society of Ireland, said: "International research shows that reliever inhaler overuse can be a major factor in asthma exacerbations and asthma-related deaths, as in the UK's *National Review of Asthma Deaths* report and GINA's *Global Strategy for Asthma Management and Prevention*. This makes the findings of this hmR Ireland research about Irish patients relying on their reliever inhaler stark and very worrying to us. One person dies every six days from asthma in Ireland.

"The research revealed that a huge proportion of people in all age groups are overusing their reliever inhalers in every county throughout Ireland, putting them at risk of a severe exacerbation or asthma-related death. Alarmingly, within five years of diagnosis, half of people become over-reliant on it. As people with asthma get older, their rate of over-reliance increases, resulting in increased levels of uncontrolled asthma. A key point at which people become over-reliant on their reliever inhaler is between year one (year of diagnosis) and year two.

"This 'year two' of asthma is when the largest increase in inhaler over-reliance occurs and we need healthcare profession-

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[1] NEW

[1]Cetrine Allergy 1mg/ml Oral Solution, available in 200ml bottle and launched in November 2019. Cetrine Allergy 10mg FCT available in 7 and 30 packs, Lorat 10mg Tablets available in 7 and 28 packs, Rhinex Relief 50 micrograms/actuation Nasal spray, suspension, available as 1 x 60 doses. Medicinal products not subject to medical prescription. For further information, SPC or to report adverse drug reactions, contact the Marketing Authorisation Holder: Rowex Ltd., Bantry, Co. Cork. Ireland. Freephone: 1800 304 400. Fax: 027-50417. Date of preparation: (01-20) CCF No: 22863

als to know this so that they can intervene to help and support their patients to have the best possible asthma management," she added.

"If you are using your reliever inhaler several times each week, you are over-reliant on it and your asthma is not controlled, according to the Global Initiative for Asthma. The exception to this is people with asthma who participate in sport/exercise; it is still recommended you use your reliever inhaler prior to warming up before exercising."

The Asthma Society is calling on all people who are over-reliant on their reliever inhaler to act now to get their asthma under control. The Society said people with asthma should take the following actions:

1. Download an Asthma Action Plan from www.asthma.ie.
2. Complete the Asthma Action Plan with their healthcare professional and speak specifically about asthma medications.
3. Call the Asthma Society's free Asthma and COPD Adviceline on 1800 44 54 64 to help understand asthma, its triggers and how to manage it, and to better understand asthma control.

Medical Director of the Asthma Society of Ireland, Mr Marcus Butler, said: "A reliever inhaler works within minutes to relieve asthma symptoms when they happen — it gives a short-lived improvement in symptoms, effectively just buying time, but can eventually fail to keep a patient safe from asthma if more appropriate and effective controller inhalers are not used on a daily basis. A controller inhaler works over a much longer duration than reliever inhalers to eventually ease the underlying airway inflammation which ultimately causes asthma symptoms. It prevents symptoms from arising several weeks and months down the road, as long as it is habitually taken.

"The UK's *National Review of Asthma Deaths* report showed that there was evidence of excessive prescribing of reliever medication — 39 per cent of those who died had been prescribed more than 12 short-acting reliever inhalers in the year before they died, and 4 per cent had been prescribed more than 50 reliever inhalers. Those prescribed more than 12 reliever inhalers were likely to have had poorly-controlled asthma."

To reduce asthma-related deaths and exacerbations, the Asthma Society of Ireland has launched its over-arching Asthma SafetyCare campaign, an initiative aiming to end asthma deaths in Ireland by making patients and the public aware of asthma management issues.

The Asthma Society has said it hopes the Asthma SafetyCare campaign will make a tangible difference to asthma deaths by combatting problematic aspects of asthma management, with this first project looking at SABA over-reliance.

The SafetyCare specific project is a healthcare professional and patient education campaign, featuring case study videos, a healthcare professional webinar, research, infographics, outreach and media engagement, aiming to educate people with asthma and their healthcare professionals of the dangers of being over-reliant on their reliever medication.

The SafetyCare project and the hmR research were supported by AstraZeneca.

ASTHMA OVERUSE BY COUNTY

County and rate of overuse (after five years)

56% Carlow	49% Roscommon
53% Waterford	48% Cork
53% Limerick	48% Cavan
52% Dublin	47% Wexford
52% Monaghan	47% Galway
52% Tipperary	47% Sligo
52% Offaly	46% Wicklow
51% Longford	45% Mayo
51% Louth	45% Kildare
51% Leitrim	44% Laois
51% Clare	44% Kilkenny
50% Westmeath	43% Meath
49% Kerry	43% Donegal

Graph shows the rate of overuse of reliever medication per county after five years of being prescribed an inhaler

The research also revealed:

- In the initial year of diagnosis, one-in-five people overuse their reliever inhaler.
- In the first year after diagnosis, there is a 6 per cent increase in the number of people using 12 or more reliever inhalers a year (2 per cent to 8 per cent) and a 17 per cent increase in the number of people using three or more reliever inhalers per year (16 per cent to 33 per cent). There is a corresponding drop of 23 per cent of people using two or less (considered the appropriate amount) reliever inhalers per year (82 per cent to 59 per cent).
- In the year after diagnosis, the following numbers of people over-use their reliever inhaler: Three out of 10 people aged 0-7, three out of 10 people aged 7-17, two out of five people aged 18-32, half the people aged 31-50, and three out of five people aged over 50.

The Asthma Society of Ireland runs a free Asthma and COPD Adviceline. Users of the service can speak to a respiratory specialist nurse who will work with them to assess if they are overusing their reliever medication and review their asthma control.

The free Asthma and COPD Adviceline is available on 1800 44 54 64.

For healthcare professionals looking to learn more on the new GINA 2019 Update and what they should be prescribing, the Asthma Society of Ireland hosted a webinar in February to answer any questions on the new GINA Guidelines and on how to recognise SABA over-reliance in patients.

Intelligently designed. Simple to use.[1,2]

The **first** and **only** ICS/LABA delivered in a breath-actuated aerosol inhaler.

flutiform® k-haler®
fluticasone propionate/formoterol

flutiform*® *k-haler*® (fluticasone propionate/formoterol fumarate) 50 µg/5 µg and 125 µg /5 µg pressurised inhalation suspension. Prescribing Information Republic of Ireland. Please read the Summary of Product Characteristics (SPC) before prescribing. Presentation** Pressurised inhalation suspension, in a breath-actuated pressurised aerosol inhaler. **Indications** Regular treatment of asthma where the use of a combination product (inhaled corticosteroid [ICS] and long-acting β_2-agonist [LABA]) is appropriate: (i) for patients not adequately controlled with ICS and 'as required' inhaled short-acting β_2-agonist (SABA) (ii) for patients already adequately controlled on both an ICS and a LABA. For adults and adolescents aged 12 years and above. **Dosage and administration** for inhalation use. Patients should be shown how to use the inhaler correctly by a healthcare professional. Patients should be given the strength of ***flutiform k-haler containing the appropriate fluticasone propionate dose for their disease severity (50 µg/5 µg per actuation is not appropriate in patients with severe asthma). The appropriate strength should be taken as two inhalations, twice daily (normally morning and evening) and used every day, even when asymptomatic. ***flutiform k-haler*** is not recommended in children under 12 years. Prescribers should be aware that in asthmatics, fluticasone propionate is as effective as some other inhaled steroids when administered at approximately half the total daily microgram dose. Patients should be assessed regularly and once asthma is controlled, treatment should be reviewed and stepped down to the lowest effective dose, or an ICS alone. ICSs alone are first line treatment for most patients. ***flutiform k-haler*** is not intended for initial treatment of mild asthma. For patients with severe asthma the ICS therapy should be established before prescribing a fixed-dose combination product. Patients on ***flutiform k-haler*** must not use an additional LABA. An inhaled SABA should be taken for immediate relief of asthma symptoms arising between doses. Patients should be advised to contact their prescriber when ***flutiform k-haler*** dose counter is getting near zero. **Contra-indications** Hypersensitivity to the active substances or to any of the excipients. **Precautions and warnings** ***flutiform k-haler*** should not be used as the first asthma treatment, to treat acute asthma symptoms or for prophylaxis of exercise-induced asthma. It should not be initiated during an exacerbation, during significantly worsening or acutely deteriorating asthma, and should not be stopped abruptly. If a patient experiences serious asthma-related adverse events or exacerbations, they should continue treatment and seek medical advice. Patients should be reviewed as soon as possible if there is any indication of deteriorating asthma control. In case of sudden and progressive deterioration, seek urgent medical assessment. Caution in patients with: pulmonary tuberculosis; quiescent tuberculosis; fungal, viral or other infections of the airway; thyrotoxicosis; phaeochromocytoma; diabetes mellitus (consider additional blood sugar controls); uncorrected hypokalaemia; predisposition to low levels of serum potassium; impaired adrenal function (monitor HPA axis function regularly); hypertrophic obstructive cardiomyopathy; idiopathic subvalvular aortic stenosis; severe hypertension; aneurysm or other severe cardiovascular disorders; unstable or acute severe asthma and other conditions when the likelihood for hypokalaemia adverse effects is increased. There is risk of potentially serious hypokalaemia with high doses of β_2-agonists or concomitant treatment with β_2-agonists and drugs that can induce or potentiate a hypokalaemic effect. Monitoring of serum potassium levels is recommended during these circumstances. Formoterol may induce prolongation of the QTc interval. Caution must be observed when treating patients with existing prolongation of QTc interval. ***flutiform k-haler*** should be discontinued immediately if there is evidence of paradoxical bronchospasm. Visual disturbance may be reported with corticosteroid use. Systemic effects with an ICS may occur, particularly at high doses for prolonged periods or when combined with potent CYP3A4 inhibitors, but are less likely than with oral corticosteroids. Possible systemic effects include Cushing's syndrome, Cushingoid features, adrenal suppression, growth retardation in children and adolescents, decrease in bone mineral density and cataract glaucoma. Children may also experience anxiety, sleep disorders and behavioural changes. Increased exposure can be expected in patients with severe hepatic impairment. Prolonged treatment with high doses of corticosteroids may result in adrenal suppression and acute adrenal crisis, particularly in children and adolescents or potentially as a result of trauma, surgery, infection or rapid dose reduction. ***flutiform k-haler*** contains a negligible amount of ethanol that does not pose risk to patients. Interactions Co-treatment with CYP3A inhibitors (e.g. ritonavir, atazanavir, clarithromycin, indinavir, itraconazole, nelfinavir, saquinavir, ketoconazole, telithromycin, cobicistat) should be avoided unless the benefit outweighs the increased risk of systemic side-effects. Caution is advised with concomitant use of non-potassium sparing diuretics (e.g. loop or thiazide), xanthine derivatives, glucocorticosteroids, L-Dopa, L-thyroxine, oxytocin, alcohol or other adrenergic drugs, including anaesthesia with halogenated hydrocarbons and digitalis glycosides, β-adrenergic drugs, known to prolong the QTc interval, such as tricyclic antidepressants or MAOIs (and for two weeks following their discontinuation), antipsychotics (including phenothiazines), quinidine, disopyramide, procainamide, antihistamines, furazolidone and procarbazine. ***flutiform k-haler*** should not normally be used with β-blockers including those that are used as eye drops to treat glaucoma. Under certain circumstances, e.g. as prophylaxis after myocardial infarction, cardioselective β-blockers could be considered with caution. **Pregnancy and lactation** ***flutiform k-haler*** is not recommended during pregnancy unless the benefits to the mother outweigh risks to the foetus. A risk to the breastfeeding infant cannot be excluded. **Side-effects** *Uncommon (<1/100) but potentially serious:* hyperglycaemia, agitation, depression, aggression, behavioural changes (predominantly in children), vision blurred, vertigo, palpitations, ventricular extrasystoles, angina pectoris, tachycardia, hypertension, dyspnoea, peripheral oedema. Please consult the SPC a full list of side-effects and those reported for the individual molecules. **Legal category** POM **Package quantities** One inhaler (120 actuations) **Marketing Authorisation numbers** PA 1688/013/004-005 **Marketing Authorisation holder** Mundipharma Pharmaceuticals Limited, Millbank House, Arkle Road, Sandyford, Dublin 18, Ireland. Tel: +353 (0)1 2063800. For medical information enquiries, please contact medicalinformation@mundipharma.ie. ® FLUTIFORM is a registered trademark of Jagotec AG, and is used under licence. ® K-HALER is a registered trade mark of Mundipharma AG. © 2018 Napp Pharmaceuticals Limited. UK/FLUT-K-18036a(1). Date of Preparation July 2019.

Adverse events should be reported to: HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie. Adverse events should also be reported to Mundipharma Pharmaceuticals Limited on drugsafetyireland@mundipharma.ie or by phone on 01 2063800 (1800 991830 outside office hours)

References: 1. https://www.medicines.ie/medicines/flutiform-k-haler-50-microgram 5-microgram-125-microgram-5-microgram-peractuation-pressurised-inhalation suspension–34603/ last accessed September 2019.
2. Bell D *et al.* J Aerosol Med Pulm Drug Deliv 2017; 30:425–34.

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Date of Item September 2019

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GOING VIRAL

An FIP emergency taskforce has released guidelines on how pharmacists should deal with the coronavirus outbreak

The roles that pharmacists in community, hospital and clinical biology can play in preventing the spread of COVID-19 (2019-nCoV) and supporting the efficient management of infection by healthcare systems have been outlined in a document published recently by the International Pharmaceutical Federation (FIP). The document was developed by an emergency taskforce set up by FIP following the World Health Organisation's declaration that the outbreak of 2019-nCoV constitutes a public health emergency of international concern.

PREVENTIVE MEASURES

"Since pharmacies are often the first point of contact with the health system, and given that cases have already been seen in a number of countries, it is important that the whole pharmacy workforce is well informed and prepared," said taskforce chair Ms Jane Dawson, who is also Secretary of FIP's Military and Emergency Pharmacy Section and Director of Health Policy for the New Zealand Defence Force. The document gives reliable information on 2019-nCoV and covers preventive measures (from how to wear a mask to effective disinfection), what equipment to stock, advice that pharmacists can give, and laboratory testing.

The taskforce also comprised a virologist, as well as pharmacists from China. FIP's member organisation the Chinese Pharmaceutical Association (CPA) had already been addressing 2019-nCoV, and had prepared guidance that includes recommendations for treatment of 2019-nCoV infection. "It is an honour for the CPA, and myself, to collaborate with FIP on an international pharmacy response to the 2019-nCoV outbreak, as well as to share the CPA's document as part of the global prevention and control work," said Prof Zhao Rongsheng of Peking University Third Hospital Pharmacy Department and Deputy Chairman of the CPA's hospital pharmacy and evidence-based pharmacy committees.

EXPERTISE

The document, *Coronavirus 2019-nCoV outbreak: Information and interim guidelines for pharmacists and the pharmacy workforce*, is downloadable in the six official United Nations languages, along with other resources on the FIP website. "Although the CPA guidance is aligned with characteristics particular to the system of pharmacy in China, it contains valuable expertise that can be used by pharmacists around the world, and it complements FIP's guidance for an international audience. The CPA has kindly agreed to share this document in English and Chinese through the FIP website," Ms Dawson said.

"As demonstrated by previous SARS-CoV and MERS-CoV outbreaks, coronavirus infections can be contained through the active engagement of decision-makers, healthcare professionals and the community. This guidance is a valuable resource to ensure preparedness of our workforce in combating this new coronavirus and perhaps future ones. It also highlights the huge benefit of international collaboration via FIP," she added.

Regarding community pharmacy, the document states: "Community pharmacies in outbreak-affected and unaffected countries are often the first point of contact with the health system for those with health-related concerns or simply in need of information and reliable advice. Community pharmacists have the shared responsibility of:

- Storing appropriate stocks of pharmaceutical products (medicines, masks, etc) to supply the demand.
- Informing and educating the public.
- Counselling.
- Referring.
- Promoting disease prevention.
- Promoting infection control.

