NHS
County Durham
Clinical Commissioning Group

NHS
Tees Valley
Clinical Commissioning Group

# County Durham & Tees Valley CCGs Pain Management Guidance for Non-Cancer Pain, including the withdrawal and use of high risk drugs in Primary Care

This document is designed to guide prescribing for persistent, non-cancer pain in primary care. Persistent pain is usually defined as pain that lasts for more than three months. Where medicines are prescribed they should be used in combination with other treatment approaches to support improved physical, psychological and social functioning.

The overall goal of treatment should be to manage symptoms sufficiently to enable patients to improve their social, emotional and physical functioning.

Managing High Risk Drugs in Primary Care adapted with thanks from Northumberland CCG, Northumberland County Council, Northumberland GPs and Addictions Services at Northumberland, Tyne and Wear.

## Nociceptive pain treatment pathway

Medications should be an adjunct to general measures such as advice about activity and sleep, physiotherapy and explanation that complete relief of symptoms is not a goal of therapy. Before prescribing review and discuss with the patient, using shared decision making and agreeing an overall management plan, incorporating drug and non-drug treatment. Non-pharmacological treatment may be effective in reducing symptoms and disability in some people with long-term (chronic) pain and can also augment and complement analgesic use. Healthcare professionals responsible for helping people manage chronic pain should be familiar with non-pharmacological interventions available including physical and psychological therapies and local availability of these services.

| | | |
|---|---|---|
| **Step 1 – self-management** | | |
| For minor pain, whether for acute or minor persistent pain, patients can usually access over the counter pain medicines such as paracetamol or ibuprofen. Patients should be encouraged to self-manage their health for minor ailments including mild pain symptoms e.g. aches and sprains, headache, period pain and back pain. | | |
| **Step 2 – regular paracetamol** | | |
| **Paracetamol** | 1g every 4-6 hours<br>Patients weighing <50kg may require dose adjustment<br>Maximum 4g per 24 hour | Effective 1st line analgesic in acute pain. Some patients may be at increased risk of toxicity at therapeutic doses, particularly those with body weight under 50kg and those with risk factors for hepatotoxicity.<br>Ensure this is prescribed at maximum dose before escalating analgesia.<br>Effervescent tablets have high sodium content (18.6mmol / tablet). Taking the maximum dose of paracetamol = 8g of sodium per day. Undertake local risk assessment before use.<br>Available to purchase over the counter (up to 100 from pharmacies). |
| **Step 3 – add NSAID** | | |
| Use the lowest possible NSAID dose for the shortest period necessary. Carefully assess benefits and risks; think about CVD, GI sensitivity, renal issues and hepatic disease.<br>All patients on NSAID at high risk of having serious GI adverse events should routinely be co-prescribed gastro-protection (lansoprazole 15mg or omeprazole 20mg). See appendix for further information. Topical NSAIDs may be recommended for localised pain, however patients should be encouraged to purchase OTC. | | |
| **Ibuprofen** | 1.2g daily in 3-4 divided doses | In line with MHRA guidance - prescribe at the lowest possible dose for the shortest period of time.<br>Ibuprofen has lowest GI risk of standard NSAIDs.<br>Daily doses less than 1200mg are not associated with increased thrombotic risk.<br>Can be used for migraine and dysmenorrhoea. |
| **Naproxen** | 500mg – 1g daily in 1-2 divided doses | Doses of less than 1g daily are not associated with increased thrombotic risk.<br>Longer duration of action than ibuprofen. For use in mild to moderate pain. Can be used for dysmenorrhoea. |
| **Step 4 – add codeine (weak opioid)** | | |
| **Codeine** | 30mg – 60mg every four hours when necessary to a maximum of 240mg daily | Review past treatment.<br>Consider potential for medication diversion.<br>Use lowest effective dose.<br>Do not use if contraindicated.<br>Consider laxatives.<br>Consider stopping NSAID if appropriate.<br>If short term do not add to repeat medication templates. |

**Codeine Non-Responders**

Approximately 5-10% of the population are believed to be poor metabolisers of codeine, and if the initial response to its introduction does not have an expected pain reduction, then consider the possibility the patient may be classed as a codeine non-responder. The absence of CYP2D6 means codeine cannot be metabolised to its active metabolite. Other drugs that utilise this gene for metabolism are also affected in this cohort; therefore avoid the use of Hydrocodone or Oxycodone.

