



# CHRONIC NON-MALIGNANT PAIN

## Top tips for MURs

- Check that the patient understands why the medication has been prescribed and check if still indicated
- Counsel patient on the intended treatment goals i.e reduction of pain to manageable / functional levels rather than a curative therapy
- Counsel patient on the need to take medication on a time contingent basis e.g. regularly and by the clock rather than according to the pain, to maintain consistent pain control
- Counsel patient on the use of balanced analgesia, where a combination of different classes of analgesics are used simultaneously to achieve more effective analgesia
- Counsel patients on long- term opioid therapy of potential side effects, including hyperalgesia, sexual dysfunction, lowered immunity and fertility
- Advise patient that when moving from one step of treatment to the next, at least 5 days should be trialled to allow transient side effects to diminish and the effectiveness of the step to be assessed
- Counsel patients receiving treatment for neuropathic pain that medication may take 2-3 weeks to take effect as doses are titrated
- Counsel patient on signs / symptoms of complications that need referral (**see red flags overleaf**)
- Counsel patient on common side effects and how they should be managed (**see overleaf**)
- Signpost patients with chronic pain to self-help leaflets and websites e.g. Arthritis care or expert patients programme
- Advise patients on non-pharmacological interventions to manage pain e.g. weight management, physiotherapy, exercise, TENS machines
- Check that patient has had annual renal and liver function tests (monitor more frequently in high risk patients e.g. in the elderly or patients with co-morbid conditions)
- Report any relevant adverse drug reactions to the Yellow Card Scheme

## Pathophysiology of pain

Pain is very common and has a significant impact on quality of life and on the economy. Pain is defined as 'An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage<sup>1</sup>.' The neurophysiological classification further describes pain in terms of whether the pain occurs in response to tissue injury (nociceptive) or due to injury within the nervous system (non-nociceptive or neuropathic).<sup>2</sup> The nociceptive pain pathway involves transduction, transmission, modulation and perception of pain from pain receptors present at nerve endings under the skin or on the walls of internal organs. Non-nociceptive pain pathways remain involved in these four stages but the processes are altered or abnormal and spontaneous pain signals can be generated in the absence of a stimulus.<sup>2</sup>

Chronic pain lasts for greater than 3-6 months. The goal of therapy for chronic non-malignant pain should be to reduce symptoms sufficiently to support improvement in physical, social and emotional functioning. Medication alone is rarely able to achieve this and patients must be encouraged to seek alternative methods of pain management e.g. physiotherapy, pacing of activity, relaxation and education.

Ensure that baseline analgesic (ideally paracetamol) is prescribed with any opioid medication due to its opioid sparing properties.

## How do medications to treat chronic non-malignant pain work?

<b>Paracetamol</b>	Postural mechanisms of action include effects on central prostaglandin inhibition, peripheral bradykinins and serotonergic systems.
<b>NSAIDs</b>	NSAIDs inhibit the enzyme cyclo-oxygenase (COX), which catalyses arachidonic acid to prostaglandins and leukotrienes. This results in reduction of inflammation, reduced temperature and an analgesic effect. Limited benefit in chronic non-malignant pain where there is less commonly an ongoing inflammatory process and limited benefit in neuropathic pain.
<b>Opioids</b>	Opioids act as opioid receptor agonist to three opioid receptors. Most opioids bind to one type of receptor preferentially, primarily the mu receptor. Differences in the opioids arise from their receptor specificity and their water and lipid solubility. Tramadol has a second mechanism of action involving an enhancement of serotonergic and adrenergic pathways. This mechanism may be useful for patients with mixed aetiology of pain e.g. nociceptive and neuropathic symptoms. Tramadol should be used with caution in elderly patients and avoided in epilepsy. Buprenorphine is a partial opioid agonist, although this is not clinically significant at systemic levels achieved using transdermal buprenorphine preparations. Oral buprenorphine is not suitable for chronic non-malignant pain management.
<b>Anticonvulsants</b>	Inhibits voltage-dependent sodium channels, resulting in decreased release of the excitatory neurotransmitters glutamate and aspartate (carbamazepine, lamotrigine and phenytoin) or increases the synthesis of GABA by modulating the enzyme glutamic acid decarboxylase (valproate, gabapentin & pregabalin). Gabapentinoids inhibit transmission via voltage-gated calcium channels, slowing transmission of neural signalling and thus reducing pain transmission.
<b>Antidepressants</b>	Monoamine reuptake inhibitors with varied specificity for noradrenaline and serotonin (tricyclic antidepressants – amitriptyline & nortriptyline) or selective serotonin and noradrenaline reuptake inhibitors (duloxetine).
<b>Lidocaine</b>	Reduces aberrant firing of sodium channels on damaged fibres under the patch. Suitable only for focal neuropathic pain symptoms. Licensed only for post-herpetic neuralgia so consult local formularies to confirm position.
<b>Capsaicin</b>	Acts in the skin to attenuate cutaneous hypersensitivity and reduce pain by defunctionalisation of nociceptor fibres and reduction of Substance P.