With regard to hospital pharmacies, the FIP states: "Hospital pharmacies in outbreak-affected and unaffected countries play an important role in:

- Storing appropriate stocks of relevant medicines and other medical products and devices to supply the demand.
- Collaborating with other healthcare professionals in providing patient care and support.
- In-hospital prevention and infection control.
- Informing and counselling.
- Ensuring the responsible use of the pharmaceutical products supplied. For example, ensuring that healthcare professionals consistently wear their masks correctly." ●

The full document is available to view or download at https://www.fip.org/file/4413

DON'T LET PAIN HOLD YOU BACK

ESSENTIAL INFORMATION

Solpa-Extra 500mg/65mg Soluble Tablets contain paracetamol and caffeine. For the treatment of mild to moderate pain. **Adults and children over 16 years**: 1-2 tablets dissolved in water every 4-6 hours. Max 8 tablets a day. **Children 12-15 years**: 1 tablet disolved in water every 4-6 hours. Max 4 tablets a day. Not suitable for children under 12 years. **Contraindications**: Hypersensitivity to the ingredients. **Precautions**: Particular caution needed under certain circumstances, such as renal or hepatic impairment, chronic alcoholism and malnutrition or dehydration. Precautions needed in asthmatic patients sensitive to acetylsalicylic acid, patients on a controlled sodium diet and with rare hereditary problems of fructose intolerance. Patients should be advised not to take other paracetamol containing products concurrently. **Pregnancy and lactation**: Not recommended during pregnancy and breastfeeding. **Side effects**: Rare: allergies. Very rare: thrombocytopenia, anaphylaxis, bronchospasm, hepatic dysfunction, cutaneous hypersentitivity reactions. Unknown: nervousness, dizziness. Further information is available in the SmPC. PA 1186/017/001. P. **MAH**: Chefaro Ireland DAC, Treasury Building, Lower Grand Canal Street, Dublin 2, Ireland. Date of preparation: April 2017.

Trying to penetrate the cloud of confusion on e-cigarette use

A new study has highlighted significant knowledge gaps on the health outcomes of e-cigarette use during pregnancy

Researchers at the RCSI University of Medicine and Health Sciences and the Coombe Women and Infants University Hospital have published a new study on the outcomes of electronic cigarette use in pregnancy.

The study found that the birth weight of infants born to e-cigarette users is similar to that of non-smokers and significantly greater than babies born to cigarette smokers. Dual users of both cigarettes and e-cigarettes had infants with a birth weight similar to smokers.

However, the study's authors, RCSI researchers Dr Brendan McDonnell and Dr Carmen Regan, cautioned that further research is needed to establish other health outcomes of e-cigarette use on mothers and babies.

OBSTETRIC OUTCOMES

"Smoking cessation and avoidance of nicotine in its entirety is still the preferable option for pregnant women. However, some women who struggle to stop smoking turn to vaping as a method of harm reduction, and continue to vape in pregnancy," said Dr McDonnell, the study's first author, Honorary Clinical Lecturer at RCSI and Bernard Stuart Fellow at the Coombe Women and Infants University Hospital.

"Although our study has found that e-cigarette use appears to have minimal impact on birth weight, the long-term foetal effects of high-dose nicotine such as that received through vaping is unclear. Questions also remain on the effects of the other compounds produced by e-cigarettes, such as aldehydes and nitrosamines on human foetal development.

"Our study highlights that further research is needed to explore other obstetric and neonatal outcomes of vaping. We recommend that all maternity units should record e-cigarette use in pregnant women to deepen our understanding of potential health impacts. Longitudinal studies extending into childhood are needed to measure developmental issues that may arise due to e-cigarette use in pregnancy."

The study included 218 women with exclusive e-cigarette use and 195 women with dual use of both cigarettes and e-cigarettes attending for antenatal care at the Coombe Women and Infants University Hospital. Infants of e-cigarette users had a mean birth weight of 3,470g, compared to 3,471g for non-smokers and 3,166g for infants of smokers. The study was funded by the Friends of the Coombe charity and by Coombe Women and Infants University Hospital.

The authors wrote: "The use of EC [electronic cigarettes] among pregnant women has increased substantially in recent years. EC are viewed positively by many pregnant women, and research suggests they are perceived as less harmful than cigarettes and useful aids for smoking cessation, despite reservations about safety and nicotine dependence.

"However, the true risks or benefits of EC use are not well understood. Longitudinal data on safety and the effect on pulmonary and cardiovascular health are lacking, as are data on the foetal effects of EC use. Nicotine is a neuro-teratogen. It crosses the placenta during pregnancy and is known to bind nicotinic acetylcholine receptors in the foetal brain, altering normal brain development."

The results showed that in socioeconomic terms, those in the 'Skilled and non-manual' category were the most prevalent e-cigarette users, followed by 'Professional and managerial' (see **Table 1** below).

NRT VS E-CIGARETTES

The researchers also pointed out that users receive a higher dosage of nicotine via e-cigarettes compared to NRT. "Smoking cessation and avoidance of nicotine in its entirety is still the preferable option for pregnant women," they wrote.

"However, smoking cessation interventions during pregnancy have limited effectiveness and many women who struggle to achieve cessation turn to EC as a method of harm reduction. This research suggests that exclusive users of EC deliver infants with a birth weight similar to that of non-smokers.

"Animal models have suggested a neuro-teratogenic role of nicotine in foetal brain development. The use of nicotine replacement therapy during pregnancy has not been shown to confer additional risks to offspring; however, the dosage of nicotine received via NRT is less than that received through EC use." ●

The research was published recently in *BJOG: An International Journal of Obstetrics and Gynaecology* and is available at obgyn.onlinelibrary.wiley.com/doi/10.1111/1471-0528.16110.

	EC users (%)	Dual users (%)	Smokers (%)	Non-smokers (%)
Professional and managerial	29.8	10.8	8.7	50.2
Skilled and non-manual	35.8	27.2	25.1	33.8
Semi-skilled and unskilled manual	12.1	17.9	15.3	13.1
Homemaker	13.0	20.5	33.8	13.1
Full-time education	4.2	4.6	2.2	2.2
Unemployed	5.1	19.0	21.8	5.5

Table 1: Socio-demographic groupings of EC users, dual users, smokers, and non-smokers using Central Statistics Office employment categories

Send your comments to **hello@irishpharmacist.ie** or by post to **Pat Kelly**, Editor, Irish Pharmacist, GreenCross Publishing Ltd, Top Floor, 111 Rathmines Road Lower, Dublin 6, D06K5F6.

The 'war against drugs' is all but lost

Your columnists Fintan Moore and Dr Des Corrigan have both touched in this issue on the apparent resurgence in use of the so-called 'party drug' cocaine. The prevalence of its use harks back to the Celtic Tiger era, when there was money sloshing around thanks to unregulated banking and building sectors and Bertie's irresponsible stewardship. I will refrain from speculating whether the bankers who were sending us letters announcing that we had been 'pre-approved for a €15,000 loan' (without actually having to apply for it) were partaking of the 'Bolivian marching powder' themselves.

The fact is — and I'm not trying to be deliberately defeatist — the so-called 'war on drugs' has been lost, if indeed it ever even began on an even playing field.

Personally I have never used cocaine — part of the reason for that is that it was simply not available to people of my ilk when I was a teenager or younger man; it was simply out of reach financially. Allow me to provide a little context from the perspective of growing up in an area that might be described as 'working class', 'economically disadvantaged', or whatever else you care to call it. Consider it 'the word on the street', if you will.

For part of my young life, I grew up in Finglas, an area whose socioeconomic circumstances are mirrored by a number of such towns in Dublin and elsewhere in cities around the country. Cocaine was simply not available; indeed, it was also a lot more unusual to encounter a heroin addict in Finglas in the 1970s. Even marijuana was considered exotic, and teenage deviants had to make do with crumbly, low-grade hashish bought down an alley and its availability was communicated by word of mouth, as the idea of having a personal phone that could be carried around with you was the stuff of a madman's dreams.

On to adulthood, whereby I left the area and spent some years in Brussels cutting my teeth as a journalist. When I returned and visited Finglas to see old friends and family members after many years, the landscape for drug misuse had changed dramatically, and not for the better. The 'street' hashish (which I was reliably informed was mixed with cement powder to bulk it up) was regarded as a quaint thing of the past and had been replaced with marijuana, the THC content of which was unlike anything the country had ever seen. Young people — professionals or otherwise — had easy access to drugs like cocaine, crack cocaine, heroin, ecstasy, mushrooms and acid, among others, and were taking advantage of this accessibility.

And there was an equally sinister development. Drug-smugglers were by then including firearms with each batch of illegal drugs bought in order to 'sweeten the deal', which as we all know has now led to vicious turf wars domestically between rival crime gangs. When I was a child and it was announced on *Garda Patrol* that a person had been shot, it was automatically assumed that 'ah, that must have been the IRA'.

This cocktail of appalling circumstances has contributed to the ever-worsening mess we are in now, and it does seem, as people in the legal profession might say, the 'toothpaste cannot be put back into the tube'.

Many healthcare professionals take issue with using combative terms such as 'the war on cancer' because it is simply misleading and the same surely applies to the 'war on drugs'. What we are faced with now is simply a damage-limitation scenario. ●

THAR AN GCUNTAR AS GAEILGE

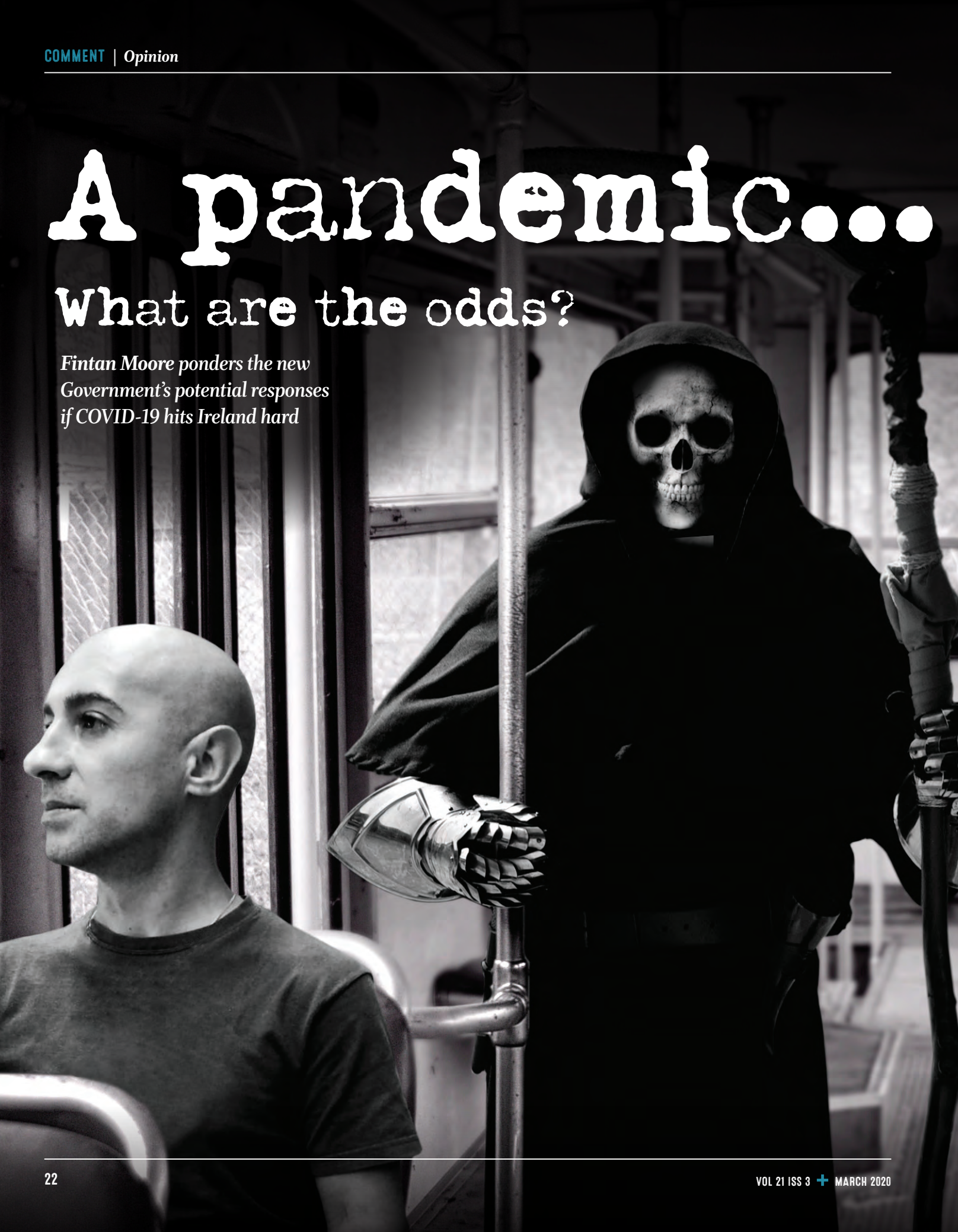
Agus mé ag scríobh an t-alt seo, níl muid ach cúpla lá amach ón toghchán. Tá an saol 's a mháthair ag súil le toradh an vótáil. Gan amhras tá brú agus neamhchinnteacht ar na bpolaiteoirí agus ar mhuintir na hÉireann. Tugann sé seo deis dúinn go léir machnamh ar an todhchaí. Is dócha go bhfuil muid go léir lonnaithe sna himeachtaí sin anois. Dé réir cosúlacht, tá athrú ag teacht. Tá tionchar mór ag na guthanna technical cosúil le Alexa, an t-idirlíon, na meáin shóisialta ar chúrsaí gnó amach anseo. Tá an tionchar seo bunaithe ar an ngaol idir margaíocht agus díolacháin. Tá tábhacht ag baint leo anois, ach sa todhchaí beidh i bhfad níos mó tábhacht ag baint leo. Mar sin, ní mór duit do chuid 'brand' a thógáil anois. Is acmhainní iontach iad an teicneolaíocht thuas luaite. Is gluais margaíocht iad. Rud nach raibh fíor blianta ó shin, is féidir le gairmithe iad féin a dhíol anois- saor in aisce. Ach an cheist atá os ár gcomhair ná 'an rud deacair é seo? An gcaithfeá a bheith iontach chun a bheith í do "Influencer"? Chun é seo a thuiscint, caithfidh muid labhair faoi spórt. Is gairm an- bhrabúsach í an chispheil, le himreoirí agus ná fireannacha a bhaineann leis, ag tuilleamh na milliúin dollar. Ach, an gciallaíonn sé seo go bhfuil cispheil brabúsach do gach duine a ghlacann páirt? Bhuel, má tá tú beag agus nach féidir leat cispheil a imirt, ar ndóigh, níl. Is meáin saor in aisce í an t-idirlíon agus mar sin is deis margaíocht saor in aisce í freisin. Mar an gcéanna le cispheil, is féidir le margaíocht ar an idirlíon a bheith brabúsach freisin. Ach, is féidir leat foghlaim conas a bheith cumasach ag na meáin shóisialta, i gcomparáid le cispheil caithfidh tú a bheith rugadh leis na scileanna. Ní mór do dhaoine staidéar a dhéanamh conas an gnó a mhargú, agus as seo amach tá sé ag éirí níos tábhachtaí gan dabht. Le teicneolaíocht nua gnímh ghnímh, ní bheidh sé ina chás de chuid Googling duine nó cuideachta a thuilleadh. Is í Alexa a roghnaíonn an cógaiseoir sa todhchaí. Caithfidh tú 'ainm' nó 'branda' láidir a bheith agat roimhe sin! Mar sin, beag beann ar thoradh ár dtoghcháin, beidh an Chógaisíocht ina gnó crua fós. Ach, is féidir linn smaoineamh ar bhealaí nua agus bealaí digiteach chun déanamh cinnte go mairfidh muid sa todhchaí.

MARK JORDAN is a community pharmacist based in Castlebar, Co Mayo. He is an elected member of the PSI Council, author of **The Weekly Nugget** on PharmaBuddy and host to the PharmaBuddy Podcast.

A pandemic...

What are the odds?