Options below should be considered for this cohort before moving on to step 5 of the treatment pathway.

**Tramadol I/R Capsules**

Tramadol uses 2 distinct pathways for its metabolism, one of which is CYP2D6. Therefore it may only be partially effective in codeine non-responders. A short course trial is recommended in patients, with a reassessment of its effectiveness advised within a month of initiating it.

Typical doses of 50-100mg up to QDS are recommended.

Tramadol as M/R can only be initiated under the advice of a pain specialist.

**Oral morphine solution 10mg/5ml**

Age appropriate dose (see table) no more than 6 times daily.

Regularly review quantities prescribed, alongside effectiveness in pain management. Consider the need for M/R morphine if patient constantly using high quantities, but also take caution around the risk of addiction, and possibility of patients who may inadvertently exceed dose limits.

| Age | Dose | |
|---|---|---|
| | **mg** | **mL** |
| **16-39 years** | 7.5 – 12.5mg | 3.75 – 6.25mL |
| **40-59 years** | 5 – 10mg | 2.5 – 5mL |
| **60-69 years** | 2.5 – 7.5mg | 1.25 – 3.75mL |
| **70-85 years** | 2.5 – 5mg | 1.25 – 2.5mL |
| **>85 years** | 2.5mg | 1.25mL |

**Low-strength buprenorphine 7-day patches**

Consider first if renal impairment, poor swallowing or morphine intolerance.

Start with Butec 5mcg/hour patch, and can increase up to 15mcg/hour. Do not increase more than once every 2-4 weeks.

If needing to consider higher doses, seek advice from specialist pain teams.

**Nefopam**

Nefopam *may* be an appropriate choice in codeine non-responders, especially where opiates are not tolerated. Nefopam prescribing in primary care must only be done so under the instruction of specialist pain teams.

See below for further information on nefopam prescribing.

See CCG statement on nefopam prescribing.

**Step 5 – review clinical assessment if no response to treatments, stop previous treatments and consider switch to strong opioid (tramadol OR morphine)**

**See APC statement –** County Durham & Tees Valley APC position on prescribing in persistent pain contains important advice for prescribers

**Initiation of strong opioids should only be considered when all other options have proven ineffective.**

Evidence shows opioids are only effective for up to a maximum of 6 months, patients should be reviewed on a regular basis.

Do not add short term opioids to repeat medication templates.

**Opioids Aware Key Messages**

Opioids Aware is a resource for patients and healthcare professionals to support prescribing of opioid medicines for pain. It is written by the Faculty of Pain Medicine in partnership with Public Health England.

- There is little evidence that opioids are helpful for long-term (chronic) pain.
- A small proportion of people may obtain good pain relief with opioids in the long term if doses can be kept low and use is intermittent, but it is difficult to identify these people at the start of treatment.
- **The risk of harm increases substantially at doses above an oral morphine equivalent of 120mg/ day, but there is no increased benefit.**
- If a patient has pain that remains severe despite opioid treatment it means they are not working and should be stopped, even if no other treatment is available.

| | | |
|---|---|---|
| • A detailed assessment of the emotional influences on the person's pain experience is essential for people with long-term (chronic) pain who also have refractory and disabling symptoms, particularly if they are on high opioid doses. | | |
| **Tramadol (CD)** | Immediate release only | Tramadol is a schedule 3 controlled drug<br>Tramadol M/R should ONLY be prescribed if advised by pain specialists<br>Tramadol and Paracetamol combination products, such as Tramacet, are non-formulary and should NOT be prescribed |
| **Morphine sulphate** | Prescribe by brand | Stop codeine/ tramadol<br>Use Zomorph capsules where available as preferred brand<br>The national threshold and for Tees Valley is to remain below 120mg daily, but across County Durham the threshold must be kept below 100mg daily |

