

Dependence Forming Medications

This bulletin provides an overview of potential Dependence Forming Medications (DFMs) and signposts to PrescQIPP resources which support medicines optimisation projects in this area.

DFMs are primarily opioids, Z-drugs (zopiclone and zolpidem), benzodiazepines, gabapentin and pregabalin.¹ Antidepressants are not addictive but may be associated with withdrawal symptoms.² Dependence in this case is defined as the need to continue taking a medicine to maintain a state of normality and avoid symptoms of withdrawal.¹

Recommendations

- Prescribers need to be aware of the harm associated with DFMs.³
- Review patients prescribed DFMs:³
 - » 120mg* morphine daily dose equivalent or greater and
 - » Pregabalin or gabapentin, long-term benzodiazepines or Z-drugs.

*SIGN guidelines state that all patients receiving opioid doses of >50mg/day morphine equivalent should be reviewed regularly (at least annually). Pain specialist advice or review should be sought at doses >90mg/day morphine equivalent.⁴
- Effective, personalised care should include shared decision making with patients and regular reviews of whether the treatment is working. Patients who want to stop using a medicine must be able to access appropriate medical advice and treatment and must never be stigmatised.²
- Prescribers need to have an open and honest discussion with the patient regarding the risks and benefits of the DFM in the short term (i.e. benzodiazepines <4 weeks; opioid analgesics <3 months) and long term. This must be recorded, information provided and the patient signposted to appropriate resources. It is necessary to improve information, informed choice and shared decision making between clinicians and patients or carers.^{2,3}
- Inappropriate limiting of medicines may increase harm, including the risk of suicide, and lead some people to seek medicines from illicit or less-regulated sources. There needs to be increased public and clinical awareness of other interventions, such as cognitive behavioural therapy.²
- Prescribers must work within their competence and consider if the patient would benefit from specialist led care or prescribing.³
- Medication needs to be reviewed regularly, added onto acute (not repeat) records and a clear indication for the medication recorded in the patient's notes. The total morphine daily dose equivalent must be recorded.³
- Prescribers should be alert to signs of drug-seeking behaviour and emerging dependence or addiction.³
- If the DFM is not benefitting the patient or if the underlying condition is resolved, review and stop the medication (with tapering if necessary), recording the reasons clearly in the patient's notes.³
- Be aware of polypharmacy and co-morbidities, for example, other DFMs, diabetes, sedatives, patients with COPD, renal disease, and older patients.³

Background

Public Health England (PHE) has published a review of the evidence for dependence on, and withdrawal from, prescribed medicines in adults who have non-cancer pain, anxiety, insomnia or depression.² The review analysed NHS prescription data in England from 2015 to 2018 for the following drug groups: benzodiazepines, Z-drugs, gabapentin and pregabalin, opioids and antidepressants. Also included are the findings from a rapid evidence assessment (REA) of articles on prescription medicine-associated harms, dependence, withdrawal, risk factors and service models published between 2008 and 2018. Documented patient experiences of taking these medicines and use of treatment services were also included.²

In England, 26% of the adult population received, had dispensed, one or more prescriptions for antidepressants (17% of the adult population), opioid (13%), pregabalin and gabapentin (3%), benzodiazepines (3%) and Z-drugs (2%). Between 2015 to 2016 and 2017 to 2018 the rate of prescribing for antidepressants increased from 15.8% of the adult population to 16.6% and for gabapentinoids from 2.9% to 3.3%. Whereas there was a small decrease in prescribing of opioids, benzodiazepines and Z-drugs. There is a higher rate of prescribing to women and older adults. However, there is a large variation in prescribing across CCGs. Greater deprivation was associated with higher prescribing rates for opioids, pregabalin and gabapentin, but lower prescribing rates for benzodiazepine and Z-drugs. Antidepressant prescribing had a weaker association with deprivation. Most people who start prescriptions receive them for three months or less, but each month there is a group of patients who continue to receive a prescription for longer. The following number of people received prescriptions continuously between April 2015 (or earlier) and March 2018:

- 930,000 antidepressants
- 540,000 opioid pain medicines
- 160,000 pregabalin and gabapentin
- 120,000 benzodiazepines
- 100,000 Z-drugs

The REA found evidence that benzodiazepines, Z-drugs, opioids, pregabalin and gabapentin are associated with a risk of dependence and withdrawal. Antidepressants are associated with withdrawal.