***Fintan Moore** ponders the new Government's potential responses if COVID-19 hits Ireland hard*



The phrase 'China Crisis' used to just refer to a synth-pop British band from back in the dim and distant 1980s, although they have shown remarkable longevity and are still touring. In a much more worrying display of longevity, the outbreak of Coronavirus, aka COVID-19, has expanded from being a localised Chinese crisis to something much bigger — and it's also still touring. At time of writing, the Italian authorities are struggling to contain it, so by the time you read this, it seems likely that other countries in Europe will also be affected. It has not officially been declared a pandemic yet, but that seems to be just a matter of time.

We've been assured by the HSE and the Department of Health that there are plans in place that will be rolled-out if and when people in Ireland start coming down with the virus. I don't like to scaremonger, but these are two organisations that can't really point to a track record of excellence when it comes to planning. Unlike with the stock market, sometimes 'past performance' is a good indicator of future gains, or in this case, losses. In fairness to them, even a well-organised and fully-resourced health service would struggle to contain a disease such as this, which has a long incubation period, various transmission possibilities, and apparently some carriers who are symptomless.

So, in a very plausible worst-case scenario, the Irish health service will be unable to contain the spread of COVID-19, and hospitals will be swamped. Patients will be advised to stay at home and be treated by their families. For most of these people, they will suffer nothing worse than a flu-like illness, but pharmacies can expect a steady footfall of these patients and their families. We will be well and truly in the firing-line on this one. So how bad might it be?

There is obviously the great unknown variable, which is how transmissible the disease might be from pharmacy customers to pharmacists and pharmacy staff. However, the approximate average mortality rate for people who contract the virus seems to be about 2 per cent, but apparently the available data is too low to give a correct percentage. Sadly, the increase in data is occurring, so that figure will become more accurate. What might be vaguely 'reassuring' for some of us is the breakdown in fatality rate by age. For people aged 10-to-49, the rate ranges from 0.2 per cent to 0.4 per cent. The rate for those aged 50-to-69 jumps to a range of 1.3 per cent to 3.6 per cent. So even if by some freak circumstance every pharmacist of a working age in the country became infected, we would still only lose a handful of us. I'm not trying to be glib or callous, but if we do hit this particular iceberg, then we will need to be hard-headed and pragmatic.

> *In a much more worrying display of longevity, the outbreak of coronavirus, aka COVID-19, has expanded from being a localised Chinese crisis to something much bigger — and [like the group China Crisis], it's also still touring*

PRIMARY ERRORS

The recent General Election that saw Sinn Féin support surge to unprecedented levels has all the usual political correspondents trying to unravel what the people were thinking. It seems that housing and health were the main reasons for voters floating to the 'dark side', but exit polls show up some anomalies — for example, contrary to what you might expect, tax cuts are desired by a higher percentage of Sinn Féin voters than Fine Gael voters. Go figure.

In relation to the desire of the public for better health services, some commentators have been blindly trotting out the old fallacy about the need for 'more primary care centres', without any critical thinking being applied. There is no evidence that the existing primary centres built in the last 20 years have actually improved health outcomes in their areas. The financial model used has the HSE as 'the pig that pays the rent' by taking enough space to generate a profit for the developer. The vast majority of these centres add no extra services to what existed before they were built. Politicians like them because they get a photo-op cutting the ribbon but in reality, they are simply a vehicle for taxpayers' money to be paid in perpetuity to private companies. Maybe a left-leaning Government might contain the right people to start questioning this model.

NOT TO BE SNIFFED AT

Anecdotally, it would appear that the country is awash in cocaine, despite the potential addiction and health risks. Matt Cooper recently expressed his bemusement at the guys he knows in their 50s who are overweight and unhealthy, yet still take cocaine — maybe the Drug Squad should infiltrate the Today FM Christmas party. Personally, I've no interest in the stuff, but tend to be agnostic about what other people choose to do for kicks — mountaineering and motorbike riding are pretty risky, but nobody's trying to prohibit them. However, cocaine use is funding the most vicious criminal gangs the country has ever seen. There is no 'Fair Trade' cocaine, so exploitation and violence exist at every level on the supply chain. Even people who wouldn't dream of wearing real fur don't mind snorting it, so perhaps there should be a more severe sentencing policy for possession of cocaine for personal use to deter people from dabbling. To be effective, a policy like this would need to be countrywide and well publicised, rather than the current haphazard situation, with widely-varying policies applied by individual judges. The status quo is a lottery in which otherwise blameless people caught in the wrong place at the wrong time and sentenced by the wrong judge can be unfairly hit with a sentence that has repercussions out of all proportion to the misdemeanour involved. ●

CONTRIBUTOR INFORMATION

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ARE WE REALLY IN THE MIDDLE OF ANOTHER

Cocaine epidemic?

Is there a resurgence in the use of what is foolishly considered by some to be a benign 'party drug', asks ***Dr Des Corrigan***

Drugs experts and media commentators have recently claimed that cocaine use is now so widespread that every town and village in Ireland is awash with the white powder. How true these claims are is difficult to judge in the absence of up-to-date, objective data. In this article, I will look at what data we do have and review the health implications of the use of a drug that many users foolishly consider a benign 'party drug'.

There is no doubt that the world production of cocaine has increased dramatically in recent years. The United Nations, in its 2019 *World Drug Report,*

stated that overall cocaine production in the three producer countries (Bolivia, Columbia and Peru) had doubled since 2013 to 1,976 tons. While seizures had also increased to 1,275 tons, that still leaves a lot of the drug available on the illicit market in the US and in Europe. Supply has definitely increased, therefore. Less up-to-date are our national figures on consumption and cocaine-related harms. The most recently published *Population Survey* dates to 2014/15 and shows that 8 per cent of adults had ever used the drug, but that only 0.5 per cent were current users, having used it in the previous month. This latter figure compares to 65 per cent who reported use of alcohol and 4 per cent who had used cannabis in the past month.

In terms of harm, the most serious is death, and cocaine-related poisoning fatalities have increased by 26 per cent to 53 in 2017 (the last year for which data is available). The number of deaths has ebbed and flowed in parallel with our national financial fortunes, giving support to the old joke that cocaine was God's way of telling you that you had too much money. What I mean is that cocaine deaths first peaked in 2008 at the height of the infamous Celtic Tiger era, only to fall back dramatically once the Great Recession kicked-in and many people no longer had the money to indulge themselves with 'nose candy'. With the ending of the financial crisis, such deaths are unfortunately back at Tiger era levels. Demand for treatment for problem cocaine use has also increased, from 8 per cent of all drug treatment cases in 2012, to 22 per cent in 2018. One of the truly worrying trends is that the smokeable form of cocaine, known as 'crack' or 'free base', accounted for 11 per cent of overall cocaine cases.

I regularly do some peer education training on behalf of a drug project in the Tallaght area with groups of young women who use crack and as a result, I have come to realise how prevalent the use of this most harmful form of the drug is in poorer and marginalised communities. What makes crack cocaine so dangerous is the fact that as the alkaloid free base, it is volatilised at relatively low temperatures in a crack pipe, allowing it to be smoked without burning it into carbonised soot. This has an immediate impact on the onset and duration of action of the drug. Whereas cocaine salts in powder form have typically an onset of action of one-to-five minutes, crack and injected cocaine produce their euphoric effects after just five seconds. On the other hand, the duration of the rewarding pleasurable effects are shorter with crack, lasting about 15 minutes for one rock or stone. Powder, on the other hand, produces a high that can last up to 90 minutes. Because of the more rapid onset of dysphoric reactions after crack, repeated use becomes rapidly established in order to avoid negative feelings, leading to compulsive, addictive patterns of use.

While addiction can develop to any form of cocaine, it occurs more rapidly with crack than with the powder. Because the dependence is psychological rather than physical, it can be more difficult to treat and medication-based therapies are largely ineffective. Counselling and cognitive behavioural therapy (CBT) seem to offer the best hope of recovery for both crack and powder addicts. Although the dependence is psychological, there are definite withdrawal symptoms, including intense craving for the drug, depression and suicidal thoughts. It is not surprising therefore that cocaine is one of the main drugs detected in those who died by hanging (114 in 2017). It is also possible that many non-poisoning deaths attributed to cardiac events (56) are also linked to cocaine use because it is well known that cocaine in whatever form has a significant impact on the cardiovascular system.

This arises from the increased energy and mental alertness that makes cocaine such an attractive drug. This creates a large increase for oxygen in the brain and the rest of the body. This is met by an increased heart rate, leading to tachycardia and at the same time, the drug acts as a vasoconstrictor, leading to hypertension and coronary artery spasm. This 'Catch-22' scenario results in heart attacks, strokes, cardiomyopathy and in some cases bowel and kidney ischaemia. The various cutting agents used by organised crime gangs to boost profits by bulking-up the powder can add to those risks. One such agent is lignocaine or lidocaine, the local anaesthetic effect of which mirrors that of cocaine and thus fools buyers into thinking they are getting high-purity drug, when in fact it might at best contain 20 per cent of pure cocaine.

Excessive exposure to lignocaine can exacerbate cardiovascular issues. Other cutting agents are also worrying. Phenacetin is another common diluent and nobody outside the cartels seems to know why it is used, since it is an analgesic banned for human use because of the kidney damage, including cancer of the kidney, it causes. The most common cutting agent at present is the anthelminthic levamisole that potentiates the effects of cocaine, possibly because its metabolite aminorex has amphetamine-stimulant effects. Unfortunately, in cocaine powder users, it also causes impairments in attention and working memory, as well as pronounced thickening of the lateral prefrontal cortex. It is also known to cause neutropaenia and agranulocytosis and skin necrosis that requires skin grafts.

Our previous experience of the Tiger era cocaine phenomenon taught us that it has a range of negative consequences arising from the direct effect of the drug on the body, but also indirectly from the way the cocaine is taken. For example, destruction of the nasal septum when the drug is snorted and the transmission of HIV and Hep C through 'Crack Lip,' when the hot pipe causes open sores through which viruses from shared pipes gain entry to the body. If, as it appears, we are in the midst of another increase in cocaine use, it would appear that as a society, we are condemned to relive the mistakes of the past. Do we really have to endure more high-profile tragedies in so-called 'celebs' before we once again realise that cocaine consumption by the wealthy, the middle-class or the marginalised is not a good idea? Sometimes I despair of my fellow human beings who, when it comes to chemical intoxication, think that it could not happen to them. Well, it can and for some unfortunates, it probably will. ●

CONTRIBUTOR INFORMATION

Dr Des Corrigan, Best Contribution in Pharmacy Award (winner), GSK Medical Media Awards 2014, is a former Director of the School of Pharmacy at TCD and won the Lifetime Achievement Award at the 2009 Pharmacist Awards. He was chair of the Government's National Advisory Committee on Drugs from 2000 to 2011. He currently chairs the Advisory Subcommittee on Herbal Medicines and is a member of the Advisory Committee on Human Medicines at the IMB. He is a National Expert on Committee 13B (Phytochemistry) at the European Pharmacopoeia in Strasbourg and he is an editorial board member of the Journal of Herbal Medicine and of FACT — Focus on Alternative and Complementary Therapy.

MISSING LINK

***Terry Maguire** wonders if we are missing the role of cyclizine in the increasing number of opioid-related deaths*

He waited until I had assembled and labelled the 11 items on his prescription and I had come out of the dispensary to give him his medicines, before bringing up what was on his mind. He had been made to feel embarrassed in our pharmacy two days ago, he claimed. He had asked to buy "sickness tablets" and had been refused. He needed me to understand how this made him feel. He was being treated as a common drug-addict. The "sickness tablets" were for his sister and he only requested them on advice of a community nurse attending his sister who was vomiting copiously and who was waiting to get a prescription for them from the GP. What really annoyed him, he continued, was that he walked the short distance to a competitor pharmacy and without any hesitation or questions was sold a strip of 10 tablets. Could I explain why this was so?

Sensing his righteous anger growing, I decided to tread carefully. Firstly, I told him, I wasn't in the pharmacy when he made the request and that the pharmacist who was had made professional decisions which I would not be over-riding. Secondly, I reminded him that we had a similar issue last year and at that time, I had told him we would not be selling cyclizine 50mg tablets any more, in line with Department of Health and Pharmaceutical Society guidance. But could I explain why another pharmacy without hesitation sold him a strip of 10, he interjected. I could not and what they did was really up to them; their business was nothing to do with me.

In that case, he said in a loud voice so other customers could overhear, he would never be in our pharmacy again; treated like a common drug addict. In a calm but assertive voice, I told him it was unfortunate he felt that way. He threw the medicine bag back onto the counter and demanded his prescriptions back.

I had reached that point, the point I never wished to reach. I had had enough and I responded accordingly. I bluntly refused, telling him the prescriptions I had just dispensed were dispensed in good faith and they were not his property, they were the property of the Government. I suggested, keeping as best as I could to a degree of professional decorum that might ensure I did not bring the pharmacy profession into disrepute, that if he wished, he could make a complaint to the Health Board and I would be very happy to address the points in his compliant when the Health Board contacted me. Confused and surprised with how assertively I took this position, he stomped off, taking the bag of medicine with him.

I have never been clear what the benefits to addicts are from the combination of cyclizine and opioids, but I do see this combination becoming more and more popular. This patient had a long-standing addiction to codeine; a combination of prescribed codeine, mainly 30/500, but also supplemented by over-the-counter 8/500 purchases.

> *The literature suggests that there is an intense CNS effect when the two are taken concomitantly. The link of course has been easily made by users, since cyclizine is indicated when opioids cause nausea, which they often do, so the combination is common*

The literature suggests that there is an intense CNS effect when the two are taken concomitantly. The link, of course, has been easily made by users, since cyclizine is indicated when opioids cause nausea, which they often do, so the combination is common. I always assumed that cyclizine merely allowed patients to take larger doses of opioids while avoiding nausea or to fend-off nausea associated with withdrawal, but it's clearly more complex than this.

A few cases of suicide have been linked to cyclizine use, but very few. For this reason, most pharmacists regard cyclizine as a relatively safe drug. Yet, as a centrally-acting anticholinergic, its use, particularly its use over a prolonged period of time, is not without risk and the potential for significant adverse events. The literature to date fails to identify cyclizine as a drug of abuse, misuse or one with significantly negative outcomes. The reason for this perhaps is that since it is deemed to be safe, it is not screened for in autopsy following suicide or opioid overdose and therefore, maybe, we are missing its role in the increasing number of opioid-related deaths currently being recorded across the British Isles.

Cyclizine abuse has been reported among opioid dependents receiving methadone, with the combination having been reported to produce strong psychoactive effects, with intense stimulation and often hallucinations. In one suicide case, cyclizine was found in a concentration far above the therapeutic range. These reports, few as they are, are questioning the safety of cyclizine, especially its potential for abuse and its toxicity in overdose. Overdose is more likely on continued use due to the tolerance that builds up, requiring higher and higher doses to achieve the same effect.

My patient returned later that day with a box of chocolates and a sheepish apology. He did not understand what had come over him; perhaps it was his worry about his sister, he suggested. He asked if we could forget all about it. The incident had caused me some considerable stress, and stress I could well do without, yet I accepted his apology and as there was no mention of us supplying cyclizine, it seemed we could move on and of course no-one would ever suggest, or even think, that he was in any way a 'common drug addict'. ●

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Terry Maguire owns two pharmacies in Belfast. He is an honorary senior lecturer at the School of Pharmacy, Queen's University of Belfast. His research interests include the contribution of community pharmacy to improving public health.

A SERIOUS BUSINESS?

How fully do our patients and fellow healthcare professionals understand that pharmacy is a serious business, asks ***Ultan Molloy***

I have just got a *Harvard Business Review* article through this morning detailing the value of having a laugh at work, "even when the work is serious", it said. This got me thinking about the work of community pharmacies, pharmacists, technicians and our teams. Is it a serious business we are in, doing 'serious work'? Also, who sees it as serious work, and what even constitutes serious work, mind you.

