

## Benzodiazepines and Z-drugs (zopiclone and zolpidem) – How to manage patients on Benzodiazepines and Z-drugs during the COVID-19 pandemic.

Please note all questions within each section are linked to each other and should be read in conjunction.

Below each question are the weblinks to the sources of evidence to support the guidance recommendation.

This guidance should be read in association with [the most up to date advice on PPE](#) (personal protective equipment) and on [reducing the risk of transmission in hospital settings](#).

Clinical question	Guidance
<b>Using benzodiazepines in patients who have COVID-19.</b>	
<b>General advice</b> <a href="#">[link1]</a> <a href="#">[link2]</a> <a href="#">[link3]</a> <a href="#">[link4]</a> <a href="#">[link5]</a> <a href="#">[link6]</a> <a href="#">[link7]</a>	<p>Benzodiazepines and Z-drugs (Zopiclone and Zolpidem) <b>have the capacity to depress respiratory drive</b>, so they should be used with caution in patients with evidence of compromised respiratory function.</p> <p>Patients taking benzodiazepines and/or rapid tranquilisation should have <b>increased physical health monitoring and this should be reflected in the patient’s individualised care plan</b>.</p> <p>Benzodiazepines are <b>contra-indicated in patients with acute pulmonary insufficiency and must be used with caution in other respiratory diseases</b>.</p> <p>Zopiclone is <b>contra-indicated in patients with respiratory failure and must be used in caution with those who have pulmonary insufficiency</b> because of the risk of respiratory depression. Zolpidem is <b>contra-indicated in patients with acute or severe respiratory depression</b>.</p> <p>The risk of respiratory depression with these drugs <b>increases with higher doses and/or parenteral use</b>. Therefore, low dose, short-acting oral medicines are preferred when required.</p> <p><b>Particular care should be taken where patients are prescribed additional sedative drugs</b>, for example the combination of opiates and benzodiazepines may significantly impair respiration. <b>Only prescribe benzodiazepines or benzodiazepine-like drugs and opioids together if there is no alternative</b>. If the decision is made to co-prescribe, the following principles are advised:</p> <ul style="list-style-type: none"> <li>• use the lowest doses possible for the shortest duration of time and carefully monitor for signs of respiratory depression</li> <li>• if there is any change in prescribing such as new interactions or dose adjustments, re-introduce close monitoring of the patient</li> <li>• if co-prescribing methadone with a benzodiazepine or benzodiazepine-like drug, closely monitor for respiratory depression for at least 2 weeks following initiation or changes to prescribing because the respiratory depression effect of methadone may be delayed</li> </ul>

- advise patients of the symptoms of respiratory depression and sedation and the need to seek immediate medical attention if these occur
- report suspected adverse drug reactions to any medicines to the [Yellow Card Scheme](#)

Benzodiazepines and related drugs (BZRD) **have been associated with a higher risk of pneumonia** (odds for developing pneumonia were 1.25-fold higher (odds ratio, OR = 1.25; 95% confidence interval (CI), 1.09-1.44) in BZRD users).

**There are no data on the impact of chronic or acute use of benzodiazepines in patients with symptoms of COVID-19 infection.**

### Treating insomnia

[\[link8\]](#)

[\[link9\]](#)

[\[link16\]](#)

#### General advice for treating insomnia.

- **Offer advice on improving sleep hygiene** (e.g. try to maintain regular sleeping patterns and keep good sleep hygiene practices, including avoiding screens before bed, cutting back on caffeine and creating a restful environment).

See these guidance from [RCPsych](#) and [NHS](#) for further details.

- A benzodiazepine or Z-drug is only considered appropriate for insomnia **when non-drug measures have failed and the patient's insomnia is severe, disabling or causing extreme distress.**
- Benzodiazepines and the Z-drugs (zopiclone and zolpidem) **should be avoided in the elderly**, because they are at greater risk of becoming ataxic and confused, leading to falls and injury.
- If a prescription is needed, offer a low dose short-acting benzodiazepine or Z-drug for a short-term period only, up to 2 weeks.

**In patients with suspected or confirmed COVID-19, prescribers should be aware that respiratory symptoms of COVID-19 can develop rapidly and therefore there should be a plan in place to regularly monitor the patient and discontinue the benzodiazepine or Z-drug should respiration become compromised.**

As **an alternative to benzodiazepines**, clinicians could consider:

- Offering **web-based CBT for insomnia** e.g. [sleepio](#).
- Offering **other pharmacological options, such as melatonin** (depending on local license and availability) – see [this document](#) for prescribing advice in the UK.

### For anxiety disorders

[\[link10\]](#)

[\[link11\]](#)

#### General advice for treating anxiety disorders.

Benzodiazepines **should only be used intermittently or short-term** when treating anxiety disorders.

They are usually reserved for patients who have not responded to at least three previous treatments. In such cases they may be used long-term for persistent, severe, distressing, and impairing anxiety symptoms, when other treatments have proved ineffective.

