RISKS ASSOCIATED WITH GABAPENTINOIDS  
(GABAPENTIN AND PREGABALIN)

Potential for abuse, misuse or diversion

The Summary of Product Characteristics (SPC) for pregabalin recognises the potential for abuse: "Cases of misuse, abuse and dependence have been reported. Caution should be exercised in patients with a history of substance abuse and the patient should be monitored for symptoms of pregabalin misuse, abuse or dependence (development of tolerance, dose escalation, drug-seeking behaviour have been reported)"².

Misuse of gabapentin and pregabalin and gabapentin has been noted for some years in clients attending substance misuse treatment and recovery services, and within secure environment settings, and has been described as producing feelings of euphoria, relaxation and calmness. It can also enhance the euphoric effects of drugs such as opiates. Currently, pregabalin appears to be more sought after for misuse than gabapentin. There is a growing illegal market, and these drugs are also being bought through online pharmacies.

The abuse liability of pregabalin has been described in Scandinavia and other parts of Europe. Pregabalin was also listed as a new recreational psychoactive substance by the relevant EU agencies in 2010. In the US pregabalin is scheduled, indicating that it has abuse potential. Gabapentin and pregabalin have been mentioned on death certificates as adjunctive substances in patients dying of drug poisoning, this has also been the case in Dorset.

Public Health England and NHS England jointly published advice for prescribers in 2014 on the risk of the misuse of pregabalin and gabapentin³. They state that prescribers should be aware not only of the potential benefits of pregabalin and gabapentin to patients, but also that the drugs can lead to dependence and may be misused or diverted.

Pregabalin and gabapentin are now highly sought after, because of both their own inherent misuse potential and their use in enhancing the effects of other drugs. There is growing unease that GPs are being targeted to supply these medicines, but are unaware of their illicit value.

Adverse effects and drug interactions

Gabapentin has been associated with a rare risk of severe respiratory depression even without concomitant opioid medicines. Patients with compromised respiratory function, respiratory or neurological disease, renal impairment, concomitant use of central nervous system (CNS) depressants, and elderly people might be at higher risk of experiencing severe respiratory depression. Dose adjustments might be necessary in these patients.⁷

In some cases, gabapentin or pregabalin is found in combination with other CNS depressants in addition to methadone and/or chlordiazepoxide prescribed for the management of opiate and/or
alcohol withdrawal. However, there are reports of respiratory failure and coma in patients taking pregabalin and CNS depressant medicinal products.

**Morphine** can increase the bioavailability of gabapentin. Caution is needed when these drugs are co-prescribed and the doses of both drugs may need to be modified. Similarly, pregabalin appears to be additive in the impairment of cognitive and gross motor function caused by oxycodone.

For **heroin** users, the combination of opioids with gabapentin or pregabalin increases the risk of death, see below.

**When heroin is used with pregabalin or gabapentin**

A recently published study concluded that for heroin users, the combination of opioids with gabapentin or pregabalin potentially increases the risk of acute overdose and death through either reversal of tolerance or an additive effect of the drugs to depress respiration.

The study used Office of National Statistics data for drug related deaths in England and Wales, and described an increase in the number of drug related deaths involving pregabalin and gabapentin, highly correlated to the increase in prescribing of these drugs. There were 137 deaths in 2015 involving heroin and either pregabalin or gabapentin – 79% of these deaths also involved opioid drugs). The study also involved interviews with heroin users, some of which described pregabalin as “easy to obtain” and suggested that it reinforced the effects of heroin.

**Formulary position and cost effective prescribing**

Pregabalin is included in the Pan-Dorset prescribing formulary:

- As an alternative to first line options in neuropathic pain, with a green traffic light status
- As a second line option in the management of epilepsy, with an amber traffic light status
- As a third line option in generalised anxiety disorder, in accordance with NICE guidance, with a green traffic light status.

Generic prescribing is strongly encouraged. Pregabalin should be prescribed as a twice daily dose as there is no clinical benefit to three times daily dosing.

**Recognising potential problems**

The following situations may indicate a possibility of increased risk to the patient from use of pregabalin or gabapentin:

- Patient is asking for earlier prescriptions or ‘losing’ prescriptions
- Sharing of medications with friends / relatives
- Regularly accessing out of hours services
- Requesting to see different GPs
- Changes in mood / behaviours of the patient with practice staff
- Patients with a history of substance / alcohol misuse or drug alcohol misuse in the family, patients with mental health problems and patients who have experienced a recent life event.
• Patients with a history of previous medicine overdose(s)
• Review patients receiving their dose in multiple capsules – consolidate their dosing to use the fewest number of capsules possible.

Prescribing safely
• It is suggested that less harmful, alternative drugs can often be first-line treatments for the indicated conditions for which pregabalin and gabapentin are now used, and may be tried preferentially in higher risk settings or in patients who may be more likely to be harmed by the drugs.
• If pregabalin or gabapentin is the most suitable treatment option prescribe in line with Dorset formulary and/or licensed indications.
• Agree clear treatment goals and regular review process before prescribing, document treatment goals and consider them at each review. Stop if not making progress towards goals.
• Prescribed doses should be within BNF range.
• Potential for misuse should be discussed with all patients.
• If misuse problems identified – prescribing should be managed by a single prescriber and consider smaller prescribing quantities with support from community pharmacist.
• If a patient is known to abuse opiates, then considerations should be given as to whether it is safe to continue prescribing Pregabalin. Pregabalin is increasingly being reported in the toxicology of drug related deaths in Dorset.
• Be aware of the risk abuse and addiction to gabapentin or pregabalin, even in those patients with no known history of abuse. Consider implementing additional monitoring of individual patients, where appropriate.
• Consider the “street value” of the drug and potential for requests for increased doses and quantities. Also consider carefully any requests from temporary residents for pregabalin, irrespective of whether it is requested alone or with other drugs.
• Review patients who are currently receiving a three times daily dosing regimen and consider whether twice daily would be suitable
• Refer to Public Health England guidance for more information and guidance.

Tapering gabapentin and pregabalin

If dependence on, misuse or diversion of pregabalin or gabapentin is suspected or identified the patient should be reviewed and concerns documented clearly. Agreement on suitable controls on access to, and maximum daily use, of the drugs being misused may be required, or specialist advice may be necessary. It may be appropriate to offer a planned withdrawal of the medication. See SPC for full information on how to reduce the dose of these agents.

If there is unequivocal evidence that pregabalin or gabapentin are being diverted they should be stopped.
References

1. Herefordshire CCG prescribing newsletter (May 2013)
   https://www.herefordshireccg.nhs.uk/your-services/medicines-optimisation/newsletters/ccg-prescribing-newsletter

2. Lyrica® 50mg capsules – summary of product characteristics, (last updated 21/03/2017) accessed on 12/07/2017 via http://www.medicines.org.uk/emc/medicine/14651