I recall a story of a pharmacist called Mrs Bourke in Dublin, whom a now ex-pharmacist friend of mine used to work for. The story goes that a lady ran in the door with a prescription, pushing it towards Mrs Bourke, saying "I need that quickly. I'm in a terrible rush", to which Mrs Bourke replied, "that's no problem dear, you better bring it with you so". Staring at Mrs Bourke in disbelief, the would-be customer listened on. "We don't do things in a rush here. Medicines are a serious business, you know." Clearly she didn't, and perhaps we forget this from time-to-time.

My friend is still a pharmacist by the way, as in, he is on the register, but after getting abused down the phone by a hospital consultant who wasn't following up on his patient's Humira consumption, he decided the craic was gone out of pharmacy for him. The local GP was writing valid prescriptions to dispense from, of course, so all good there. That happened some time back, at the start of what appears to be a trend of pharmacists leaving the profession. Certainly, pharmacists staying in it, who have an interest in patient care somewhat proportionate to the salaries that they hope to command, are few and far between.

Doctors, of course, are in a serious business. Surely we can't argue otherwise. Life and death and all that. There's a level of trust there that's needed from patients, and pharmacists are even more trusted than patients' GPs, according to some surveys. The till can be the complicating factor perhaps. Paranoia can kick in that 'you are just selling me stuff', but there is an antidote in the majority of cases. Advise on the most safe and effective medicines for the symptoms that the patient presents with, let them decide on the severity and choose from their options, and if they want something just for their throat, or for their nose, throat and chest, then they can decide.

Let's think link-advising with integrity, rather than link selling, with more tenuous links to patient care.

ON PERCEIVED VALUE

€50 for a seven-minute slot in a GP surgery, or €6.99 for some Advil cold and flu, where appropriate of course, following a 'free' consultation. Surely it's a no-brainer, if a head cold is the diagnosis. What is the perceived value, however, is the thing to consider. Much like our "I'm in a terrible rush" lady, one can readily argue that 'free' isn't going to be valued at the counter when it comes to pharmacist advice. At the tail end of 10 years of FEMPI, we nearly had another round of cuts, demonstrating unfortunately that any 'vision' for pharmacy appears to be solely cultivated and embraced on our side of the fence at present.

A couple of talented local musicians have stopped playing "for the craic" in the local for some time now. They're gigging musicians, depending on it for their income, and the 'why would I spend €25 to see him in the Claregalway Hotel when i can just drop in down the road to the local on a Thursday evening' was killing their income and the perceived value.

PILE THEM HIGH AND SELL THEM CHEAP... JUST 'A CONDUIT FOR DRUG DELIVERY'

Market forces, and ones positioning in the market of course, determine the perceived value of a product or service. I used to get frustrated at colleagues competing solely on price. Okay, I still do, but there's a place for everyone, or at least that's the theory. Just 20 per cent or so of medicines are paid for by patients visiting the pharmacy, with the rest paid for by the State — still what appears to be a little known fact. If we were to actually do the 80/20 in terms of which is more important, no doubt stretching our mental arithmetic skills in this case, then I would continue to be very, very, concerned at what nearly happened before Christmas to pharmacy payments. I'm neglecting, of course, the unexplained patients whose phased fees were just stopped without explanation. Rather than nearly, they actually happened, and this appears to have gone unacknowledged and unnoticed in the media. More PCRS bullying behaviour too, mind you, led no doubt from certain characters in there. Respect for the profession? Indeed. Maybe it needs to be better earned at the same time, and an acceptance of what has been accepted as best efforts to date have not proved to be good enough.

OMNIPRESENCE

Remember this month to dispense, check, do the paperwork, ensure regulatory compliance, look after the business needs, staff etc... and of course be available for patients. When Irene says she is from "all over" in *Me, Myself and Irene*, Jim Carrey replies: "Omnipresence. I like that in a woman!" Are we trying to be omnipresent, and yet not really present in any one place, and if so, what determines and sets our priority?

SURE, IT'S ONLY A BIT OF CRAIC

We'll know the story of our Government for the coming months by the time this is published, or perhaps we'll be preparing for another election. Interesting times, when candidates who go on holidays through the election period and can't get elected to local councils end up in our Dáil. Sure, it's only a bit of craic, isn't it? If you're down this way, look me up and we'll hit the pubs in Galway and get a few pints in for Donegal Tuesday with our local Sinn Féin candidate.

Lowering the voting age to 16 was talked about some time back, wasn't it? Which just wouldn't be on, of course, as they'd be missing out on the craic. One of our friend's daughters gave our Sinn Féin friend a vote "because he's cute". Sure why not, isn't it all a bit of craic? Although, on my wife's advice, any political aspirations I had have been now well and truly put to bed. ●

CONTRIBUTOR INFORMATION

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Rheumatoid arthritis

AUTHOR:
CIARA GAVIN MPSI

***Ciara Gavin MPSI** takes a clinical look at the prevalence, symptoms and treatment options for patients with rheumatoid arthritis and how pharmacists can help*

BACKGROUND

Rheumatoid arthritis is a common, chronic systemic inflammatory condition affecting around 1 per cent of the population.[1] The condition manifests in patients as joint pain, stiffness and swelling.[2] Rheumatoid arthritis (RA) primarily affects the small joints of the hands and feet.[3] Due to the cartilage and bone destruction caused by untreated or progressed RA, it is recommended to commence treatment as soon as possible after diagnosis, and ideally within three months.[2,3,4]

INVESTIGATIONS

Laboratory tests

Once a clinical diagnosis is made, laboratory tests are ordered to help confirm diagnosis and determine prognosis:

- Rheumatoid factor (RF):[3] This protein is produced by the immune system when it attacks healthy tissue and is identified in a laboratory test.[5] RF is positive in 60-to-70 per cent of patients with RA. It is generally tested at first presentation or diagnosis and does not need to be repeated if positive. The higher values symbolise worse prognosis.[6] About 5 per cent of patients without rheumatoid arthritis can also test positive for the protein.[5]
- Anti-CCP antibodies:[3] Anti-cyclic citrullinated peptide antibody (anti-CCP) is a marker present in about 70 per cent of patients with RA.[7] Those with anti-CCP positive laboratory tests are very likely to develop RA, but not everyone with RA will have anti-CCP antibodies present.
- Patients with both positive results for RF and anti-CCP antibodies are more likely to have severe RA.[5]
- ESR or CRP:[3] Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) are both non-specific laboratory tests which can measure inflammation levels in the body. These are often measured during RA diagnosis.[5,8]

Imaging

- X-rays:[3] Scans of a patient's affected joints are conducted to identify any erosion visible.

Assessing disease activity

- Disease activity measurement is important for assessing and identifying treatment plans for the patient. By quantifying disease activity, it is recognised as a tool for measuring treatment success also. There are several composite measures of disease activity developed and validated, but the most commonly used is the *'28 joint count disease activity scale'* – DAS28.[4]
- Scores of >5.1; >3.2 to ≤5.1 or ≤3.2 indicate the presence of high, moderate or low disease activity, respectively[4]

Treatment

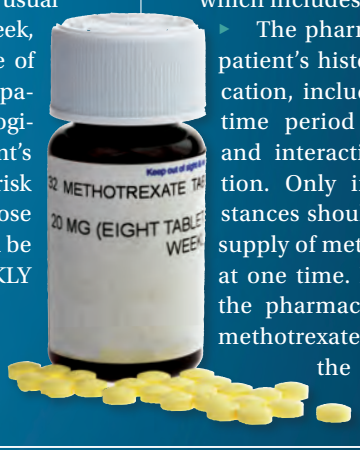
Treatment aims for RA are to control the symptoms and signs of RA and limit radiological damage; therapy should be started as soon as possible.[4, 5]

Steroids and non-steroidal anti-inflammatory drugs (NSAIDs) are used to control pain and the initial inflammatory process at the commencement of treatment[9,3] and also can be used for acute flares during treatment.[4]

cDMARD: Conventional disease-modifying anti-rheumatic drugs monotherapy are first-line treatment.[3] cDMARDs offered are: Methotrexate, leflunomide, sulfasalazine and hydroxychloroquine.[3, 4, 5]

Short-term glucocorticoids via oral, intramuscular or intra-articular administration can be used to bridge treatment when commencing a cDMARD.[3]

Methotrexate is often the cDMARD of choice first-line[3, 4, 5] and is used either as monotherapy or in combination with another DMARD in approximately 70 per cent of RA treatment. Methotrexate is a folic acid antagonist and is classified as an antimetabolite cytotoxic agent.[10] The usual starting dose is 7.5mg once a week, up-titrated to a maximum dose of 20mg once-weekly based on the patient's response and haematological toxicity, as reviewed by patient's blood tests.[10] Due to the serious risk of toxicity associated with overdose of methotrexate, patients should be informed this is a ONCE-WEEKLY administration.



Patients should inform their doctor or pharmacist immediately if they experience any of the following symptoms:[10, 11]

- Sore throat/other infections.
- Fever/chills.
- Mouth ulceration.
- Easy bruising or bleeding.
- Diarrhoea.
- Vomiting.
- Unexplained rash.
- Breathlessness.
- Dry, persistent cough.

Due to the high-risk nature of the supply of methotrexate to patients in Ireland, The PSI published guidance for pharmacists which includes the following points:[11]

- The pharmacist must ***review*** the patient's history of dispensed medication, including an assessment for time period since last dispensing and interaction review of medication. Only in exceptional circumstances should more than a month's supply of methotrexate be dispensed at one time. If a patient presents to the pharmacy known to be taking methotrexate, they should be seen by the pharmacist, irrespective of the nature of the advice being sought.
- Product labelling must be clear for the patient. It is recommended to state the number of tablets, total dose, weekly interval and day of week on the dispensed medication, ie, take 6 x 2.5mg tablets (15mg in total) once a week on a Friday. The use of 'as directed' is not suitable.
- The ***dispensed*** product should always be double-checked.
- At the point of ***supply***, the pharmacist should personally supply the methotrexate to the patient or carer, should verbally confirm the dose and reinforce the labelled instructions. The pharmacist must offer to counsel the patient every time a supply is made.

If a patient has not achieved the treatment target aim of remission or low disease activity despite dose escalation of single agent cDMARD, then a combination 'step-up strategy' is recommended where an additional cDMARD is commenced.[3]

If a patient has moderate-to-severe disease activity at initial presentation, or has not adequately responded to cDMARD alone, they are offered methotrexate plus a

biological agent or targeted synthetic disease-modifying antirheumatic drug.

Biological agents

Biological agents, including TNF inhibitors, B-cell modulators, T-cell modulators and IL-6 inhibitors have improved the success of RA treatment and control in the recent era by modulating the inflammatory response.[9]

TNF-α is a cytokine involved in the inflammation process in RA. It has been found that the presence of TNF-α plays an extremely central role in the inflammation and bone degradation with RA,[9] as it induces local inflammation and pannus formation, which leads to erosion of the cartilage and bone destruction. TNF-α inhibitors have expanded treatment options for RA. The TNF-α inhibitors block the chronic inflammation process.

TNF-α inhibitors used in the treatment of RA include:

- **Etanercept:** 50mg subcutaneously once-weekly or 25mg subcutaneously twice-weekly.
- **Infliximab**: 3mg/kg intravenous infusion at weeks 0, 2, 6, and then every eight weeks thereafter (the dose and/or frequency can be increased if incomplete response).
- **Adalimumab:** 40mg every two weeks subcutaneously.
- **Golimumab**: 50mg subcutaneously once monthly; or 2mg/kg intravenous infusion at weeks 0 and 4, and then every eight weeks thereafter.
- **Certolizumab pegol**: 400mg subcutaneously at weeks 0, 2, and 4, and then 200mg every two weeks or 400mg every four weeks thereafter.

IL-6 inhibitors

- **Tocilizumab:** 4mg/kg intravenous infusion every four weeks, may increase to 8mg/kg every four weeks if necessary, maximum 800mg/dose; body weight <100 kg: 162mg subcutaneously every two weeks initially, increase to 162mg once weekly if necessary; body weight ≥100kg: 162mg subcutaneously once-weekly.
- **Sarilumab:** 200mg subcutaneously every two weeks.

T-Cell modulator

- **Abatacept**: Body weight <60 kg: 500mg intravenous infusion at weeks 0, 2, and 4, and then every four weeks thereafter; body weight 60-100kg: 750mg intravenous infusion at weeks 0, 2, and 4, and then every four weeks thereafter; body weight >100kg: 1,000mg intravenous infusion at weeks 0, 2, and 4, and then every four weeks thereafter.

B-Cell modulator

- **Rituximab:** 1,000mg intravenous infusion on days one and 15, may repeat course every 16-to-24 weeks if inadequate response.

Targeted synthetic DMARDs

JAK inhibitors: Janus kinase inhibitors block the intracellular enzyme that transmit signals from cytokines which drive the inflammatory cellular response in rheumatoid arthritis.

- **Tofacitinib:** 5mg orally (immediate-release) twice-daily.
- **Baricitinib**: 2mg or 4mg orally once-daily.

Upadacitinib: 15mg orally once-daily.

For further information on the management of rheumatoid arthritis, see the National Institute of Health and Care Excellence guidelines (2018).

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Methofill®

Methotrexate

NEW Self Inject Device from Accord Healthcare

Lower acquisition cost vs Metoject® Pen[1]

ABBREVIATED PRESCRIBING INFORMATION

Please refer to the Summary of Product Characteristics (SmPC) before prescribing **Methofill (Methotrexate) 7.5mg, 10mg, 12.5mg, 15mg, 17.5mg, 20mg, 22.5mg, 25mg, 27.5mg and 30mg, solution for injection in pre-filled injector.** Each pre-filled injector contains 7.5, 10, 12.5, 15, 17.5, 20, 22.5, 25mg, 27.5mg or 30 mg methotrexate.

Indications:

Active rheumatoid arthritis in adults. Polyarthritic forms of severe, active juvenile idiopathic arthritis, when response to nonsteroidal anti-inflammatory drugs (NSAIDs) is inadequate. Severe recalcitrant disabling psoriasis, not adequately responsive to other therapy such as phototherapy, PUVA, and retinoids, and severe psoriatic arthritis in adults. Mild to moderate Crohn's disease alone or in combination with corticosteroids in adults refractory or intolerant to thiopurines.

Dosage and Administration:

Adults with rheumatoid arthritis: Recommended initial dose is 7.5mg of methotrexate once weekly, administered subcutaneously. May be increased gradually by 2.5mg per week. Weekly dose of 25mg should not be exceeded. Doses exceeding 20mg/week are associated with significant increase in toxicity. Response to treatment expected after approximately 4 – 8 weeks. Upon achieving therapeutically desired result, reduce dose gradually to lowest effective maintenance dose. *Children and adolescents below 16 years with polyarthritic forms of juvenile idiopathic arthritis*: Children with body surface area below 0.75m^2 cannot be treated with this product. Recommended dose 10 - 15mg/m. body surface area (BSA)/once weekly by subcutaneous injection. Weekly dosage may be increased to 20mg/m^2 body surface area/once weekly. Increase monitoring frequency if dose increased. Refer patients to rheumatology specialist in the treatment of children/adolescents. Use in children < 3 years of age not recommended. *Psoriasis vulgaris and psoriatic arthritis*: Administer test dose of 5 – 10mg parenterally, one week prior to therapy to detect idiosyncratic adverse reactions. Recommended initial dose 7.5mg once weekly subcutaneously. Increase dose gradually. Do not exceed weekly dose of 25mg. Doses exceeding 20mg per week are associated with significant increase in toxicity. Response to treatment expected after approximately 2 – 6 weeks. Upon achieving therapeutically desired result, reduce dose gradually to lowest effective maintenance dose. Increase dose as necessary but do not exceed maximum recommended weekly dose of 25mg. Exceptionally a higher dose might be clinically justified, but should not exceed a maximum weekly dose of 30mg. *Crohn's Disease*: Induction treatment 25mg/week subcutaneously. Response to treatment expected after approximately 8 to 12 weeks. Maintenance treatment 15mg/week subcutaneously. *Renal impairment*: Use with caution. See SPC for dose adjustments based on creatinine clearance. *Hepatic impairment*: Use with great caution, if at all, in patients with significant current or previous liver disease, especially if due to alcohol. If bilirubin is > _5mg/dl (85.5 µmol/l), methotrexate is contraindicated. *Elderly patients*: Consider dose reduction. *Third distribution space (pleural effusions, ascites)*: Half-life can be prolonged, dose reduction or discontinuation may be required.