| **Avoid use and review patients** | |
|---|---|
| **Co-codamol** | Co-codamol is not recommended and its use is discouraged due to inflexibility in dosing. Paracetamol and codeine should be prescribed separately. If co-codamol is used, this should be in tablet form, not the effervescent preparation which has a higher salt content. |
| **Co-proxamol** | Co-proxamol should not be prescribed under any circumstances for new patients; existing patients should be converted to alternative analgesics. Co-proxamol has an unfavourable adverse-events profile, particularly toxicity in accidental and intentional overdose. The MHRA Drug Safety Update (January 2011) further confirms the cardiac risks associated with co-proxamol. NHS England (November 2017) supports the deprescribing of co-proxamol. |
| **Dihydrocodeine** | Dihydrocodeine is not recommended for regular use (either alone or in combination with paracetamol as co-dydramol) has a shorter half-life and the effects are more likely to lead to abuse. |
| **Diclofenac** | Diclofenac is not recommended due to its risk of cardiovascular effects. Diclofenac is contraindicated in patients with established ischaemic heart disease, peripheral arterial disease, cerebrovascular disease, or congestive heart failure. MHRA (2014): Diclofenac: new contraindications and warnings |
| **COX-2 inhibitors** | Cox-2 inhibitors are not recommended because of their risk of adverse cardiovascular effects. Etoricoxib is contra-indicated in certain patients with hypertension due to its cardiovascular risk profile. MHRA (2015): Cox-2 selective inhibitors and non-steroidal anti-inflammatory drugs (NSAIDs): Cardiovascular safety |
| **Indometacin** | Prescribing of indometacin is not recommended. |
| **Nefopam** | Nefopam should not be initiated for acute or chronic pain, or continued post discharge following secondary care acute initiation. Only continue nefopam in line with recommendations of the specialist pain service. Review existing patients - assess benefits versus adverse effects and consider stopping; withdraw slowly over 1-2 weeks following chronic use. Adverse effects are common, nefopam is toxic in overdose and has abuse potential through its psychostimulant-like effects. Nefopam may be useful in the case when patients cannot tolerate opioids. CCG position statement regarding nefopam. |
| **Rubefacients** | Prescribing of topical rubefacient preparations is not recommended. Topical rubefacient preparations may contain nicotinate and salicylic acid compounds, essential oils, capsicum, and camphor which are all irritant. The evidence available does not support the use of topical rubefacients in acute or chronic musculoskeletal pain. Rubefacients should not be offered to treat osteoarthritis. Stop any prescribing.<br>NICE states that capsaicin patches should not be used for neuropathic pain in non-specialist settings, unless advised by a specialist. |
| **Tapentadol** | Prescribing of tapentadol is not recommended.<br>This should only be prescribed with specialist pain service input when other treatments (e.g. morphine) have failed in persistent pain patients. |
| **Buprenorphine patches** | Reserved only for patients unable to tolerate the side effects of oral opiates or have difficulty swallowing, have compliance issues, or renal impairment. Large risk of overdose in opioid naïve patients. Buprenorphine 5mcg/hr patches are approximately equivalent to 12mg oral morphine per day. Buprenorphine 35mcg/hr patches are approximately equivalent to 84mg oral morphine per day[1]. |
| **Fentanyl patches** | Not recommended. Fentanyl patches are highly addictive and have limited value in non-malignant chronic pain therefore should only be used on the recommendation of a pain specialist. |

[1] PrescQIPP Bulletin 218 (February 2019). Reducing opioid prescribing in chronic pain.

| | |
|---|---|
| **Oxycodone** | Not recommended first-line. Oxycodone and morphine sulphate have similar safety and efficacy profiles, however morphine sulphate is significantly less costly than oxycodone. There is a lack of evidence from high quality comparative trials that other opioids have advantages over morphine in terms of either efficacy or side effects. |
| **Oxycodone/ naloxone (Targinact®)** | Not recommended. Randomised controlled trials have only compared with standard-release oxycodone, NOT with other strong opioids such as morphine, with regular laxatives. There is no data showing that combined oxycodone and naloxone reduce the need for laxatives in the long-term. |

