The College of Psychiatry of Ireland
Coláiste Síciatrachta na hÉireann

A consensus statement on the use of Benzodiazepines in specialist mental health services

EAP Position Paper

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Benzodiazepines are used in Primary Care, when prescribed by General Practitioners. There are practice guidelines available for General Practitioners in prescribing them.[1] This paper focuses on the use of Benzodiazepines in Specialist Mental Health Services.

General Information:

Benzodiazepines (BDZ) are drugs which work within the central nervous system and their main effect is to reduce anxiety and agitation quickly. The major clinical advantages of benzodiazepines are that they are highly effective in reducing anxiety, they work quickly; and they have few unwanted side effects. Unwanted side effects include a general slowness of mental and bodily movements; this is seen especially in the elderly. With long term use, tolerance (whereby the person needs more medication to produce the same effects) and dependence (where the person finds they start to need the drug and without it they develop withdrawal effects) can become major disadvantages. Unwanted effects can largely be prevented by keeping dosages minimal and courses short (ideally 4 weeks maximum) and by careful patient selection. Paradoxical reactions (unexpected increases in **agitated or** aggressive behaviour secondary to drug treatment) are rare.

Benzodiazepines are **also** sedative. When prescribed, patients should be warned of the risks associated with combining benzodiazepines with other sedative drugs or alcohol, and of the possible adverse effects on driving or operating machinery. Benzodiazepines are licenced for use for 4 weeks only; prescribing for longer than 4 weeks is known as off-label prescribing. Off-label prescribing should usually be limited to consultant-level specialists who are familiar with all the alternatives and prevailing expert opinion. In some circumstances it may be appropriate to continue this prescribing in Primary Care (general practitioner-level), but best practice is by mutual agreement between both parties concerned. It is important to tell the patient that the drug is being used off-label and why it is thought to be appropriate to use the drug.

Benzodiazepines work by increasing the efficiency of a natural brain chemical, GABA, to decrease the excitability of neurons. This reduces the communication between neurons and, therefore, has a calming effect on many of the functions of the brain.

Benzodiazepines can be placed into one of three groups by how quickly it is eliminated from the body. Short-acting compounds examples are, midazolam, and triazolam. Intermediate acting examples are alprazolam, flunitrazepam, clonazepam, lorazepam, nitrazepam, and temazepam. Long-acting compound examples are diazepam, clorazepate, chlordiazepoxide, and flurazepam.

Generally shorter acting compounds are better for the elderly, where the longer acting compounds may build up over time. Short acting compounds are more likely to become habit forming or create dependency.

Indications for Use

Caution should be exercised in prescribing benzodiazepines. Benzodiazepines prescribing should never be purely symptom orientated, but should be used in conjunction with treatments for any underlying disorder. It is vital to check whether the person might have a tendency to misuse drugs or alcohol, or a history of same, and if so should a referral be made to a specialist addiction psychiatry service.

Withdrawal from alcohol

Benzodiazepines are recognised as the treatment of choice for alcohol withdrawal. In this context the dosage should be tapered and discontinued within one week. Benzodiazepines are cross-tolerant with alcohol. This means people who are addicted to alcohol have a strong likelihood of becoming addicted to benzodiazepines. Benzodiazepines also have anticonvulsant properties.[12,13]

Anxiety Disorders

The principal indication for benzodiazepines is for short-term treatment (2 to 4weeks) of anxiety disorders.[2]

or panic disorder, benzodiazepines should not be used as a first line treatment option but are an option for treatment resistant cases.[3] They should be used with care in post-traumatic stress disorder (PTSD).[4] Benzodiazepines have no benefit on the course of bereavement and may inhibit psychological adjustment.[5] While benzodiazepines have been studied and utilized to treat these conditions they are not part of recommended first-line therapy for any of them. However, it is acceptable to use benzodiazepines as adjuncts during initial treatment while waiting for definitive therapy with longer term medications and psychotherapy to take effect. Continuing Benzodiazepines beyond 4 weeks will often result in loss of effectiveness, the development of tolerance, dependence and potential for withdrawal syndromes, persistent adverse side effects, and interference with the effectiveness of definitive medication and counselling. This should be discussed with the patient before prescribing. Benzodiazepines taken for more than 2 weeks continuously should be tapered rather than discontinued abruptly. If in the judgment of the clinician, the patient will have difficulty stopping the benzodiazepines after the 2 to 4 week acute treatment period, then benzodiazepines should not be prescribed.

Benzodiazepines will usually be reserved for the treatment of patients who have not responded to at least two treatments (such as after non-response to both an SSRI (selective serotonin reuptake inhibitor) and a psychological treatment) but concerns about potential problems in long-term use should not prevent their use in patients with persistent, severe, distressing and impairing anxiety symptoms.[6] There are a minority of people, who benefit from long term use of benzodiazepines, who do not develop tolerance, and attempts to reduce benzodiazepines results in a relapse.[6]

Insomnia

Benzodiazepines are effective for the short term treatment of insomnia. Non benzodiazepines (Z) hypnotics may be associated with less side effects. The recommendation is that all hypnotics are only prescribed for 2 – 4 weeks.