Contraindications:

Hypersensitivity. Severe liver impairment. Alcohol abuse. Severe renal impairment (creatinine clearance less than 30 ml/min). Pre-existing blood dyscrasias. Serious, acute or chronic infections Ulcers of oral cavity and known active gastrointestinal ulcer disease. Pregnancy, breast-feeding. Concurrent vaccination with live vaccines.

Warnings and Precautions: Clearly inform patients that therapy should be administered **once a week**, not every day. Supervise patients so that signs of possible toxic effects or adverse reactions are detected and evaluated with minimal delay. Treatment should be initiated and supervised by physicians with knowledge and experience in use of antimetabolite therapy. Possibility of severe/fatal toxic reactions, patients should be fully informed by physician of risks and recommended safety measures. Use in children under 3 is not recommended. *Before beginning or reinstituting treatment*: Complete blood count with differential and platelets, liver enzymes, bilirubin, serum albumin, chest x-ray and renal function tests. If clinically indicated, exclude tuberculosis and hepatitis. *During therapy (at least once a month during the first six months and every three months thereafter)*: Examine mouth and throat for mucosal changes. Complete blood count with differential and platelets. Profound drop in white-cell or platelet counts indicates immediate withdrawal of treatment and appropriate supportive therapy. Advise patients to report signs and symptoms of infection. Monitor patients taking haematotoxic medicinal products (e.g. leflunomide) closely with blood count and platelets. Liver function tests: Do not start treatment if abnormality of liver function tests or liver biopsy present. Stop treatment if abnormalities develop. Treatment may be recommenced if liver function returns to normal. Evaluate need for liver biopsy in psoriasis therapy. Temporary increases in transaminases have been reported. Consider dose reduction or discontinuation in the case of a constant increase in liver-related enzymes. Additional hepatotoxic medicinal products should not be taken unless clearly necessary and consumption of alcohol should be avoided. Monitor liver enzymes closely in patients taking other hepatotoxic products. The same should be taken into account with the simultaneous administration of haematoxic products. Monitor renal function. Where renal function may be compromised (e.g. the elderly), monitor more frequently particularly when concomitant medicinal products affect the elimination of methotrexate, cause kidney damage or can lead to impairment of blood formation. Dehydration may also intensify methotrexate toxicity. Respiratory system: Be alert for symptoms of lung function impairment. Pulmonary effects require quick diagnosis and discontinuation of methotrexate. Pulmonary symptoms (especially dry non-productive cough) or a non-specific pneumonitis occurring during methotrexate therapy may be indicative of a potentially dangerous lesion and require interruption of treatment and careful investigation. Acute or chronic interstitial pneumonitis, often associated with blood eosinophilia may occur and deaths have been reported. This lesion can occur at all dosages. Methotrexate may impair response to vaccination and affect result of immunological tests. Particular caution needed in presence of inactive, chronic infections (e.g. herpes zoster, tuberculosis, hepatitis B or C). Vaccination using live vaccines must not be performed. Malignant lymphomas may occur in which case therapy must be discontinued. Concomitant administration of folate antagonists has been reported to cause acute megaloblastic pancytopenia. Radiation induced dermatitis and sun-burn can reappear (recall-reaction). Psoriatic lesions can exacerbate during UV-irradiation and simultaneous administration of methotrexate. Methotrexate elimination is reduced in patients with a third distribution space (ascites, pleural effusions) requiring careful monitoring for toxicity and dose reduction or discontinuation of methotrexate. Pleural effusions and ascites should be drained prior to initiation of methotrexate. Diarrhoea and ulcerative stomatitis require interruption of therapy. Products containing folic acid, folinic acid or derivatives may decrease effectiveness. Treatment of psoriasis with methotrexate should be restricted to severe recalcitrant, disabling psoriasis not adequately responsive to other forms of therapy and only when diagnosis established by biopsy and/or after dermatological consultation. Encephalopathy / Leukoencephalopathy have been reported in oncologic patients. The absence of pregnancy should be confirmed before methotrexate is administered. Contains less than 1 mmol sodium (23 mg) per dose, i.e. essentially "sodium free". Methotrexate has minor or moderate influence on ability to drive and use machines. **Pregnancy and Lactation:** Contraindicated in pregnancy and lactation. It has been reported that methotrexate treatment could lead to abortion. Women getting pregnant during therapy should receive medical counselling about risk of adverse reactions for the child. Effective contraception (women and men) is required during treatment and for at least 6 months thereafter. Women who wish to become pregnant should consult a genetic counselling centre. Men should seek advice about sperm preservation before starting therapy. **Adverse events include: Adverse events which could be considered serious include:** *Common:* Leukopenia, thrombopenia, pneumonia, interstitial alveolitis/ pneumonitis often associated with eosinophilia, *Uncommon*: Pharyngitis, pancytopenia, precipitation of diabetes mellitus, pancreatitis, cirrhosis, fibrosis and fatty degeneration of the liver, renal impairment, gastrointestinal ulcers and bleeding. *Rare*: Pericarditis, pericardial effusion, pericardial tamponade, thromboembolic events, pulmonary fibrosis, acute hepatitis, renal failure, anuria, anaphylactic shock, allergic vasculitis, conjunctivitis, sepsis, hypogammaglobulinaemia. *Very rare*: Acute aseptic meningitis, lymphoma, agranulocytosis, convulsions, paralysis, retinopathy, haematemesis, toxic megacolon, hepatic failure, Stevens-Johnson syndrome, toxic epidermal necrolysis (Lyell's syndrome). *Frequency unknown:* Bone marrow suppression, pulmonary toxicity, hepatotoxicity, renal toxicity, neurotoxicity, leukoencephalopathy, encephalopathy. **Other Very Common adverse events:** Stomatitis, dyspepsia, nausea, loss of appetite, abdominal pain, abnormal liver function tests (increased ALAT, ASAT, alkaline phosphatase and bilirubin). **Other Common adverse events**: Anaemia, headache, tiredness, drowsiness, oral ulcers, diarrhoea, exanthema, erythema, pruritus. See SPC for details of other adverse events. **Shelf Life:** 24 months. **Pack size:** 7.5mg/0.15ml; 10mg/0.20ml; 12.5mg/0.25ml;15mg/0.30 ml;17.5mg/0.35ml; 20mg/0.40ml; 22.5mg/0.45ml; 25mg/0.50ml; 27.5ml/0.55ml; 30mg/0.60ml. **Marketing Authorisation Holder (MAH):** Accord Healthcare Limited, Sage House, 319 Pinner Road, North Harrow, Middlesex, HA1 4HF, United Kingdom. **MA Number:** PA 1390/099/002, 003, 004, 005, 006, 007, 008, 009, 010, 011. **Legal Category:** POM. Full prescribing information including the SPC, is available on request from Actavis Ireland Ltd, a subsidiary of Accord Healthcare Ltd, Euro House, Little Island, Co. Cork, Tel: 021-4619040 or www.accord-healthcare.ie/products. Adverse reactions can be reported to Medical Information at Accord Healthcare Ltd. via E-mail: medinfo@accord-healthcare.com or Tel: +44(0)1271385257. **Date of Generation of API:** June 2018 UK&IE/MET/0027/06-18

Adverse events should be reported. Reporting forms and information can be found on the HPRA website (www.hpra.ie), or by e-mailing medsafety@hpra.ie. Adverse events should also be reported to Medical Information via email: medinfo@accord-healthcare.com or tel: 0044 (0)1271 385257.

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Date of Preparation: July 2018 UK&IE/MET/0012/04-18(1)

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Heart Health

***Dr Donna Cosgrove PhD MPSI** provides a clinical overview of the complexities of cardiovascular disease*

Dr Donna Cosgrove PhD MPSI

INTRODUCTION

Cardiovascular disease (CVD) describes disease of the heart and blood vessels caused by the process of atherosclerosis, and includes coronary heart disease (CHD), stroke, and other circulatory diseases.[1] CVD is the most common cause of death in Ireland, accounting for 36 per cent of all deaths.[2] According to the WHO, more than 17 million people worldwide died from CVD in 2008. The largest number of deaths relate to CHD and are mainly due to myocardial infarction (7.3 million).[2] Strokes were responsible for 6.2 million.[3] Of these deaths, more than three million occurred before the age of 60 and could have largely been prevented. CVD also has significant cost implications: The cost to the NHS in England was estimated at £7,880 million in 2010.[1]

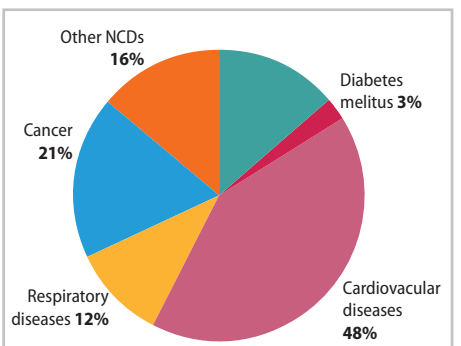

FIGURE 1: Distribution of global non-communicable diseases[3] by cause of death (both sexes)

ATHEROSCLEROSIS AND CORONARY HEART DISEASE

Atherosclerosis is an inflammatory process that affects the cardiovascular system.[3] CHD occurs when the coronary blood vessels are blocked by a build-up of cholesterol: This causes narrowing of the lumen and makes the inner surfaces of the blood vessels irregular and less pliable, which is detrimental to regular blood flow.[2,3]

When the blood vessel endothelium is exposed to raised levels of low-density lipoprotein (LDL), cholesterol and additional substances like free radicals, the endothelium becomes permeable to lymphocytes and monocytes. These cells migrate into the wall of the blood vessel, resulting in a series of reactions and attracting LDL cholesterol to the site. This cholesterol is engulfed by monocytes, which are then transformed into macrophages. Smooth muscle cells migrate to the site from deeper layers of the vessel wall (the media). Then, a fibrous cap, consisting of smooth muscle and collagen, is formed.[3] At the same time, the macrophages involved in the original reaction begin to die, forming a necrotic core. These lesions (atheromatous plaques) grow bigger as cells and lipids accumulate in them and begin to bulge into the vessel lumen. As the process continues, thinning of the fibrous cap and a fissuring of the endothelial surface of the plaque occur, which may cause rupture. With rupture, lipid fragments and cellular debris are released into the vessel lumen and exposed to thrombogenic agents on the endothelial surface, resulting in the formation of a thrombus.

If the thrombus is big enough, and a coronary blood vessel or a cerebral blood vessel is blocked, the blood flow to the heart is cut off. The decrease in the supply of oxygen and nutrients causes chest pain (angina) due to ischaemia[3] and can damage the heart muscle, resulting in a heart attack (MI). Symptoms of MI include sweating; light-headedness; nausea; and breathlessness, like angina, although not relieved by a nitrate spray.

Although LDL cholesterol tends to build up on the walls of the coronary arteries, increasing risk of heart disease, HDL cholesterol carries cholesterol away from the cells and back to the liver, where it is broken down or excreted. The current recommendation for healthy cholesterol levels is a total blood cholesterol level of less than 5mmol/litre, a HDL level of >1mmol/litre, and an LDL level of under 3mmol/litre.[2]

RISK FACTORS

The atherosclerotic process can start to develop before adulthood. There is strong evidence that tobacco use, physical inactivity, unhealthy diet, excessive alcohol intake, hypertension, diabetes, raised blood lipids, obesity, poverty, low educational status, advancing age, male gender, genetic disposition and psychological factors all contribute to this process.[1,3] Behavioural risk factors for atherosclerosis such as tobacco use, physical inactivity, an unhealthy diet, and harmful use of alcohol are risk factors for many non-communicable diseases (NCDs), not just atherosclerosis, thus a large percentage of NCDs are preventable through the reduction of these risk factors.

Hypertension

Hypertension affects more than one billion individuals worldwide. It puts a strain on the heart, contributing to CHD and causing an estimated 9.4 million deaths every year.[2,5] The benefits of decreasing blood pressure are long established based on observational studies and trials of hyper- and normotensive patients. A review of studies concluded that a 10mmHg reduction in systolic blood pressure has been shown to reduce the risk of major CVD events by 20 per cent, CHD by 17 per cent, stroke by 27 per cent, heart failure by 28 per cent, and all-cause mortality by 13 per cent.[5] This was evident across multiple groups of patients, which suggests that blood pressure-lowering provides benefits that are somewhat generalisable. Even patients with lower blood pressure at baseline benefitted from these notable effects. The authors of this review[5] suggest a case-by-case assessment by clinicians of each patient's risk factors to decide on the blood pressure level at which to start antihypertensive medication, rather than a decision based on an arguably arbitrary fixed threshold for blood pressure, which is just a single risk factor for CVD.

The best approach to reduce blood pressure, however, is still unclear: Generally, the commonly-prescribed antihypertensives are effective overall in contributing to preventing cardiovascular disease, but there are some modest but significant differences between treatments in terms of specific clinical outcomes: Calcium channel blockers appear to be more effective than other classes of drugs for stroke prevention, whereas diuretics work better for prevention of heart failure. Beta blockers appeared to be inferior to other classes of antihypertensives for the prevention of major cardiovascular disease events, stroke, renal failure, and all-cause mortality.

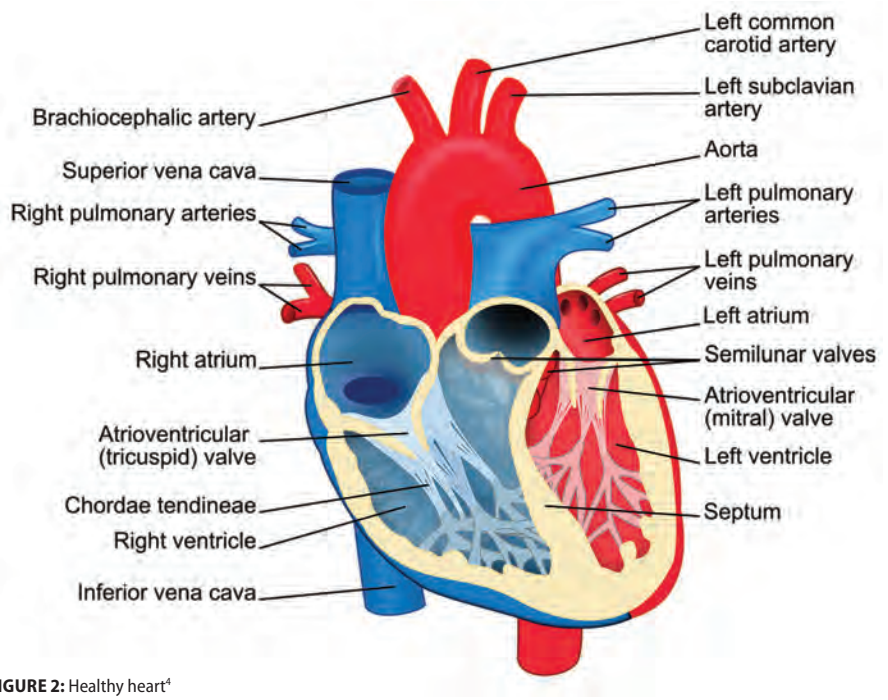

FIGURE 2: Healthy heart[4]

Smoking

Tobacco use is a huge contributor to the development of health problems, including heart attacks, strokes, sudden death, heart failure, aortic aneurysm and peripheral vascular disease.[3] Smoking increases the risk of heart disease by 24 per cent. Carbon monoxide and nicotine present in cigarette smoke place a strain on the heart by increasing heart rate and risk of blood clots, and additional chemicals also damage the lumen of the coronary arteries.[2]

Physical activity

Regular physical activity can prevent obesity. Insufficient physical activity not only contributes to heart disease, but is the fourth-leading risk factor for mortality. According to the WHO Global Atlas on cardiovascular disease prevention and control, 31.3 per cent of adults aged 15 or older are not sufficiently active, a figure that may have increased since its publication in 2011. People who do not engage in enough physical activity have a 20-to-30 per cent increased risk of all-cause mortality compared to those who engage in at least 30 minutes of moderate-intensity physical activity most days of the week.[3] Participating in 150 minutes of moderate physical activity each week (or 75 minutes of vigorous intensity aerobic activity, or a mix of both) can reduce the risk of ischaemic heart disease by approximately 30 per cent and the risk of diabetes by 27 per cent.[3]

Alcohol

There is a complex relationship between alcohol consumption and CHD/cerebrovascular disease. There is a direct relationship between higher levels of alcohol consumption and binge-drinking (60 or more grams alcohol per day) with risk of CVD. Low levels of drinking alcohol, conversely, may be associated with a reduced risk of negative cardiovascular outcomes. Various mechanisms have been suggested for the protective effect, ie, beneficial effects of alcohol on the HDL cholesterol level, throm-

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Dose (mg/day)	5	10	20	40	80
Fluvastatin	-	-	21%[1]	27%[1]	33%[2]
Pravastatin	-	20%[1]	24%[1]	29%[1]	-
Simvastatin	-	27%[1]	32%[2]	37%[2]	42%[3,4]
Atorvastatin	-	37%[2]	43%[3]	49%[3]	55%[3]
Rosuvastatin	38%[2]	43%[3]	48%[3]	53%[3]	-

TABLE 1: Reduction in low-density lipoprotein cholesterol according to NICE guidance. 1 = low intensity, 2 = medium intensity, 3 = high intensity. 4 = increased risk of myopathy (high dose simvastatin): consider only when patients have not achieved treatment goals on lower doses with consideration of risks and benefits[1]

bolytic profile and platelet aggregation.[3] If alcohol is consumed, the recommended weekly limit of 14 standard drinks should be adhered to, with these units spread out over at least three days. Binge drinking should always be avoided.[2]

Diet

People at high risk of or with CVD should be advised to reduce their saturated fat intake and increase their mono-unsaturated fat intake. Unsaturated fat will help reduce cholesterol levels.