## Neuropathic pain treatment pathway

| | | |
|---|---|---|
| **Step 1 – self-management** | | |
| For minor pain, whether for acute or minor persistent pain, patients can usually access over the counter pain medicines such as paracetamol or ibuprofen. Patients should be encouraged to self-manage their health for minor ailments including mild pain symptoms. | | |
| **Step 2 – amitriptyline** | | |
| **Amitriptyline** | 10mg to 75mg at night | Increase by 10mg to 25mg weekly. Ensure patient tolerates does at each step before increasing dose. Advise patient to take at approx. 8pm; if morning sedation is problematic the dose may be taken earlier in the evening.<br>Pain relief may be seen after 7 days, however trial for at least 4-5 weeks if tolerated.<br>If it is not tolerated or if ineffective over the trial period withdraw gradually over 1-2 weeks.<br>Particular caution should be given to initiating in the elderly as they are more susceptible to side effects.<br>Amitriptyline can be useful if patient is having difficulty sleeping at night. |
| **Step 3 – switch to gabapentin if no/ partial response**<br>**See APC statement –** County Durham & Tees Valley APC position on prescribing in persistent pain contains important advice for prescribers | | |
| **Gabapentin (CD)** | 1200mg to 3600mg daily | Gabapentin is licensed for use in peripheral neuropathic pain.<br>Start at a low dose and titrate slowly.<br>Caution when used in patients with any degree of renal impairment. Caution also in those with diabetes as it may affect blood glucose readings.<br>Caution in 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. See MHRA Drug Safety Update for further details.<br>Gabapentin is a controlled drug, therefore maximum 28 day prescribing. |
| **Step 4 – switch to duloxetine if no response** | | |
| **Duloxetine** | 30mg to maximum 120mg daily | Consider ahead of gabapentin in diabetic patients.<br>Review past treatment.<br>Consider potential for medication diversion.<br>Use lowest effective dose.<br>Do not use if contraindicated.<br>Consider laxatives.<br>Consider stopping NSAID if appropriate. |
| **Step 5 – review clinical assessment if no response to treatments, stop previous treatments and consider pregabalin**<br>**See APC statement –** County Durham & Tees Valley APC position on prescribing in persistent pain contains important advice for prescribers | | |
| **Pregabalin (CD)** | 75mg to 300mg twice daily | Pregabalin does not have a therapeutic advantage over gabapentin.<br>Consider risk of diversion and/or misuse before prescribing.<br>Pregabalin is a controlled drug, therefore maximum 28 day prescribing. |

**Step 6 – refer to specialist**

For people awaiting referral after initial treatments have failed, consider prescribing a short course of tramadol for pain relief. Prescribe tramadol cautiously, bearing in mind the potential for misuse. Tramadol is a schedule 3 controlled drug.

**Avoid use and review patients**

| | |
|---|---|
| **Nortriptyline** | Not recommended first-line. May be considered when other tricyclics have not been tolerated.<br>There is no evidence of increased efficacy although nortriptyline may have a lower side effect profile than amitriptyline as it is less anticholinergic.<br>The same titration schedule as amitriptyline can be followed; however the maximum dose advised is 75mg daily. |
| **Topiramate** | On specialist advice only |
| **Lidocaine patch** | Only licensed for post herpetic neuralgia, where it can be considered first-line. Not recommended in other circumstances. |
| **Capsaicin cream** | Generally not recommended, although may consider in osteoarthritis of hand and knees. |
| **Morphine in neuropathic pain** | Not recommended. |

**Trigeminal Neuralgia -** Carbamazepine taken during the acute stages of trigeminal neuralgia reduces the frequency and severity of attacks. Satisfactory pain relief may be achieved in 70% or more of patients. Carbamazepine should be commenced as the first line agent. If this is contraindicated, ineffective, or there are intolerable side effects, consider early referral for neurosurgical advice and commence alternative agent as for neuropathic pain such as gabapentin.