Acute Mania or Hypomania
Benzodiazepines are used in treating Acute Mania or Hypomania, as an adjunct to Antipsychotic or Mood stabilising medication.

Use in Psychosis
Benzodiazepines are used in the treatment of Psychosis. Where a person with psychosis is extremely distressed, and needs to be calmed quickly, then benzodiazepines are commonly used for what is described as Rapid Tranquillisation, either alone[7], or in combination with an antipsychotic; a significant minority of patients with established psychotic illness fail to respond adequately to antipsychotics alone, and this can result in benzodiazepines being prescribed on a long term basis.[10] There is limited evidence that some treatment resistant patients may benefit from a combination of antipsychotics and benzodiazepines, either by showing a very marked antipsychotic response or by allowing the use of lower-dose antipsychotic regimens.[11]

Catatonia
Benzodiazepines are the treatment of choice in Catatonia**.** Numerous studies and case reports indicate that benzodiazepines are rapidly effective, safe and easily administered and are therefore regarded as first-line treatment.[11]

Special populations:
Pregnancy
There is a low but established risk of teratogenicity with benzodiazepines use in pregnancy.[14-16] Ideally these medications should be gradually discontinued before a planned pregnancy and this possibility should be discussed with any woman of childbearing age for whom they are being prescribed. If a woman discovers she is pregnant and is taking benzodiazepines, she should be advised of the risks and usually have them gradually withdrawn as soon as possible. However, as always, a risk benefit analysis should be undertaken, and if other treatments such as relaxation, anxiety management, sleep hygiene and Cognitive Behaviour Therapy (CBT) are not effective, sometimes benzodiazepines are justified. Severe and persistent anxiety, in itself, can be a significant risk to foetal health. Specialist advice should be sought if necessary.

Old Age
The use of benzodiazepines in older people have been associated with adverse effects including marked sedation and psychomotor impairment, as well as an increased risk of hip fracture and motor vehicle crash, as well as the development of tolerance, dependence and withdrawal.[19,20,21.]. The reduced drug clearance as we age may be responsible for the increased susceptibility to adverse events. Adverse effects are reduced by using short acting benzodiazepines. Depression in older people can present with anxiety symptoms, this should be treated with anti depressants and psychological therapies, rather than benzodiazepines. Prescribing for residents in continuing care facilities present special difficulties. The use of benzodiazepines is less when staff receives education in geriatric care and where the organisational culture is supportive. Long term residents in continuing care settings need to have their medication reviewed regularly in line with best practice and HIQA guidelines. Benefits associated with

successful reduction in rates of benzodiazepine use include increased mobility and alertness, reduced incontinence and improved well being.[22]

People with an Intellectual Disability

The risks of benzodiazepines use includes sedation, and therefore increased risk of falls, and in addition inability to engage with activities during the day, so impacting on quality of life. For those who lack capacity to consent to treatment, pending enactment of Irish capacity legislation, reference should be made to relevant Medical Council Guidance and the prescriber should consult with carers and appropriate parties in order to determine the best interests of the patient.

Patients in Prison or Forensic Settings.

Doctors working in prison settings (where substance misuse problems occur in 65-70% of inmates) come under particular pressure to prescribe benzodiazepines. There is evidence that much of the medication prescribed in these settings is misused, sold on to others in exchange for other drugs, endangering the unintended end users. The most common cause of death in prison now is accidental overdose, typically of smuggled opiates combined with diverted benzodiazepines, and so benzodiazepines are not prescribed unless there is clear evidence of withdrawal from alcohol or benzodiazepines, when detoxification is appropriate.

Substance Misuse Services / Addiction Psychiatry Services.

Many service users attending the addiction services commonly misuse benzodiazepines in large quantities with other drugs in order to enhance their effects, to experience euphoric effects and an altered state of consciousness. They are also taken to treat withdrawals from other drugs including heroin, alcohol and cocaine. Other reasons for taking benzodiazepines by substance misusers include self medication for underlying symptoms of anxiety, panic attacks, phobic disorders, depression, post-traumatic stress disorder, memories of past abuse, and psychotic symptoms as part of a schizophrenic illness or not. Individuals with a diagnosis of emotionally unstable personality disorder tend to misuse and become dependent on benzodiazepines to manage associated psychic distress that they experience.