Foods high in unsaturated fat include oily fish, avocados, nuts and seeds, sunflower, rapeseed, olive and vegetable oils.[2] Wholegrain varieties of starchy food are preferred, and daily intake of sugar and food products containing refined sugars should be reduced. At least five portions of fruit and vegetables should be consumed per day, and two portions of fish per week, including a portion of oily fish, and at least four-to-five portions of unsalted nuts, seeds and legumes.[1] Dietary salt consumption is an important contributor to hypertension and cardiovascular risk, and daily intake should not exceed 6g.[3]

MAINTAINING CARDIAC HEALTH

Several prospective human studies have demonstrated the cardioprotective effect of fish, ie, the Physicians' Health Study, which followed 20,551 male physicians for up to 11 years.[6] A 52 per cent reduction of sudden cardiac death in males who consumed fish once a week was reported compared to those who ate fish less than once a month. This cardioprotective effect has been attributed to its content of the omega-3 fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA).

One meta-analysis of clinical trials investigating the cardioprotective effect of omega-3 supplements showed significant effects on triglycerides, blood pressure, heart rate and CRP, with small, significant increases in both LDL-C and HDLC, although the authors say that the quantity of EPA and DHA required for these effects is still unknown.[6]

Conversely, a Cochrane review[7] of the use of long-chain omega-3 fats (79 trials involving over 112,000 people) found no evidence to suggest that they have any important positive or negative effects on mortality, CVD events or other measures of cardiovascular health. There was evidence that increasing ALA (in, ie, walnuts or enriched margarine) probably slightly reduces CVD risk, but effects were very small.

The review concludes that supplemental long-chain omega-3 fats are probably not useful for preventing or treating cardiovascular disease, although long-chain omega-3 fats can help to reduce serum triglycerides and raise HDL a little.

Regardless of the reported lack of association of omega-3 with heart health, fish and seafood are nutrient-dense and rich in a variety of other nutrients (such as vitamin D, calcium, iodine, selenium), so are useful foods, even without the potential cardiovascular benefits. NICE guidelines advise against recommending omega 3 oils for CVD prevention, and likewise for plant stanols or sterols.[1]

TREATMENT OF CARDIAC DISEASE

In severe cases of CHD, surgical procedures to treat blocked arteries are sometimes required, such as coronary angioplasty or a coronary artery bypass. In a small number of people, a heart transplant may be performed. However, in most cases, patients can successfully manage CHD with medicines, ie, ACE inhibitors, channel blockers, beta blockers, low-dose aspirin, nitrates and statins.[2] The NICE guideline groups statins into three different intensity categories according to the percentage reduction in LDL cholesterol they produce: Low intensity if the reduction is 20-to-30 per cent; medium intensity is 31-to-40 per cent; and high intensity is above 40 per cent.

In addition to adherence to prescribed regimens, it is important for individuals being treated for, or at risk of, CVD to keep the behavioural risk factors in mind and reconsider their lifestyle in light of these.

Self-care is an integral part of daily life and is all about the individual taking responsibility for their own health and well-being with support from the people involved in their care.

Self-care includes the daily actions undertaken in order to stay fit and maintain good physical and mental health, prevent illness or accidents, and care more effectively for minor ailments and long-term conditions.[2]

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Dr Donna Cosgrove PhD MPSI

IBD & IBS

***Dr Donna Cosgrove PhD MPSI** looks at the risk factors and mechanisms of disease in inflammatory bowel disease and irritable bowel syndrome, including treatment of symptoms and an overview of clinical research data*

MICROBES IN GUT HEALTH

The brain interacts with the gut through the gut-brain axis (GBA). Disturbances in this and in the microbial landscape in the intestine contribute to the pathogenesis of gastrointestinal (GI) disorders, including irritable bowel syndrome (IBS) and inflammatory bowel disease (IBD).[1] In normal circumstances, bacteria in the GI tract mainly consists of firmicutes (64 per cent), bacteroidetes (23 per cent), proteobacteria (8 per cent), and actinobacteria (3 per cent), and are important for priming the immune system, breakdown of dietary substrates inaccessible to host enzymes, and detoxification of xenobiotics.[1,2]

'Dysbiosis' is the term given to the disturbance of gut microbiota. Gut viruses have also been identified, primarily *Podoviridae*, *Siphoviridae* and *Myoviridae*. The GI microbial flora cohabits through a relationship of symbiosis, or 'commensalisms'. It is believed that the microbiota in an infant is derived from its mother's microbes during vaginal delivery or Caesarean section.

IRRITABLE BOWEL SYNDROME

IBS has an estimated prevalence of 10-to-15 per cent worldwide and in some populations is more common in women than in men (ie, North America), though not all.[3,5] IBS is based on symptoms and is defined by the presence of abdominal pain or discomfort, with altered bowel habits. It is

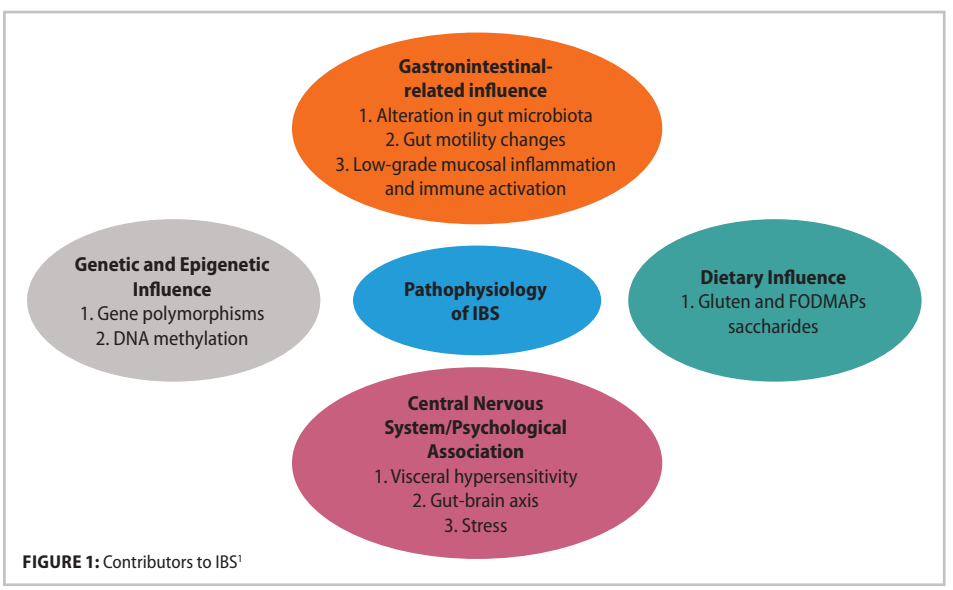

FIGURE 1: Contributors to IBS[1]

diagnosed when the symptoms are not attributable to any alternative disorder being present, with the onset often occurring during adolescence. Women more commonly report IBS with abdominal pain and constipation (IBS-C) whereas men more so report diarrhoea (IBS-D)-type symptoms. The predominant subtype experienced by an individual can change over time, as well as symptom severity: It is a chronic relapsing disease.[3]

The main symptoms of IBS are:

- Abdominal cramping.
- Loose/frequent stools.
- Constipation.
- Bloating.
- Discomfort or pain.
- Flatulence.

Symptoms can be brought on by food intake/specific food sensitivities. Other symptoms include mucus in stools, lack of energy, nausea, backache, urinary symptoms, and incontinence.[3] Importantly, IBS shows comorbidity with psychiatric disorders such as anxiety, depression and somatoform disorders, which can profoundly impact on quality of life.

IBS AETIOLOGY

Dysfunction of the innate immune system contributes to low-grade inflammation in IBS.[1] In IBS patients, activation of the immune system in the colonic mucosa is observed, along with infiltration of immune cells and release of inflammatory cytokines (particularly IL-6, TNF-a, and IL-1b), although the cause for this is unclear. In healthy individuals, the mucus epithelium barrier in the GIT means that microbes are confined to the intestinal lumen, and immune responses maintain barrier integrity. However, once the barrier is damaged by an influx of inflammatory mediators, this causes an alteration in the intestinal environment and changes the gut microbiota composition. This alteration of gut integrity and immunity may contribute to IBS. Combination of this low-grade mucosal inflammation with visceral hypersensitivity and impaired bowel motility leads to IBS. Visceral hypersensitivity (increased pain sensation in the bowel due to physiological stimuli) is a large factor: Patients with visceral hypersensitivity tend to have lower colonic distension pain threshold, and a normal stimulus will intensify pain. The prevalence of this hypersensitivity in IBS patients can vary from 33-to-90 per cent, occurring more frequently in IBS-D patients. The cause of this hypersensitivity is due to multiple factors, including dysbiosis, brain-gut communication, diet, psychological factors, genetics, inflammation, immunological factors and altered intestinal permeability.

IBS TREATMENT

Identifying the patient's predominant bowel complaint helps guide treatment choice. Subtyping IBS by Predominant Stool Pattern can help with this:

1. IBS with constipation — hard or lumpy stools ≥25%; loose or watery stools <25% of bowel movements.
2. IBS with diarrhoea — loose or watery stools ≥25%; hard or lumpy stools <25% of bowel movements.
3. Mixed IBS — hard or lumpy stools ≥25%; loose or watery stools ≥25% of bowel movements.[3]

Management interventions for IBS include pharmacological treatments (ie, antispasmodics, antidiarrheal, low-dose antidepressants, probiotics, etc), modifications in lifestyle and dietary changes.[4]

PHARMACOLOGICAL THERAPIES

Loperamide is specifically useful in IBS-D because it reduces stool frequency, increases stool consistency, and can be used prophylactically.

Antispasmodics can be useful in IBS when there is an exaggerated gastrocolonic reflex. This is partially cholinergically mediated. Hyoscine has an antispasmodic effect useful in these cases. Peppermint oil is also an antispasmodic, with calcium channel-blocking properties.

Diet is very important in IBS as food and breakdown products can affect gut physiology. Ingestion of FODMAPs (fermentable oligosaccharides, disaccharides, monosaccharides and polyols) are easily fermentable by gut bacteria into methane and hydrogen gasses, and are associated with bloating and abdominal pain in about 70 per cent of patients, regardless of IBS subtype.[1] FODMAPs may cause GI distension and stimulate abnormal intestinal motility due to osmotic increase in fluid volumes and are found in foods such as wheat, onions, some fruits and vegetables, sorbitol, and some dairy, among others.

Soluble fibre like ispaghula can improve symptoms, unlike insoluble fibre like wheat bran, which contains FODMAPs. NICE guidance recommends limiting the intake of insoluble fibres and starch, with ispaghula powder (a soluble fibre) or foods high in soluble fibre being encouraged, particularly for IBS-C.[1]

Osmotic laxatives such as lactulose can be useful in IBS-C as it pulls water back into the bowel to soften the stool. However, they do not reliably improve pain or bloating.

Antidepressants work in multiple ways to help symptoms: They affect pain perception, mood and motility. Serotonin plays a role in GIT motility, and altered levels are found in patients with IBS.[1] Most trials so far have not separated out the subtype of IBS patients recruited, so recommendation by IBS subtype is not possible. However, because TCAs prolong gut transit times, whereas SSRIs decrease transit time, it may be the case that TCAs would be more effective in IBS-D, and SSRIs of greater benefit in IBS-C, although this has not yet been investigated.[5] Some of the strongest evidence for the pain-modifying effects of antidepressants in chronic painful disorders comes from studies looking at serotonin and norepinephrine reuptake inhibitors (SNRIs) duloxetine and milnacipran, but neither of these have been tested in IBS trials to date.

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Product Information
Buscopan® 10mg Coated Tablets Product Information
Presentation: Tablets containing hyoscine butylbromide 10mg. **Indications:** Relief of spasm of the gastrointestinal tract and for the symptomatic relief of Irritable Bowel Syndrome. **Dosage and administration:** For spasm of the gastrointestinal tract: adults and children over 12 years: 2 tablets four times daily. For Irritable Bowel Syndrome: initially 1 tablet three times daily, increasing if necessary to 2 tablets four times a day. **Contraindications:** hypersensitivity to any component, myasthenia gravis, mechanical stenosis in the gastrointestinal tract, paralytical or obstructive ileus, megacolon, narrow angle glaucoma. **Warnings and precautions:** In case severe, unexplained abdominal pain persists or worsens, or occurs together with symptoms like fever, nausea, vomiting, changes in bowel movements, abdominal tenderness, decreased blood pressure, fainting or blood in stool, medical advice should be sought immediately. Buscopan should not be taken for extended periods without investigating the cause of abdominal pain. Use with caution in conditions characterised by tachycardia; those susceptible to intestinal or urinary outlet obstruction; pyrexia. Warn patients to seek medical advice if they develop a painful red eye with loss of vision whilst or after taking Buscopan 10mg Coated Tablets. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take Buscopan 10mg Coated Tablets since the tablet coat contains sucrose. Advise patients to consult their doctor before taking if: this is the first time they have symptoms of IBS, age over 40 years and some time since the last attack of IBS or the symptoms are different; recent rectal bleeding; severe constipation; nausea or vomiting; loss of appetite or weight; difficulty or pain passing urine; fever; recent travel abroad. Advise patients to consult their doctor if they develop new symptoms, or if symptoms worsen, or if they do not improve after 2 weeks of treatment. **Interactions:** The anticholinergic effect of drugs, e.g. tri- and tetracyclic antidepressants, antihistamines, quinidine, amantadine, antipsychotics (e.g. butyrophenones, phenothiazines), disopyramide and other anticholinergics (e.g. tiotropium, ipratropium, atropine-like compounds) may be intensified by Buscopan 10mg Coated Tablets. Co-administration with a dopamine antagonist may diminish the effect of both medicines. The tachycardic effects of beta-adrenergic agents may be enhanced by Buscopan 10mg Coated Tablets. **Pregnancy and lactation:** Use during pregnancy and breastfeeding is not recommended. **Side effects:** Uncommon: dry mouth, tachycardia, skin reactions (e.g. urticaria, pruritus), dyshidrosis, constipation. Rare: urinary retention. Not known: anaphylactic shock, anaphylactic reactions, dyspnoea, rash, erythema, other hypersensitivity, visual accommodation disturbances. **Pack sizes:** 20 and 40. **Legal category:** P. **Product authorisation number:** PA 540/181/2. **Product authorisation holder:** sanofi-aventis Ireland Ltd., Citywest Business Campus, Dublin 24, Ireland. Tel 01403 5600, email: IEmedinfo@sanofi.com. For further information please see Summary of Product Characteristics. **Date of revision:** January 2020.
Adverse events should be reported. Reporting forms and information can be found at www.hpra.ie. Adverse events should also be reported to Sanofi Ireland Ltd. on 01403 5600 or email IEPharmacovigilance@Sanofi.com

1: IMS data - April 2019

SAIE.BUSC.17.11.0234(2) - February 2020

Psychological therapies appear to be effective for the treatment of IBS. These therapies modify cognitive, behavioural, and emotional responses to symptoms. This results in a reduction in IBS symptoms, improved quality of life and, with CBT in particular, enabling patients to target maladaptive thoughts and behaviours that exacerbate or maintain these symptoms.