**Carbamazepine**

Slowly introduce carbamazepine, starting from 100mg daily, and increasing every 3-4 days, up to the maximum 1600mg dosage daily (in divided doses), depending on tolerability and efficacy. Trial for a period of up to 3 months to establish if effective in patient, increasing to maximum dosing where possible. If treatment does not have desired therapeutic effect, consider an alternate neuropathic pain agent and refer the patient to specialist pain service.

| Day | Breakfast | Lunch | Evening | Night |
|---|---|---|---|---|
| Day 1 | | | | 100mg |
| Day 2-4 | 100mg | | | 100mg |
| Day 5-7 | 100mg | | | 200mg |
| Day 8-10 | 200mg | | | 200mg |
| Day 11-13 | 200mg | 100mg | | 200mg |
| Day 14-16 | 200mg | 200mg | | 200mg |
| Day 17-19 | 200mg | 200mg | 100mg | 200mg |

Suggested carbamazepine dosing schedule

# Managing High-Dependency Risk Drugs in Primary Care

Suggestions to assist prescribers reducing and stopping prescriptions for **benzodiazepines, z-drugs, opiates and gabapentinoids** when:

- A patient is requesting help to come off one or more of these medications and it is clinically appropriate for them to do so
- Or You, as the prescriber, are satisfied that a patient no longer needs the medication
- Or Following a risk benefit analysis, the risks of continued prescribing outweigh any potential benefits as agreed by both the patient and the prescriber

## Assessment

These are suggestions only and should follow comprehensive assessment to ensure that one or more of the above criteria are met.
During assessment, consider the following:

1. The original indication for prescribing the drug and reasons for why it is no longer necessary or why the risks of prescribing outweigh the benefits. Discuss with patient the rationale for reducing and stopping the drug.
2. Discuss any concerns and whether an alternative medication is appropriate or not.
3. Timing. Successful outcomes will be more likely if physical and psychological health and personal circumstances are stable.
4. Be prepared to negotiate with some options for the patient to choose so that they gain some sense of control.
5. Be prepared to pause reductions but set a resumption date (do not leave open ended) and avoid reversing any reductions.

## High Risk Situations include:

Poly-pharmacy, especially combinations of CNS depressants. Gabapentinoids with opiates are currently of particular concern given an increase in prescriptions for these drugs and the combination has been implicated in drug related deaths/respiratory arrest. Also to be considered:

1. Whether there is co-morbid illicit drug or alcohol use
2. Sedation or intoxication resulting from the drug(s)
3. Suspicion of diversion or other misuse
4. Suspected / untreated sleep apnoea, >50 years, high BMI, loud snore

## Monitoring and Compliance:

Toxicology (urine drug screening) may be useful depending on what question you want to answer (it is not qualitative). However, have a clear plan for how you will act if the result is negative (when you thought it would be positive) or positive (when you thought it would be negative).
If patients struggle – discuss whether additional psychosocial support from the Addictions Service (NRP) may be helpful – n.b. some patients who struggle to come off opiates may warrant referral to the Addiction Service for consideration of OST (methadone or buprenorphine) with subsequent structured reduction. Also consider whether alternate pain relief may be necessary.
If considered high risk with high concern - consider short prescriptions (daily or weekly if necessary). Be clear from the outset that there will no concessions if medication is lost, stolen etc.
Be prepared for regular reviews to monitor progress with positive feedback and projected completion dates.
If possible, it is useful if patients are monitored/followed up by same GP with clearly documented plans.

## Tips for GPs

Be prepared:

- To be flexible
- Take the long view
- To pick your battles

Consider sequence of reduction if patient is on more than one drug – there is some evidence that more than one drug can be reduced at a time but generally the recommendations are to keep other prescriptions stable whilst reducing.
Negotiate with the patient but if possible start with the most risky / least beneficial drug first. There may be no right or wrong answer for this.

## Opioids

**Indications for use:** Moderate to severe pain (e.g. codeine phosphate, dihydrocodeine, tramadol, morphine, buprenorphine), severe pain (e.g. oxycodone) chronic intractable pain (e.g. fentanyl), acute pain (e.g. codeine, morphine), adjunct in the treatment of opiate dependence (e.g. buprenorphine, methadone, Suboxone).

**Considerations:**

- Opioids may be useful in managing acute pain in some situations especially if used on a prn rather than regular basis. However, chronic pain is complex and often influence by psychological factors and there is little evidence that opioids are then beneficial particularly as tolerance and dependence can rapidly develop with requests for escalating doses.
- **A maximum of 120mg morphine equivalent dose in 24 hours** is recommended by the British Pain Society and above this dose, harm may increase with no increase in benefit. If the patient still describes significant pain at and above this dose, it is likely that the pain is not opioid sensitive and the opioids should be reduced and stopped (even if no other treatment is available).
- It is important to discuss the patient's fears around reducing opiates and also discuss whether expectations of becoming pain free through medication is realistic. Mental ill-health and emotional difficulties should be identified and adequately treated.
- Consider discussion with Addiction Services (and other specialists) if necessary particularly for patients at high risk of harm (e.g. in pregnancy, dual diagnosis) or patients with an opioid use disorder or other illicit drug use or alcohol misuse. Offer psychosocial support (via Addictions Services) if necessary.

