FINAL DRAFT EXECUTIVE SUMMARY

Guidance for the use and reduction of misuse of benzodiazepines prescribing and other hypnotics and anxiolytics in general practice

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Section 1: Introduction

- Benzodiazepines are widely prescribed in clinical practice short-term for a variety of conditions and their anxiolytic and hypnotic efficacy has been well established
- The combination of effectiveness and risks of long-term use is the reason why benzodiazepines cause us such a headache in clinical practice.
- With benzodiazepines, there is often a wide divergence between published guidelines and clinical practice
- Should only be prescribed for maximum of 2-4 weeks but many people are prescribed for much longer
- The number of people taking prescribed benzodiazepines worldwide is enormous and over 1 million people in the UK are on long-term
- Up to half of long-term users have difficulties in stopping benzodiazepines because of withdrawal symptoms
- Over the last decade the level of combined benzodiazepine and Z-drug prescribing has remained stable but that of benzodiazepines used for anxiety has steadily risen, as has Z drugs replacing BZ for sleep disturbances

Section 2.1 Properties and clinical actions

- There are a large number of benzodiazepines available, all have similar properties, although their potency greatly varies
- Benzodiazepines are rapidly and fully absorbed orally, leading to peak effects within a half-hour to 2 hours of ingestion
- The more fat-soluble drugs (e.g. diazepam) are absorbed faster and enter the central nervous system more rapidly hence are generally associated with increased abuse potential.
- Those with long half-lives such as diazepam and nitrazepam are more likely to produce residual effects such as sedation and falls the next day.
- Rapid-onset drugs are associated with ‘good’ subjective effects, and therefore result in psychological reinforcement every time they are taken and higher dose leads to a better ‘buzz’.
- The actions of benzodiazepines are mediated by enhancing the activity of gamma-aminobutyric acid (GABA), which is an inhibitory neurotransmitter that transmits messages from one neuron to another. Benzodiazepines bind to receptors on the GABA-A receptor complex and can directly or indirectly affect almost every part of brain function unselectively. This “inhibitory” effect is responsible for the characteristic effects of sedation, amnesia and motor incoordination.
- Tolerance is a physiological reaction and the body responds so the original dose of the drug has progressively less effect and a higher dose is required to obtain the original effect.
- The rate of development of tolerance may vary for different drug effects, such as relief of anxiety, sedation and pleasure, can develop at different speeds, and can vary between individuals.

- Many different people of all ages and both genders use benzodiazepines. They cover a spectrum of people ranging from therapeutic users to pleasure-seekers.

Section 3 Treatment of Insomnia, anxiety

- Insomnia is an important, common, usually long-term health problem that requires accurate diagnosis and effective treatment and anxiety symptoms may range from mild and transient without daytime functional impairment, to severe and persistent causing significant distress.
- Treatment for both should start with addressing underlying problems and then using: talking therapies, cognitive behavioural therapies and self-help.
- Drug treatment can include benzodiazepines, Z-drugs and SSRIs but drugs should not be first-line treatment for most occasions.
- They may be indicated in very few specific situations such as an acute crisis with a clear endpoint or a predicted acute crisis.
- Benzodiazepines should be used in the lowest dose and for the shortest time, maximum 2-4 weeks.
- Benzodiazepines and other similar drugs are not indicated for the long-term treatment of anxiety or insomnia, unless in rare cases where the patient has been proven to have treatment-resistant anxiety or insomnia.
- The use of benzodiazepines is inappropriate to treat short-term mild anxiety.
- Benzodiazepines primarily relieve and suppress symptoms, rather than being curative for any disorder.
- The “Z” drugs were developed as hypnotics to overcome the side effects associated with benzodiazepine therapy, although their potential to cause tolerance, dependence and withdrawal symptoms was known from the beginning
- Melatonin can be used for insomnia in adults aged 55 and over for up to13 weeks.
- Caution must be used when prescribing benzodiazepines, Z-drugs and other related drugs to any patient, but more so when there is a current or past history of substance abuse or personality disorder.
- Having once started it is harder to stop and hence the prescriber and the patient must have a plan for not using longer than 2 – 4 weeks or use very intermittently.
- Discuss fully before issuing short-term that it is one-off, the risks of driving etc, and explain long-term risks
- Prescribing for patients with established benzodiazepine dependence, is more controversial, and abrupt withdrawal of prescribed benzodiazepines carries significant risks

Section 4 Adverse effects and specific problems with long-term use

- Benzodiazepines and related drugs are usually effective when first prescribed and nearly all the disadvantages and problems come from long-term use.
- These can be associated with considerable physical, mental and social health problems and hence long-term use should be avoided.
- Relapse can occur with all drugs of dependence, but is low with benzodiazepines.
- With slow reduction and psychological support, most patients lose their anxiety, panics, agoraphobia etc.
- Increased anxiety can be caused by the benzodiazepines or when reducing long-term use.
- Long-term use of benzodiazepines has been associated with long-term cognitive effects, memory impairment, emotional blunting, weakening of coping skills and amnesia, which gradually disappear in most people 6-12 months after stopping.
- Long-term benzodiazepine users will sometimes develop depression, for the first time after prolonged use, which will resolve within 6 months or a year of stopping the drug.
- Benzodiazepines may also aggravate depression and can precipitate suicidal tendencies in depressed patients