Exercise encourages regular bowel movements. People with IBS should be encouraged to increase their physical activity, even by as little as a 20-minute walk every day.

INFLAMMATORY BOWEL DISEASE

IBD refers to ulcerative colitis (UC) and Crohn's disease (CD), both relapsing and remitting diseases characterised by chronic GIT inflammation.[6] The prevalence of IBD is between 5-and-20 per cent and it is more common in women and younger people. UC affects mainly the rectum (95 per cent) and colon, but CD can affect any part of the tract from the mouth to the anus. IBD affects all age groups but there are two main peaks of onset: Between the ages of 25-to-35, and between the age of 60 and 80.[6,8]

Symptoms of IBD include:

- Diarrhoea.
- Abdominal pain.
- Tenderness.
- Weight loss.

In UC, blood is more likely to be present, with a feeling of rectal urgency or tenesmus. The mucosal and submucosal layers of the colon are affected. As CD is a transmural disease, occurring across the entire wall of the organ, this leads to complications like intra-abdominal abscesses, fistulas, linear clefts and strictures, in turn causing intestinal obstruction.

IBD AETIOLOGY

The full mechanism behind IBD development is still unclear, however genetic factors and environmental factors both contribute, stimulating a sustained abnormal immune response that results in disruption of the intestinal mucosa. Some 235 genetic regions have been associated with IBD susceptibility. Less-diverse microbiota profiles have been demonstrated in UC patient samples.[2]

IBD TREATMENT

The extent, location and severity of the disease determine the treatment approach.[3] In acute IBD, the goal of treatment is to treat the symptoms and induce clinical remission while improving quality of life. Afterwards, treatment is tailored to maintain this.[7]

Aminosalicylates are more effective in UC than in CD. Mesalazine (5-aminosalicylic acid) delivers anti-inflammatory effects in the GIT or rectal delivery. The aminosalicylate sulfasalazine is made up of mesalazine coupled to a sulfapyridine and is broken down by colonic bacteria when administered orally. This leads to mesalazine delivery within the large intestine, although sulfapyridine is associated with side-effects. Drugs that do not contain sulfapyridine are available, ie, olsalazine (a molecule in which mesalazine is bonded to a second mesalazine).

Corticosteroids are potent anti-inflammatories. Prednisolone, hydrocortisone, and methylprednisolone are useful to achieve remission in acute IBD, especially where aminosalicylate therapy has failed. These are not useful in relapse prevention or for long-term use due to side-effects (bone disease, diabetes, infection risk). The corticosteroid budesonide is better tolerated than conventional steroids and is effective at inducing remission in both UC and CD.[7]

Immunosuppressants, including the thiopurines (azathioprine and 6-mercaptopurine), are used for both UC and CD. These drugs are not useful for inducing remission as their full effect can take up to six months. However, these drugs are associated with serious adverse effects (ie, pancreatitis, allergic reaction, infection, bone marrow suppression). Methotrexate can be used in CD maintenance therapy as an

alternative to azathioprine, although it has its own side-effects.

Biologics — TNF blockers and leucocyte adhesion inhibitors: Drugs that inhibit the effects of TNF-α, ie, infliximab, are reserved for moderate-to-severe IBD refractory to other therapies. People treated with biologic agents may over time experience a loss of efficacy, thought to be due to the development of antibodies to the drug. Adalimumab, certolizumab, and golimumab are alternatives for patients who cannot tolerate, or have become resistant to, infliximab. Natalizumab reduces inflammation through inhibiting the adhesion of alpha-4-beta-7 integrin to the receptors on endothelial gut cells.

For inducing remission in UC, NICE guidance recommends initial use of aminosalicylates. For treating CD, NICE guidelines recommend monotherapy with a conventional corticosteroid to induce remission.[9] More specific guidance for additional circumstances and monitoring (ie, for neutropaenia) is recommended in the NICE guidelines.

Antibiotics are known to influence several disorders, including IBD, by modulating the host microbiota. Antibiotics can potentially ameliorate the microbial environment of patients with IBD both by decreasing proinflammatory bacteria and by increasing beneficial ones.[2] Several antimicrobial drugs have been investigated in patients with UC for the induction and/or maintenance of disease remission, ie, ciprofloxacin, metronidazole, tobramycin and rifaximin, to varying degrees of success. Currently, there is no firm evidence to support a routine role for antibiotics in IBD.

Probiotics have been investigated in IBD and IBS, with the aim of reversing dysbiosis.[2] However, a Cochrane review of many studies showed that probiotics were not more effective than placebo or active comparators in inducing the remission of active UC. When only a subset of studies (the randomised controlled trials only) were pooled, probiotics were shown to be effective in the induction of remission (RR 1.80). In rare cases, probiotics have also been shown to cause sepsis in patients with UC, therefore they should be used with caution, particularly in severe disease. Only limited data are available for probiotic application in CD, however, none of them have shown efficacy. Synbiotics refer to the combination of probiotics. In theory, these should be more potent than the probiotic or prebiotic components used on their own.[1] Another medical treatment, faecal microbiota transplantation (FMT), involves the administration of faecal microbiota into the intestinal tract of a recipient. This therapeutic approach was practiced in ancient China since the 4th Century. The physician Ge Hong suggested to patients with severe diarrhoea to use fresh stool as a choice of treatment. More recent studies indicate that FMT appears to be a moderately effective treatment for patients with active UC. Further study of more targeted, specific probiotics and synbiotics in IBD and IBS is needed, along with refinement of some other treatments.

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MAZDA'S NEW TAKE ON SUCK-SQUEEZE-BANG-BLOW

***Morgan Flanagan Creagh** reviews the new Skyactiv-X motor special, which combines petrol and diesel processes with a spattering of hybrid technology*

The Mazda-3 was reviewed last year and at that time, I advised shrewd *Irish Pharmacist* readers to hold their fire and wait for the release of the Skyactiv-X engine, which Mazda implied was going to be a revolution in fuel economy. Here we have the follow-up, as I was lucky enough to test the new saloon model, which I think is a little less stylish than its hatchback brother. The car has a 2.0-litre, four-cylinder petrol engine, which produces 180hp and 224nm of torque. It is also equipped with Mazda's mild Hybrid system that they say reduces fuel consumption and increases fuel economy. It does this by recycling energy recovered during braking to power an electric motor that assists the engine, though I must admit I didn't notice anything particularly hybrid-like about the driving experience.

What makes this new Skyactiv-X motor special is that it has a new take on the whole suck-squeeze-bang-blow business, as it combines petrol and diesel processes, with the aforementioned spattering of hybrid technology.

In a normal petrol engine, gasoline is sucked into the cylinder, where it is compressed and ignited using a spark. The resulting explosion created by igniting the fuel and air mixture causes the cylinder to move, which sets in motion the chain reaction that results in drive. Alternatively, in diesel engines the fuel and air are squirted into a cylinder and are heavily compressed until the mixture reaches its pressure-induced flashpoint, at which point it ignites, explodes, and pushes the cylinder, eventually moving the vehicle.

To make this new motor, Mazda has added some diesel systems to their petrol engine by compressing the gasoline at a much higher ratio, generating a leaner burn, which causes a reduction in both emissions and fuel usage. The Skyactiv-X engine is the world's first commercial petrol unit to combine the spark ignition of a petrol engine with the compres-

TECH SPECS

POWER ▸ 180hp

TORQUE ▸ 224Nm
0-100km/h 8.2 sec

TOP SPEED ▸ 216km/h

CLAIMED CONSUMPTION ▸
5.6l/100km (50.4mpg)

CO2 EMISSIONS ▸ 127g/km

MOTOR TAX ▸ €190

PRICE ▸ €37,270 as tested
Mazda 3 starts at €28,320

sion ignition of a diesel, and Mazda claims it has led to fuel economy of 5.6l/100km, or 50.4mpg.

Mazda loves mad motors like the Wankel rotary it used in its RX cars, and it's interesting to see some lateral thinking in regard to modern engines. My test car was frugal, but I found the engine idle noise to be jarring. I initially thought the car was broken until I remembered the diesel technology in its DNA. With the radio off, the rattle-n-hum was not a fun experience and I found myself hoping for the stop-start system to kick in and silence the orchestra.

The saloon model is more spacious, especially for back-seat passengers, as it doesn't have the sloping profile of the hatchback. Mazda built this car, so it feels balanced, handles wonderfully and the gearbox is a little gem. However, I feel a little short-changed regarding the 180hp as I really had to work the motor to find this power. Perhaps I'm just longing for a Mazdaspeed3 to arrive on the press fleet.

The cockpit is stylishly designed and uses decent-quality plastics. My test model had some lovely cream leather, heated seats that were very handy for cold winter backsides and were accompanied by a heated steering wheel, which really came into its own during the cold test week. The Bose sound system was tremendous, despite being attached to the Mazda infotainment system, which is not my favourite. The parking cameras seemed to be very high-resolution and the test car had the very useful overhead parking camera, which stitches together images from cameras all around the vehicle to build an augmented reality parking assistant.

The Mazda-3 starts at €28,320 but the model I tested will set you back €37,270. Personally, I don't think Mazda have managed to divert fuel economy-focused, prospective buyers away from hybrid or plug-in hybrid offerings with their new Skyactiv-X motor.

NAPPY RASH

Caldesene Powder gets a new look for a new generation

Caldesene Medicated Powder has been the gold standard for the treatment and prevention of nappy rash for over 45 years. Clonmel Healthcare has just unveiled its new, brighter branding and packaging that will make Caldesene, the leading nappy rash product, look even more impactful on the shelves in Irish pharmacies.

Clonmel Healthcare has invested extensively in a full brand audit on Caldesene. During the process all stakeholders were consulted, including pharmacists, HCPs and new parents to discuss their experiences of baby's nappy rash and current treatment trends.

A bolder design has been created, while ensuring the recognisable Caldesene look is retained. The front of the packaging has been decluttered, so consumers can understand the core message — Caldesene medicated powder prevents and treats nappy rash — quickly and easily. The new design uses strong and warm colours that are appealing and attention-grabbing for the retail environment. The inviting pink and teal colours on the packaging are still marked with the signature Caldesene heart shape to offer familiarity to consumers, and the new baby graphic portrays the company's family values at point of sale.

Marketing Director Mr Martin Gallagher said: "We have created a new image to highlight that Caldesene prevents and treats nappy rash, and it should be used at every change. It was so important to us that we maintained the brand heritage, whilst conveying to the consumers that this is still the same great product that they have grown up with. The product has not changed in any way. This new modern, attractive packaging is attention-grabbing and clearly communicates the product on-shelf."

Clonmel Healthcare aims to improve the way they communicate and make Caldesene more relevant and accessible for today's audience. In order to communicate the values of Caldesene to a whole new generation of parents, they have also introduced the new supporting tagline: 'Tender care at every change.'

To engage the consumers with the new look, Caldesene will run a substantial advertising campaign including radio advertising, visual media, online marketing, a new Caldesene website, in-store POS and attendance at all significant trade shows.

'Look at me, I'm a big girl now'
Chloe admires a photo from her first Caldesene photoshoot two years ago

For further information, to receive product imagery or to speak to Mr Martin Gallagher, contact Ms Ann-Marie Sheehan, Aspire PR, Tel: 087 2985569/01 8275181 or email annmarie@aspire-pr.com.

CYSTIC FIBROSIS

Cystic Fibrosis Ireland to set the scene for cystic fibrosis in the 2020s at April Annual Conference

Dr Preston Campbell, former President and Chief Executive Officer of the Cystic Fibrosis Foundation in the United States, and a leading medical expert in cystic fibrosis (CF), has been announced as the keynote speaker at the forthcoming Cystic Fibrosis Ireland annual conference taking place in Galway from Friday 3 April-Sunday 5 April.

Aimed at people with CF, their families and friends, registration for the conference in the Ardilaun Hotel, Taylors Hill, is now open at **www.cfireland.ie**. Ireland has the highest incidence of CF in the world, with almost 1,400 people diagnosed with the disease. The conference comes ahead of Cystic Fibrosis Ireland's annual flagship fundraising appeal, 65 Roses Day, on Friday 10 April, where people can lend their support by buying a purple rose for €2 or by donating online at **www.65RosesDay.ie**.

Vision for a new decade

Dr Campbell's address will offer a world view of CF developments underway. Dr Campbell, who has more than 25 years' experience providing direct clinical care to people with CF, including at the John Hopkins CF Care Centre and Vanderbilt's CF Care Centre in the US, stepped down from his position as President and Chief Executive Officer of the Cystic Fibrosis Foundation last December. During his time at the Foundation, Dr Campbell was responsible for overseeing the Foundation's research, drug discovery and development programmes. These resulted in the approval of 12 CF therapies, including four treatments that address the basic defect in CF, most recently Trikafta, which will benefit 90 per cent of people with the disease. Dr Campbell also oversaw the Foundation's network of CF care centres, which are recognised by the National Institutes of Health as a model of care for chronic disease. With nearly every CF drug available today having been made possible because of Cystic Fibrosis Foundation support, Dr Campbell has a unique insight into what promising developments lie ahead.

In addition to Dr Campbell's keynote, there will be a number of other presentations on a range of topics, including:

- Positive mental health by Dr Alistair Duff, Head of Psychological Services, St James's University Hospital, Leeds.
- Superbugs by Prof John Moore and Prof Cheri Millar, clinical microbiologists at Belfast City Hospital.
- Gene editing by Dr Patrick Harrison, Senior Lecturer, University College Cork.
- Diet research by Dr Audrey Tierney, Director for the MSc in Human Nutrition and Dietetics, University of Limerick.
- Relaxation by Charlotte Farragher and Rory Murphy, instructors at Tuam Yoga and Pilates Studio.
- The impact of new drug therapies in children and gastrointestinal CF developments by Prof Paul McNally, Consultant, Children's Health Ireland, Crumlin Hospital.

Not there yet…

Mr Philip Watt, Chief Executive, Cystic Fibrosis Ireland, comments: "People with cystic fibrosis in Ireland are living longer lives than ever before. Indeed, in recent years we have seen steady advances in treatment and care with the development of dedicated centres of CF care, the funding of cutting-edge drug therapies and the continued success of the lung transplant programme. While these developments have been very positive, we are by no means there yet, and it's important to remember that there are still people with CF for whom, because of their specific genetic make-up, the latest drug therapies do not apply and for whom progress will be reliant on further research, including gene editing/Crispr, which is still at a relatively early stage.

"This conference, at the start of a new decade, provides us with an opportunity to see more clearly what is on the horizon for CF and to set forth a new vision for where CF care needs to be. Ireland is number one in the world in terms of incidence of CF. We have some of the most severe strains of CF. It's only right therefore that Ireland also strives to be number one worldwide for the best healthcare, the best quality of life, and the best outcomes for people with CF. We have still some way to go to realise this ambition."