**Reduction regimes:**

- The rate of reduction should be negotiated with the aim of both keeping the patient comfortable and also having some sense of control. It is useful to continue to stress the benefits of coming off the medication.
- A decrease of 10% of the original dose per week is a reasonable starting point. Some patients who have taken opiates for a long time might find slower reductions (e.g., 10% per month) easier. Warn patients about loss of tolerance and the dangers of rapidly returning to previous doses. Reduce more gradually when the dose is down to the last 30%.
- Adjust the rate and duration of the reduction according to the patient's response. It ultimately does not matter how long the reduction takes as long as reductions continue at a regular rate.
- Don't reverse the reduction however, the rate may be slowed or paused while monitoring and managing withdrawal symptoms.
- Once the smallest available dose is reached, the interval between doses can be extended and opioids may be stopped when taken less than once a day.
- Various regimes are available for patients on combinations of modified and immediate release preparations. Discuss with the patient and negotiate according to what they find most useful.
- Consider referral to Specialist Addictions Services if patients do not manage to reduce on a regular basis for consideration of OST (methadone or buprenorphine) and they are agreeable to referral.

### Opioids Aware

Opioids Aware, a project from the Faculty of Pain Medicine and Public Health England, contains specific information relating to the clinical use of opioids for pain that aims to support prescribers and patients in making a fully informed decision to use, or not use opioids.

Opioids Aware resources to support clinicians:

- Patient Assessment. What should be included in a full pain history?
- Dose Equivalence and Changing Opioids. Opioid rotation or switching may be considered if a patient obtains pain relief with one opioid and is suffering severe adverse effects. Switching from one opioid to another should only be recommended or supervised by a healthcare practitioner with adequate competence and sufficient experience.
- Tapering and Stopping Opioids. When to stop; preparing the patient and strategies for dose reduction.
- Opioids and Driving. New drug driving legislation came into force in England and Wales in 2015. If your driving is impaired for any reason, including taking medicines, it is illegal to drive. All opioid medicines have the potential to impair driving. A patient information leaflet is also available from the Faculty of Pain Medicine.
- Faculty of Pain Medicine Checklist for Prescribers. Includes sections on what to discuss with the patient when considering opioid treatment, documentation, responsibility for prescribing, and arrangement for review.

Opioids Aware Information for Patients:

- About Pain. Information about acute, chronic, neuropathic and cancer pain
- Thinking About Opioid Treatment for Pain. Things to think about when considering opioid therapy.
- Taking Opioids for Pain. Answers to frequently asked questions about taking opioid medicines.

## Gabapentinoids – pregabalin and gabapentin

**See APC statement –** County Durham & Tees Valley APC position on prescribing in persistent pain contains important advice for prescribers

**Indications for use:** Licensed in the UK and USA for the treatment of epilepsy and neuropathic pain and in the US for fibromyalgia. In the UK pregabalin is also licensed for the treatment of generalised anxiety disorder.

**Considerations:**

1. Avoid prescribing gabapentinoids to anyone with an active drug or alcohol problem if at all possible. There is a risk that some patients may wish to accumulate supplies with a view to taking excessive doses for a psychoactive effect.
2. If dependence to pregabalin or gabapentin, or other misuse or diversion, is suspected or identified, the patient should be reviewed and the concerns discussed empathically and documented clearly. Of particular concern is use of gabapentinoids with opiates (some evidence that morphine may increase the bioavailability of gabapentin).
3. Specialist advice may be appropriate and Addiction Services (NRP) may be able to offer psychosocial support while patients are being weaned off their prescription.
4. If there is a confirmed diagnosis of epilepsy – liaise with neurology.