The following factors contributed to the risk of harms associated with dependence and the short-term discontinuation or longer-term withdrawal symptoms:

Opioids

- High initial dose
- Baseline pain intensity rated 5-6 or 8-10 on a 0-10 scale (zero=no pain, 10=pain as bad as could be)
- Duration of treatment greater than 90 days
- Prior or concurrent use of benzodiazepines, NSAIDs or pregabalin
- Mental health diagnosis

Benzodiazepines

- White ethnicity
- Low income
- Two or more different benzodiazepines prescribed together
- Short-acting benzodiazepines

The patient experience documents found that patients felt there was a lack of information on the risks of medication. They described not being offered any non-medicinal treatment options and their treatment not being reviewed sufficiently.²

The British Medical Association (BMA) issued recommendations that a national helpline, specialist support centres and clear guidance on tapering and withdrawal management should be developed collaboratively with input from professional groups and patients.⁵

Prescribers must be responsible for prescribing and ensure safety of prescribing.³ Some people are more at risk from DFM's including those with COPD, elderly and debilitated, diabetes, CKD, mental health problems, substance misuse issues, and homeless or at risk of homelessness.³

Further resources

This bulletin should be read in conjunction with the following PrescQIPP bulletins and support tools:

Hypnotics and anxiolytics

- [PrescQIPP Bulletin 258 Hypnotics and support tools](#)
- [PrescQIPP Silver Annual Award Winner 2019 - Blue-folder clinics to facilitate reduction of inappropriate opioid, pregabalin, hypnotic and benzodiazepine prescribing to improve patient outcomes East Norfolk Medical Practice](#)
- [PrescQIPP Bulletin 184 Behavioural change strategies](#)

Opioids, pregabalin, gabapentin

- [PrescQIPP Opioids aware webinar](#)
- [PrescQIPP Opioids aware audit webinar](#)
- [PrescQIPP Bulletin 218 Reducing opioid prescribing in chronic pain](#)
- [PrescQIPP Silver Award Winner 2019 - Blue-folder clinics to facilitate reduction of inappropriate opioid, pregabalin, hypnotic and benzodiazepine prescribing to improve patient outcomes East Norfolk Medical Practice](#)
- [PrescQIPP Annual Award Winner 2019. High dose opiate reduction in Great Yarmouth and Waveney NHS Great Yarmouth and Waveney CCG](#)
- [Reducing opiate prescribing in pain NHS Great Yarmouth and Waveney CCG](#)
- [PrescQIPP Opioid management of pain in secondary care webinar](#)
- [PrescQIPP Bulletin 149 Non-neuropathic pain](#)
- [PrescQIPP Bulletin 119 Pregabalin in neuropathic pain](#)

Antidepressants

- [PrescQIPP Bulletin 237 Antidepressants](#)
- [PrescQIPP Polypharmacy and deprescribing webkit](#)

General

- [Bulletin 254. Polypharmacy and Deprescribing](#)
- [Bulletin 254. Polypharmacy and deprescribing - antidepressant deprescribing algorithm](#)
- [Bulletin 252: Supporting the World Health Organisation Medication Without Harm Challenge - Focus on dependence forming medicines](#)
- [PrescQIPP Polypharmacy and deprescribing webkit](#)

Additional PrescQIPP resources:

- [Fentanyl lozenges briefing](#)
- [Opioid deprescribing algorithm](#)
- [Opioid deprescribing case study](#)
- [Patient letter- drug dependency prescription](#)
- [Benzodiazepine deprescribing algorithm](#)

References

1. Cartagena Farias J, Porter L, et al. Prescribing Patterns in Dependence Forming Medications. Public Health Research Consortium. 2017. Available at http://qna.files.parliament.uk/qna-attachments/825285/original/PHRC_014_Final_Report.pdf Accessed 02/06/19
2. Public Health England. Dependence and withdrawal associated with some prescribed medicines. An evidence review. 2019. Available at https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/829777/PHE_PMR_report.pdf Accessed 25/09/19
3. Royal College of General Practitioners. Top Ten Tips: Dependence Forming Medications. April 2019. Available at <https://www.rcgp.org.uk/clinical-and-research/resources/a-to-z-clinical-resources/dependence-forming-medications.aspx> Accessed 02/06/19
4. Scottish Intercollegiate Guidelines Network. Management of Chronic Pain. SIGN 136. December 2013. Revised August 2019. Available at https://www.sign.ac.uk/assets/sign136_2019.pdf Accessed 02/06/19
5. BMA. Supporting individuals affected by prescribed drugs associated with dependence and withdrawal. December 2018. Available at <https://www.bma.org.uk/collective-voice/policy-and-research/public-and-population-health/prescribed-drugs-dependence-and-withdrawal> Accessed 02/06/19

 Briefing	https://www.prescqipp.info/our-resources/bulletins/bulletin-256-dependence-forming-medications/
 Implementation tools	
 Data pack	High dose opioids data pack Benzodiazepines data pack Hypnotics data pack Pregabalin and gabapentin data pack
Infographics	High dose opioids infographic Benzodiazepines infographic Hypnotics infographic Pregabalin and gabapentin infographic

Information compiled by Anita Hunjan, PrescQIPP CIC, January 2020 and reviewed by Katie Smith, PrescQIPP CIC January 2020. Non-subscriber publication April 2021.

Contact help@prescqipp.info with any queries or comments related to the content of this document.

This document represents the view of PrescQIPP CIC at the time of publication, which was arrived at after careful consideration of the referenced evidence, and in accordance with PrescQIPP's quality assurance framework.

The use and application of this guidance does not override the individual responsibility of health and social care professionals to make decisions appropriate to local need and the circumstances of individual patients (in consultation with the patient and/or guardian or carer). [Terms and conditions](#)