For more details on registration for Cystic Fibrosis Ireland's Annual Conference and AGM, telephone 01 4962433 or email **info@crireland.ie**. Those not in a position to attend the conference can view proceedings online, where they will be streamed live at **www.cfireland.ie**.

HEALTH SUPPLEMENTS

Pure ingredients, ethically sourced, vegan friendly

Naturalife, Ireland's leading health supplement supplier, has relaunched One Nutrition, an innovative range of premium supplements, each containing the purest of ingredients, ethically sourced and now presented in almost 100 per cent recyclable packaging.

The One Nutrition range consists of 14 products focusing on three areas: Recovery, Wellness and Superfood, which all play an important role in keeping the body in great shape on the inside and out. The vegan friendly brand has been created for the consumer who is seeking superior, natural nutritional products with no unnecessary additives and presented in recyclable amber glass jars protected by recyclable card boxes.

Formulated in Ireland by Mr Darragh Hammond, Mr Dominic Galvin (pictured) and their technical team — achieving 360° sustainability and a minimal environmental impact is at the heart of the brand's philosophy.

Commenting on the relaunch of One Nutrition, founder Mr Hammond said: "With each passing year, we are seeing more and more people take a proactive approach to their overall health and wellbeing and increasingly looking towards preventive measures over cures. Recent research shows that 72 per cent of Irish adults consider vitamins and minerals to be an important part of a healthy diet. Consumers are more aware of their nutritional needs and the environmental impact of their choices, which now includes demanding vegan-friendly, sustainably-packaged, ethically-sourced and free from varieties. It is our overriding aim to meet all these criteria where possible across all our products and we are 99 per cent there."

One Nutrition Health Supplements;
TOP RIGHT: Dominic Galvin and Darragh Hammond

With more than seven-in-10 Irish consumers believing vitamins and minerals are an important part of a healthy diet, the vegan-friendly brand was created with the modern consumer in mind. The 20-year-old company Naturalife, based in Rathnew, Co Wicklow, has relaunched this pared-back natural sustainable range in a bid to satisfy modern consumer demand. The sustainably packaged range also incorporates free from ingredients to produce nutritional supplements that are both good for the individual and good for the planet.

Hero products in the range include the following, which are all vegan friendly as well as gluten, soy and dairy free:

- B12-Max, a highly absorbable vitamin B12 spray to support immune system, energy levels and red blood cell formation, particularly useful for those following a vegan diet. Vitamin B12 contributes to normal red blood cell formation, to the reduction of tiredness and fatigue to normal energy yielding metabolism and to the normal function of the immune system.
- D3-Max A, plant-based high-strength vitamin D oral spray supporting the immune system, bone health and muscle function, it's delicious orange flavour means it tastes great too. Vitamin D contributes to the normal function of the immune system and to the maintenance of normal bones and muscle function.
- Q10-Max, a high strength Co-enzyme Q10, which also contains thiamine to support energy and heart health. Suitable for those taking statin drugs which are known to deplete CoQ10 levels. Thiamine contributes to the normal function of the heart and normal energy yielding metabolism.
- Ocean Mag, Natural Atlantic sea sourced magnesium helps support normal muscle function and energy, suitable for those exercising regularly. Magnesium contributes to normal muscle function and energy-yielding metabolism.

SLEEP AID

Perrigo launches Nytol's first clinically proven sleep aid for Ireland

Perrigo has launched Nytol's first clinically proven sleep aid onto the Irish market. Nytol One-A-Night is now available over the counter in pharmacy to help customers suffering from temporary sleep disturbance. An online survey conducted in 2019 shows that over six-in-10 adults in Ireland have difficulties getting to sleep, or staying asleep at night, with women more likely to suffer than men and stress being the main cause for sleep problems. "That's a significant cohort of people who would benefit from pharmacy support," said Ms Catherine O'Connor, Brand Manager, Perrigo. "The research also showed that Irish people consider getting enough sleep the number-one priority in maintaining good health and wellness, yet the majority claim to be getting less hours' sleep than what they perceive to be 'healthy'."

Sleep problems usually get better by changing sleeping habits, but when everyday coping mechanisms and non-pharmacological strategies have not worked, Nytol One-A- Night can be taken for up to seven nights to help get the sleep pattern back on track. Each tablet contains 50mg Diphenhydramine Hydrochloride, which can help those suffering from temporary sleep disturbance.

If the problem persists, please refer your customer to their GP.

For more information about Nytol and useful tools to assist in the conversation with your customers in pharmacy, talk to your Perrigo business representative.

RARE DISEASE DAY

Patient groups come together to urge action on rare diseases

To mark Rare Disease Day, *An Easyguide to Rare Diseases in Ireland* was launched at the event in the presence of the Minister for Health, Simon Harris. The guide has been produced by the Rare Disease Taskforce, which incorporates RDI, HRCI and IPPOSI. The guide provides information on rare diseases in Ireland, insights on living with a rare disease through personal testimonies, as well as further sources of information and support for rare diseases. The Easyguide together with the '10 Priorities for the Next Programme for Government' can be viewed at www.rdi.ie/rdeasyguide-2020/. Pictured at the launch is Ms Bernadette Gilroy, parent of a child with PKU.

DERMATOLOGY

New campaign for Salatac Gel treatment

With summer on the horizon, Dermal will be launching a new campaign to advertise Salatac Gel to the general public in national newspapers and magazines. As warts and verrucas are highly contagious and easily transmitted in pools and changing rooms, the new campaign, running in April/May, will focus on children at a swimming pool.

Each complete Salatac Gel kit contains:

- **Treatment gel containing salicylic acid, with a specially designed nozzle for easy, targeted application.**
- **An emery board to remove hardened skin.**
- **Patient information leaflet with usage instructions.**

Topical salicylic acid treatments such as Salatac Gel have been shown to be as effective as cryotherapy. It forms a waterproof barrier over the lesion, meaning no plasters are required, and transmitting the wart or verruca to others is less likely. According to Dermal, it is a proven, convenient and painless first-line treatment for patients with warts and verrucas this summer.

DEPRESSION

Nasal spray approved in Europe for adults with treatment-resistant major depressive disorder

- SPRAVATO▼ esketamine nasal spray offers the first new mechanism of action for an antidepressant in 30 years.
- EC approval is based on data from a clinical trial programme in adult patients with treatment-resistant major depressive disorder, including five phase 3 trials.
- Treatment with esketamine nasal spray plus a newly initiated oral antidepressant was associated with a significant reduction in depressive symptoms, with the onset of efficacy as early as day two, with approximately half of all treated patients achieving remission after four weeks of treatment spray, in combination with a selective serotonin reuptake inhibitor (SSRI) or serotonin and norepinephrine reuptake inhibitor (SNRI), for adults living with treatment-resistant major depressive disorder (TRD). According to the approval, patients are considered to have TRD if they have not responded to at least two different treatments with antidepressants in the current moderate-to-severe depressive episode.

Major depressive disorder (MDD) affects approximately 40 million people across Europe and is the leading cause of disability worldwide. For these patients, the main goal of treatment is to relieve the symptoms of depression, and ultimately achieve remission, with few, if any, symptoms of depression remaining. However, about one-third of patients with MDD do not respond to currently available treatments.

"MDD is a debilitating illness that can have profound emotional, functional and economic impact on both those who suffer and their loved ones," said Prof Ted Dinan, Professor of Psychiatry and Principal Investigator in the Alimentary Pharmabiotic Centre at University College Cork. "I have seen patients who have been suffering with MDD for a really long time and have tried multiple different treatments, which can take weeks or even months to show any kind of effect. The fast-acting nature of esketamine nasal spray makes it a welcome new treatment option for individuals who need it most."

The approval of esketamine is based on data from a clinical trial programme in patients with TRD, including over 1,600 patients treated with esketamine. The five phase 3 trials included three short-term studies, one randomised withdrawal and maintenance of effect study, and one long-term safety study. These data demonstrated that treatment with esketamine nasal spray plus a newly-initiated oral antidepressant was associated with a greater reduction in depressive symptoms compared to a newly-initiated oral antidepressant plus placebo nasal spray, in adult patients (18-to-64 years), with the onset of efficacy as early as day two. Approximately 70 per cent of esketamine-treated patients responded to treatment, with a ≥50 percent symptom reduction. Furthermore, approximately half of all treated patients achieved remission at the end of the four-week studies. Continued treatment with esketamine nasal spray plus oral antidepressant reduced the risk of relapse by 70 per cent among patients with stable response and by 51 per cent in patients in stable remission, compared to continuing treatment with oral antidepressant alone.

"Esketamine nasal spray represents a new way to manage TRD with a new mechanism of action," said Mr Laurent de Saint Sernin, General Manager, Commercial Operations, Janssen Sciences Ireland UC. "Janssen is committed to reducing the devastating burden caused by serious mental health and neurodegenerative diseases, and we are proud to be bringing an innovative new treatment option which will help to address an acute unmet need." He added: "Janssen Sciences Ireland UC are looking forward to working with the relevant authorities and the local reimbursement process to make esketamine nasal spray available to Irish patients and to ensure the safe and appropriate therapeutic use of this treatment."

Across the five phase 3 and one phase 2 clinical trials, esketamine nasal spray demonstrated a favourable benefit-risk profile, with sustained efficacy and no new safety concerns were observed over a period of up to one year. The most commonly observed adverse events in TRD patients treated with esketamine were dizziness, nausea, dissociation, headache, somnolence, vertigo, dysgeusia, hypoaesthesia, and vomiting. These side-effects were generally mild-to-moderate, transient (typically resolving within two hours) and occurred on the day of dosing.

Esketamine is an antagonist of the N-methyl-D-aspartate (NMDA) glutamate receptor and is understood to work differently than other currently available therapies for MDD. It is thought to help restore synaptic connections between brain cells in people with TRD, allowing for more activity and communication between specific regions of the brain. Based on results from clinical trials, this increase in activity and communication is thought to help improve the symptoms of depression. EC approval is valid in all 28 member states of the European Union, as well as the European Economic Area countries (Norway, Iceland and Liechtenstein).

*based on 25% reduction in cravings at nearly 3 hours

Nicorette Icy white 4mg Medicated Chewing Gum. For the treatment of tobacco dependence by relieving nicotine craving and withdrawal symptoms, thereby facilitating smoking cessation in smokers motivated to quit. Helping smokers temporarily abstain from smoking . In smokers currently unable or not ready to stop smoking abruptly. Gum may also be used as part of a programme to reduce smoking prior to stopping completely.. **Dosage:** ***Smoking cessation:*** The gum should be used whenever there is an urge to smoke. Not more than 15 pieces of the chewing gum may be used each day. If not successful after 12 weeks the patient should be encouraged to make a fresh attempt to stop smoking. ***Temporary Abstinence:*** See full prescribing information. ***Gradual cessation:*** See full prescribing information. **Contraindications:** Use in non-smokers, Use in persons hypersensitive to nicotine or any ingredient in the formulation. **Special Warnings and Precautions:** The benefits of quitting smoking outweigh any risks associated with correctly administered NRT. A risk-benefit assessment should be made by an appropriate healthcare professional for patients with the following conditions: - Cardiovascular disease: Dependent smokers with a recent myocardial infarction, unstable or worsening angina including Prinzmetal's angina, severe cardiac arrhythmias, recent cerebrovascular accident, and/or who suffer with uncontrolled hypertension should be encouraged to stop smoking with non-pharmacological interventions (such as counselling). If this fails, Nicorette Gum may be considered but as data on safety in this patient group are limited, initiation should only be under close medical supervision. Renal and hepatic impairment: Use with caution in patients with moderate to severe hepatic impairment and/or severe renal impairment as the clearance of nicotine or its metabolites may be decreased with the potential for increased adverse effects. Gastrointestinal Disease: Nicotine may exacerbate symptoms in patients suffering from oesophagitis, gastric or peptic ulcers and NRT preparations should be used with caution in these conditions. Phaeochromocytoma and uncontrolled hyperthyroidism: Nicotine, both from NRT and smoking, causes the release of catecholamines from the adrenal medulla. Therefore, Nicorette should be used with caution in patients with uncontrolled hyperthyroidism or pheochromocytoma. - Diabetes Mellitus. Patients with diabetes mellitus should be advised to monitor their blood sugar levels more closely than usual when smoking is stopped and NRT is initiated, as reductions in nicotine-induced catecholamine release can affect carbohydrate metabolism. Patients with diabetes mellitus may require lower doses of insulin as a result of smoking cessation. - Smokers who wear dentures may experience difficulties in chewing Nicorette Gum. The chewing gum may stick to and may in rare cases damage dentures. Transferred dependence: Nicotine in any dose form is capable of inducing a dependence syndrome after chronic use and is highly toxic after acute use. However, dependence with Nicorette Gum is a rare side-effect and is both less harmful and easier to break than smoking dependence. Danger in children: Doses of nicotine tolerated by smokers can produce severe toxicity in children that may be fatal. Products containing nicotine should not be left where they may be handled or ingested by children.. **Undesirable Effects:** See full prescribing information for full list of undesirable effects. Immune System Disorders: Hypersensitivity - Common Anaphylactic reaction - Not known. Psychiatric Disorders – Abnormal Dreams – Uncommon. Nervous System Disorders: Headache - Very Common, Burning sensation, Dysgeusia, Paraesthesia – Common. Eye Disorders: Blurred Vision, Lacrimation increased – Common. Cardiac Disorders: Palpitations, Tachycardia - Not known. Vascular Disorders: Flushing, Hypertension – Uncommon. Respiratory, Thoracic and Mediastinal Disorders: Cough, Throat irritation - Very common. Bronchospasm, Dysphonia, Dyspnoea, Nasal Congestion, Sneezing, Throat tightness – Uncommon. Gastrointestinal Disorders: Hiccups, Nausea - Very common. Abdominal pain: Diarrhoea, Dry mouth, Dyspepsia, Flatulence, Salivary hypersecretion, Stomatitis, Vomiting – Common. Eructation Glossitis, Oral mucosal blistering and exfoliation, Paraesthesia oral – Uncommon. Dysphagia, Hypoaesthesia oral, Retching – Rare. Dry throat, Gastrointestinal discomfort Lip pain - Not known. Skin and Subcutaneous Tissue: Hyperhidrosis, Pruritus, Rash, Urticaria Disorders – Uncommon. Erythema - Not known. Musculoskeletal and Connective Tissue Disorders: Pain in jaw – Uncommon. Muscle tightness - Not known. General Disorders and Administration Site Conditions: Fatigue – Common. Asthenia, Chest discomfort and pain, Malaise – Uncommon. Allergic reactions including angioedema - Rare. **MA Holder:** Johnson & Johnson (Ireland) Limited, Airton Road, Tallaght, Dublin 24, Ireland. **MA Number:** PA 330/37/9 **Date of Revision of the Text:** June 2018. **Legal Category:** Products not subject to medical prescription. Further information available upon request from Johnson & Johnson (Ireland) Ltd. IRE/NI/20-4097

Konverge Plus is indicated for the treatment of essential hypertension as an ***add on therapy*** in adult patients whose blood pressure is not adequately controlled on the combination of olmesartan medoxomil and amlodipine taken as dual-component formulation. **Konverge Plus** is indicated as ***substitution therapy*** in adult patients whose blood pressure is adequately controlled on the combination of olmesartan medoxomil, amlodipine and hydrochlorothiazide, taken as a dual-component (olmesartan medoxomil and amlodipine or olmesartan medoxomil and hydrochlorothiazide) and a single-component formulation (hydrochlorothiazide or amlodipine).

Legal Category: POM. **Marketing Authorisation Numbers:** PA 865/17/1-3 and PA 865/19/1-5. **Marketed by:** A. Menarini Pharmaceuticals Ireland. **Further information:** Available on request from A. Menarini Pharmaceuticals Ireland Ltd, Castlecourt, Monkstown Farm, Monkstown, Co. Dublin or may be found in the SmPC available at **www.medicines.ie Co-promoter:** DAIICHI SANKYO IRELAND LTD., Riverside One, Sir John Rogerson Quay, Dublin 2, Ireland. **Date of Item:** October 2018 **Item Code:** IR-KON-04-2018

Daiichi-Sankyo

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