**Reduction regimes:**

Product characteristics for gabapentin and pregabalin indicate that both drugs can be discontinued over one week. Caution in epileptic patients. A more gradual dose taper allows observation of emergent symptoms that may have been controlled by the drug. Suggested tapering regimes:

- **Pregabalin**: reduce the daily dose at a maximum rate of 50-100mg/week.
- **Gabapentin**: reduce the daily dose at a maximum rate of 300mg every four days.
- There is currently no evidence for the use of any substitute adjunctive medications in the management of withdrawal from gabapentinoids.

## Benzodiazepines and z-drugs

**Indications for use:**

**(i) Benzodiazepines:** As an adjunct in epilepsy (clobazam, clonazepam), short term use in anxiety (chlordiazepoxide, diazepam, lorazepam), muscle spasm (diazepam), alcohol withdrawal (chlordiazepoxide, diazepam), short term use in insomnia (temazepam, lormetazepam).

**(ii) Z-drugs:** For short term use in insomnia (zopiclone, zolpidem).

Take the following into considerations before commencing withdrawal:

- Any symptoms of anxiety, depression, insomnia.
- Whether the patient is willing to engage with the process, can attend regular reviews and has adequate social support.
- Any alcohol or illicit drug misuse or dependence, history of withdrawal seizures (consider specialist advice or referral).
- Although lacking an evidence base, converting to diazepam may be useful if the patient is on short acting benzodiazepines, sedative hypnotics or preparations that do not allow small reductions in dose. Diazepam is also useful as its long half-life allows for a once daily dose. Many conversion tables are available.

**Reduction regimes:**

The same approach is recommended for reducing z-drugs and benzodiazepines. There is no specified time frame. Negotiate a gradual drug withdrawal that is flexible taking into account the original indication for prescription, dose of drug and length of time on drug. Set the regime but be prepared to adjust the reduction dependent on any withdrawal symptoms:

Withdraw gradually dose tapering at a rate of 5 – 10 % reduction every 2 weeks (this will allow a slowing of the reduction at lower doses).

- Can maintain on a dose for a negotiated period if the patient is struggling but avoid putting the dose back up.
- Accept that withdrawal can take months to a year or longer.
- Review frequently (detect problems early and provide advice and encouragement).
- There is no evidence to support the use of adjunctive drug therapy to assist withdrawal.

## References and Links


1. NICE Clinical Knowledge Summaries – Benzodiazepine and z-drug withdrawal (April 2015). https://cks.nice.org.uk/benzodiazepine-and-z-drug-withdrawal
2. Advice for prescribers on the risk of the misuse of pregabalin and gabapentin. Public Health England (December 2014). https://www.gov.uk/government/publications/pregabalin-and-gabapentin-advice-for-prescribers-on-the-risk-of-misuse
3. Guidance for opioid reduction in primary care. Oxford Pain Management Centre and Oxford University Hospitals NHS Foundation Trusts (December 2017) https://www.ouh.nhs.uk/services/referrals/pain/documents/gp-guidance-opioid-reduction.pdf
4. Opioids Aware https://www.rcoa.ac.uk/faculty-of-pain-medicine/opioids-aware
5. CDC Guideline for Prescribing Opioids for Chronic Pain www.cdc.gov/drugoverdose/prescribing/guideline.html
6. Drug Misuse and Dependence. UK Guidelines on Clinical Management (DH 2017). https://www.gov.uk/government/publications/drug-misuse-and-dependence-uk-guidelines-on-clinical-management
7. MHRA Drug Safety Update volume 11, issue 3; October 2017: 2. https://www.gov.uk/drug-safety-update/gabapentin-neurontin-risk-of-severe-respiratory-depression

# Opioid Equivalent Doses[2]

## Opioid equivalence to morphine

| Drug | Dose – Faculty of Pain Medicine[2] | Dose – BNF "Prescribing in Palliative Care"[11] | Dose – SIGN[12] |
|---|---|---|---|
| **Morphine Equivalence** | 10mg | 10mg | 10mg |
| **Oral Codeine** | 100mg | 100mg | 100mg |
| **Oral Dihydrocodeine** | 100mg | 100mg | Not Stated |
| **Oral Tramadol** | 100mg | 100mg | 50mg |
| **Oral Tapentadol** | 25mg | Not Stated | Not Stated |
| **Oral Oxycodone** | 6.6mg | 6.6mg | 5mg |