Patients dependent on both benzodiazepines and opiates have been found to be more psychologically vulnerable than those dependent on benzodiazepines alone and may have an increased incidence of depression and self harm. Prescribing of benzodiazepines to substance misusers requires competency in this form of treatment with appropriate supervision and in most cases is best provided by secondary/ tertiary treatment services. Prescribing of a benzodiazepines detoxification programme should occur when there is clear evidence of benzodiazepine dependence.[24,35] There needs to be appropriate assessment of dependence prior to commencement of detoxification[26] i.e. positive benzodiazepine urine results and baseline benzodiazepines levels done, education provided about the risks of benzodiazepines, engagement in counselling, clear treatment goals agreed and regular review of progress.

Recommended targeted psychological interventions that have been recommended include anxiety management, relaxation techniques, anger management, motivational enhancement approach, maintaining a diary of drug use, identifying triggers and maintaining factors for benzodiazepines use,

problem solving techniques, managing insomnia, exploring other ways of coping, relapse prevention strategies and Cognitive Behavioural Therapy[24,25]

The UK Clinical Guidelines on *Managing Drug Misuse and Dependence*[27] clearly outlines the need to convert sedative hypnotics/benzodiazepines to an equivalent dose of diazepam and that the lowest dose of diazepam that will prevent withdrawal symptoms should be prescribed. The recommended rate of detoxification include reducing in proportions of 1/8th of daily dose (between 1/10th and ¼) every 1-2 weeks or every month depending on the patient's response and that the time needed for detoxification can vary from 4 weeks to a year or more.

There are circumstances when the longer term prescription of benzodiazepines maybe considered desirable because the alternative is deemed less beneficial. This maybe in **substance misusers with** chronic treatment resistant anxiety, or in patients who have established dependency and are unable to withdraw successfully.[28] There are a group of substance misusers dependent on benzodiazepines who can benefit from a low dose prescription of benzodiazepines in the longer term, where they no longer abuse benzodiazepines or crave benzodiazepines and where attempts at detoxification lead to a relapse of their increased benzodiazepines use. As part of their care-plan it is recommended that they are reviewed regularly and asked to consider a detoxification programme from benzodiazepines at regular intervals (at least annually) [29] On review of the treatment of co-occurring disorders with opioid addiction, SAMHSA / CSAT:Treatment Improvement Protocols (TIP No. 43): Medication assisted Treatment for Opioid Addiction in Opioid Treatment Programme [30, 31] it was recommended that patients with a history of benzodiazepines abuse should not be disallowed from previously prescribed benzodiazepines provided that they are monitored carefully and have stopped their earlier abuse. It was recognised that ongoing use maybe as a means to reduce the symptoms of co-occurring disorders i.e. anxiety disorders, mood disorders, personality disorders, schizophrenia and other psychotic disorders.

Children.

Although infrequently used, Benzodiazepines may have a very important role to play in managing children with similar presentations to adults, i.e. manic presentations, acute agitation associated with psychosis, or short term treatment of acute and debilitating anxiety, or as part of PTSD or generalised anxiety. Children and adolescents may also present with severe agitation or aggressive behaviour in the context of a learning difficulty, pervasive developmental disorders (Autism/Aspergers) or severe psychological reactions to stressful life events such as abuse and trauma. Such rapid tranquilisation may be necessary in the interest of the safety of the patients and those around them. When used such interventions are always of the shortest duration possible and regularly reviewed. Informed parental consent and assent are desirable whenever possible, unless one needs to act under common law due to the urgency of the situation. All psychotropic medication used in children is generally initiated by a specialist in Child Mental Health and as part of a multi-modal treatment approach.

Good Practice Guidelines:

- This paper outlines the risks and benefits of benzodiazepine use in specific groups.

- Where benzodiazepine prescription is indicated, the prescriber should ensure all risks and benefits are explained fully to the individual. For those who lack capacity to consent to treatment, pending enactment of Irish capacity legislation, reference should be made to relevant Medical Council Guidance and the prescriber should consult with carers and appropriate parties in order to determine the best interests of the patient.

- At the time of benzodiazepine prescription renewal or medication review, the physician should discuss the risks of long-term benzodiazepine and the benefits of discontinuation (on cognition, mood, sleep, and energy level) and advise the patient to reduce or discontinue the benzodiazepines. For some patients this will be difficult or impossible, and there may be some cases where the psychiatrist, in partnership with the patient agrees that continuing the benzodiazepine medication is the best course of action. There are a group of people, for whom maintenance medication for their mental illness may include a low dose of benzodiazepines. These people do not develop tolerance to the drug, do not require higher doses, or develop craving for the drug, and yet attempts to reduce the benzodiazepines results in a relapse in the mental illness. For these people remaining on the benzodiazepines is appropriate.

- The College of Psychiatry recommends that members who prescribe benzodiazepines should follow good practice guidelines for their use.[23] This includes conducting regular audit of practice. Standards of practice should ensure short term use of benzodiazepines, using the lowest dose possible and where their use has been for longer than four weeks, clear evidence of education on reducing with a view to discontinuing, and if this is not possible clear documentation on reasons for continuing prescription.

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