Withdrawing treatment when significant symptoms of anxiety are present is likely to make symptoms worse and is therefore unlikely to succeed. However, when symptoms are reasonably well controlled and stable it may be possible to attempt careful drug withdrawal.

In patients with suspected or confirmed COVID-19, prescribers should be aware that respiratory symptoms of COVID-19 can develop rapidly. Therefore, there should be a plan in place to regularly monitor the patient and reduce or discontinue the benzodiazepine should respiration become compromised.

This must be balanced against the risk of rapid withdrawal of benzodiazepines in long term users which may lead to significant rebound anxiety. See further advice below.

#### For acute agitation / rapid tranquilisation

[\[link12\]](#)

[\[link13\]](#)

[\[link14\]](#)

[\[link17\]](#)

If a patient with suspected or diagnosed COVID-19 is acutely disturbed and there are **no signs of respiratory compromise (decreased or increased respiratory rate) cardiovascular disease or decreased level of consciousness**, then medication, including benzodiazepines, can be used with caution.

**Benzodiazepines should not be used when a patient has acute pulmonary insufficiency.**

- **Where possible, use short-acting medication** (such as lorazepam) as the patient's physical health condition may deteriorate rapidly.
- **Oral medication is preferred** and should be offered as first line.
- **Parenteral medication is more likely to cause dose related side effects**, such as respiratory depression.
- **Ensure immediate access to flumazenil** if benzodiazepines are given.

In patients with suspected or confirmed COVID-19, prescribers should be aware that respiratory symptoms of COVID-19 can develop rapidly. Therefore, there should be a plan in place to regularly monitor the patient and reduce or discontinue the benzodiazepine should respiration become compromised.

**Benzodiazepines can be considered in treating anxiety, agitation or delirium in the context of COVID-19, including end of life care.** Again, short-acting medications such as lorazepam are preferable and the above considerations should be taken into account.

As benzodiazepines may cause respiratory depression, haloperidol may be preferred in COVID delirium. If antipsychotics are contra-indicated, low dose lorazepam can be used, although it is not licensed for delirium. Prescribe flumazenil if needed.

#### General advice for patients/carers on managing medications and prescriptions during COVID-19

[\[link17\]](#)

In the UK, PHE advises patients as follows:

- Keep taking your medication.
- You might be able to order repeat prescriptions by phone, or online using an app or website if your doctor's surgery offers this.
- Ask your pharmacy about getting your medication delivered or think about who you could ask to collect it for you if you are self-isolating or shielding. The NHS website has more information about [getting prescriptions for someone else](#) and [checking if you have to pay for prescriptions](#).
- Continue to order your repeat prescriptions in your usual timeframe. There is no need to order for a longer duration or larger quantities.
- Your GP practice (or clinical team) may move your prescriptions to repeat dispensing arrangements, so you only have to contact your pharmacy to get a repeat of your medicine rather than your practice.
- Be careful about buying medication online. You should only buy from registered pharmacies. You can check if a pharmacy is registered on the [General Pharmaceutical Council website](#).

- You can contact [NHS 111](#) in England if you're worried about accessing medication.

#### Advice on withdrawing benzodiazepines.

##### Factors to consider when withdrawing benzodiazepines

[\[link15\]](#)

**Abrupt termination of benzodiazepines after extended use can precipitate withdrawal symptoms** e.g. headaches, muscle pain, extreme anxiety, tension, restlessness, confusion and irritability. In severe cases the following symptoms may occur: derealisation, depersonalisation, hyperacusis, numbness and tingling of the extremities, hypersensitivity to light, noise and physical contact, hallucinations or epileptic seizures.

**Rebound insomnia and anxiety may also occur.** It may be accompanied by **other reactions** including mood changes, anxiety or sleep disturbances and restlessness. Since the risk of withdrawal phenomena/rebound phenomena is greater after abrupt discontinuation of treatment, **it is recommended that the dosage is decreased gradually.**

##### How to taper the dose

[\[link11\]](#)

The two potential approaches for withdrawal are **slow dose reduction of the person's current benzodiazepine or Z-drug, or switching to an approximately equivalent dose of diazepam, which is then tapered down.**

##### Switching to diazepam should be considered for:

- People using the **short-acting potent benzodiazepines** (alprazolam and lorazepam).
- People using preparations **that do not easily allow for small reductions in dose** (alprazolam, flurazepam, loprazolam and lormetazepam).
- People experiencing difficulty or who are **likely to experience difficulty withdrawing directly** from temazepam, nitrazepam, or Z-drugs, due to a high degree of dependency (associated with long duration of treatment, high doses, and a history of anxiety problems).

**Withdrawal should be gradual** (dose tapering, such as 5-10% reduction every 1-2 weeks, or an eighth of the dose fortnightly, with a slower reduction at lower doses), **and titrated according to the severity of withdrawal symptoms.**

For advice on suggested withdrawal schedules see [this document](#).