**References:**

[2] Faculty of Pain Medicine. Supported by Public Health England. Opioids Aware: A resource for patients and healthcare professionals to support prescribing of opioid medicines for pain. Available at https://fpm.ac.uk/opioids-aware accessed 30/09/20

[11] Joint Formulary Committee. British National Formulary (online) London: BMJ Group and Pharmaceutical Press; August 2018. Available at https://bnf.nice.org.uk/ accessed 30/09/20

[12] Scottish Intercollegiate Guidance Networks. SIGN. Management of chronic pain. Guideline 136. Last updated August 2019. Available at https://www.sign.ac.uk/our-guidelines/management-of-chronic-pain/ accessed 30/09/20


## Transdermal Opioids

Transdermal opioids – approximate equivalence of buprenorphine patches with oral morphine

| | | | | | | |
|---|---|---|---|---|---|---|
| **Oral morphine mg/day** | 12 | 24 | 48 | 84 | 126 | 168 |
| **Transdermal buprenorphine mcg/hr (change every 7 days)** | 5 | 10 | 20 | | | |
| **Transdermal buprenorphine mcg/hr (change twice weekly-apply every 72hours or 96 hours)** | | | | 35 | 52.5 | 70 |

Transdermal opioids – approximate equivalence of fentanyl patches with oral morphine

| Fentanyl Patch Dose (microgram/hour) | Oral Morphine Dose (mg/day) |
|---|---|
| **12** | **30** |
| **25** | **60** |
| **50** | **120** |
| **75** | **180** |
| **100** | **240** |

See Opioids Aware - Dose Equivalent and Changing Opioids for further information on dose conversions

[2] PrescQIPP – Reducing opioid prescribing in chronic pain

# Management of Medication Related Side Effects

## Proton Pump Inhibitors – advice on when to initiate a PPI with an NSAID

Where an NSAID is indicated, and to reduce the risk of gastrointestinal adverse effects, the lowest effective dose for the shortest duration of treatment should be used. As PPIs have become widely used, evidence has started to emerge regarding their long-term safety and potential for adverse effects. Clinicians should consider the risks and benefits when considering prescribing long term PPIs and ensure regular review.

All patients on NSAIDs at high risk of having serious GI adverse events should routinely be co-prescribed gastro-protection.
High risk factors are:

- Patients >45 years of age receiving long-term regular NSAID
- Patients ≥65 years of age receiving short-term of intermittent NSAID
- Dual antiplatelet therapy
- Past history of PUD
- Concomitant oral anticoagulant/ antiplatelet/ NSAID

Or have two or more risk factors:

- ≥65 years of age
- Oral corticosteroid use
- Dyspepsia or GORD symptoms
- SSRIs

Severe co-morbidity (malignancy, HF (NYHA III-IV), significant liver or renal disease (e.g. CKD 4&5 and cirrhosis)

Lansoprazole or omeprazole are the preferred formulary choices for gastro-protection.
Licensed doses of proton pump inhibitors used for gastro protection for people who require continued NSAID treatment:

| Proton Pump Inhibitor | Dose for NSAID prophylaxis |
|---|---|
| Lansoprazole | 15–30 mg once daily |
| Omeprazole | 20 mg once daily |
| Esomeprazole | 20 mg once daily |
| Pantoprazole | 20 mg once daily |

## Management of opioid induced constipation

At least 40% of patients experience constipation whilst taking opioid-based analgesia. Patients should be given general advice about fluid intake, exercise and eating plenty of fruit and vegetables.
If medication is necessary, the combination of a stimulant and osmotic laxative are the most appropriate treatment for opioid induced constipation (i.e. to avoid bulk forming laxatives which are usually the mainstay of constipation treatment).

Suggested regime:

- Senna 15-30mg at night **and**
- Laxido® sachets 1-3 sachets per day

Other options are docusate sodium and sodium picosulphate. If patient presents with faecal impaction then Laxido® up to 8 sachets per day is the first line of treatment.

Specialist only drugs for constipation due to opioid usage:
Naloxegol should be prescribed only on the advice of a specialist.
Methylnaltrexone is a non-formulary drug.