- Benzodiazepines occasionally cause paradoxical excitement with increased anxiety, insomnia, nightmares, and hallucinations at the onset of sleep, irritability, hyperactivity or aggressive behaviour.
- Use of benzodiazepine and Z-drug hypnotics is associated with an increased risk of many physical health conditions and death.
- Long-term use can cause withdrawal symptoms in many people – between 30 and 45%.
- Withdrawal symptoms can take almost any psychological and / or somatic form, but can be considered as falling into three main groups: anxiety symptoms, such as anxiety and agitation; distorted perceptions such as abnormal body sensation and major incidents such as fits, which are all rare.
- The risk of withdrawal symptoms increases with longer use and higher doses and use of high-potency benzodiazepines, in patients with chronic psychiatric and personality problems and those with chronic physical health problems.
- A history of current or past alcohol or other sedative-hypnotic dependence, or a family history of these is also significant.
- The protracted withdrawal syndrome occurs in a minority (up to 15%) of patients who develop a post-withdrawal syndrome on detoxifying from benzodiazepines. Most have taken benzodiazepines for many years.
- Withdrawal is possible in most patients who are dependent on benzodiazepines once problems related to prolonged use of benzodiazepines and other drugs are explained and discussed. Consideration needs to be given as to when and how to detoxify and extra help and services may be needed.
- Remember to ask about alcohol, as some patients may simply substitute alcohol for the benzodiazepine
- Before starting a reduction tackle any underlying problems, ensure any physical or psychiatric health problems treated and give the patient information about the problems of long-term benzodiazepine use and explain the process of withdrawal and possible effects.
- Tailor the dose reduction to the individual and taper it. There should be no hurry
- Assess the need for additional support and therapies and monitor frequently enquiring about general progress and withdrawal and rebound symptoms.
- If patients experience difficulties with a dose reduction, encourage them to persevere and suggest delaying the next step down. Do not revert to a higher dosage.
- If withdrawal symptoms might be a problem, consider substitution of short- or medium-acting benzodiazepines by long-acting compounds (diazepam)
- There are no drugs that can act as a substitute for benzodiazepines and are generally best avoided. Rarely and in certain circumstances antidepressants, beta-blockers, mood stabilizers, melatonin can help with some symptoms.
- The decision to prescribe longer-term benzodiazepines should be rare and made with care. If patients are prescribed long-term benzodiazepines, they are inevitably put at risk of all the negative effects including cognitive impairment etc.
- Unfortunately, most often, long-term benzodiazepine use results from inadvertent continuation of short-term prescriptions and started many years ago before all problems of their long-term use were known

Part 2 Section 5

- People of all ages and both genders use and misuse benzodiazepines, for many different reasons and there is much commonality of use and treatment for long-term use but there are some specific problems in specific groups including: patients with a mental health problem, the “therapeutic dose” users and people who tend to use high-doses, may use illicit benzodiazepines and other illicit drugs and / or alcohol are seeking pleasure.
- About half of the population does not find the effects of benzodiazepines either positive or reinforcing.

- Benzodiazepines are used much less in the treatment of mental illness than they used to be but are still prescribed extensively, particularly at the time of acute admission. Benzodiazepines are used in the treatment of acute agitation or behavioural disturbance, whether due to psychosis, delirium or other causes.
- Benzodiazepines have proven value in alcohol detoxification. The use of benzodiazepines in people who drink outside of the detoxification context is less clear. But care is needed as their use is higher in alcohol problems.
- We also know that people who drink moderately or harmfully but not light drinkers, have an increased liking for the effects of benzodiazepines hence care needs to be taken in all people who use about 4 units / week
- Benzodiazepine use / abuse is a serious problem in people who use drugs, especially for polydrug users and there is little evidence to guide practitioners.
- As well as taken orally, they can be snorted and / or injected.
- Up to 90% of attendees at drug treatment services reported their use in a 1-year period and over half report using illicit benzodiazepines in the last 3 months.
- People who use benzodiazepines, along with other illicit drugs and / or alcohol generally are using them for a different reason that is reward. They tend to increase rather than dampen activity in the brain reward centres.
- They are also used to alleviate withdrawal symptoms from other drugs, especially crack and / or heroin. They are more likely to be taken in binges.
- But people who use drugs may also use benzodiazepines as self-medication to improve their mood or their coping skills.
- Benzodiazepine use leads to higher rates of risk behaviour and social dysfunction, and problems may lead to fatal overdose.
- Prescribing for people who are using high doses and those who use illicit drugs develop tolerance quickly and will often escalate their dose.
- It is important to use psychological interventions and not prescribing in patients who binge-use benzodiazepines.
- In high-dose users all benzodiazepines are converted to diazepam and it is rarely appropriate to start a dose of more than 30 mg diazepam daily.
- All patients should be offered detoxification in the same way as other patients. Trials show that high-dose users are equally successful as others,
- A few people have a long-term opioid and benzodiazepine problem and do not stabilize on opioid substitution medication alone.
- When considering longer-term prescribing this must always be balanced against the risks, especially the negative effects on memory and cognitive skills.
- Women are more often prescribed than men, in pregnancy it is best to detox and this can be done at any stage.
- Older people are prescribed more and about 15% over 65 years take regularly, which is not recommended, as they are more sensitive to side-effects, pseudo-dementia, cognitive changes and increased falls.