## Lifestyle issues

- Counsel patient on reducing alcohol intake to within safe limits (up to 14 units a week, spread evenly over 3 more days, with several alcohol free days)
- Counsel patient on healthy eating, exercise & weight loss (if BMI > 25kg/m<sup>2</sup>) – advise patients to complete 30 minutes of aerobic exercise three to five times a week, reduce caffeine intake to no more than 5 cups a day and recommend 5 portions of fruit and vegetables a day
- Advise patients who smoke the benefits of stopping smoking and how to access pharmacy smoking cessation services or Stop Smoking Wales

## Red flags that need referral

- Any signs of respiratory depression
- Any changes in sleep pattern including snoring, vivid dreams, nightmares
- Worsening of pain symptoms in spite of increasing medication doses – especially with opioids
- Increased agitation, confusion or hallucinations, pinpoint pupils, sedation
- Any symptoms suggestive of gastrointestinal bleeding (anaemia, black stools or dark, coffee ground vomiting)
- Any headaches which have developed or worsened while taking opioids
- Any cardiovascular symptoms (bradycardia, tachycardia, palpitations, postural hypotension)
- Any loss of libido, erectile dysfunction in men, or amenorrhoea in women
- Suicide ideation and behaviour
- Pregnancy as risk of teratogenicity & breastfeeding as risk of toxicity to infant

## What are the common side effects to look out for?

Gastro-intestinal disturbances including discomfort, nausea, vomiting, occasionally bleeding & ulceration – <b>more commonly seen in NSAIDs, duloxetine and weak opioids (codeine, dihydrocodeine &amp; tramadol)</b>	Take medication with milk, water or food as may reduce symptoms. Refer to GP for change of formulation, medication or addition of gastro-protection if persistent.
Anticholinergic side-effects (especially dry mouth, constipation, blurred vision and confusion), sedation - <b>more commonly seen in tricyclic antidepressants, anticonvulsants and opioids</b>	Advise newly prescribed patient that side effects usually only last 3 weeks, if not tolerated refer to prescriber.
	Advise patient to drink plenty of water, avoid sugary drinks and chew sugar free chewing gum if dry mouth persists.
	Advise patient to increase fibre, water intake and exercise or recommend an osmotic and stimulant laxative if constipation persists.
	Advise patient that close up vision can be affected and to see an optician if a problem. Warn of care with driving or operating machinery if experiencing drowsiness.
Diarrhoea – <b>commonly seen with tramadol</b>	Refer to prescriber if not tolerated.
Insomnia, sleep disturbance, abnormal dreams - <b>more commonly seen in duloxetine</b>	Give sleep hygiene advice and if persistent refer to prescriber for medication review.
Increased blood pressure, CV events, hyperkalaemia & fluid retention – <b>more commonly seen in NSAIDs</b>	Refer to prescriber for review of therapy.
Weight gain, anorexia, increased appetite - <b>commonly seen with gabapentinoids</b>	Give patient lifestyle advice and refer to prescriber if not tolerated.
Burning sensation, skin irritation – <b>commonly seen with capsaicin cream</b>	Advise patients that this will diminish over time. Refer to prescriber if not tolerated.
<b>See MUR quick guide for NSAIDs and Opioids for more details of side effects of these two medications</b>	

## Potential serious drug interactions?

Drugs used to treat chronic non-malignant pain interact with a range of other medications such as: alcohol, antibacterials, anticoagulants, antidepressants, antiepileptics, antifungals, antihistamines, antipsychotics, antivirals, aspirin, beta-blockers, cytotoxics, ciclosporin, dopaminergics, diuretics, lithium, memantine, methotrexate, sympathomimetics – **See BNF Appendix 1: Interactions for more details**

## Where can you find more information?

- Analgesics – BNF sub-section 4.7
- Pain: treatment and management distance learning packs that can be found on WCPPE website (<http://www.wcppe.org.uk>)
- NICE guidance CG96 Neuropathic pain - pharmacological management: quick reference guide: CG88 Low back pain: Early management of persistent non-specific low back pain:CG59 Osteoarthritis; CG79 Rheumatoid arthritis can be found on NICE website (<http://www.nice.org.uk>)
- Clinical Knowledge Summaries (<http://www.cks.nice.org.uk>)
- National Prescribing Centre (<http://www.nps.nhs.uk>)
- Opioids for persistent pain: Good practice ([http://www.britishtainsociety.org/book\\_opioid\\_main.pdf](http://www.britishtainsociety.org/book_opioid_main.pdf))

## References

1. Pain terminology. International Association for the Study of Pain (IASP). Available from [http://iasp-pain.org/AM/Template.cfm?Section=Pain\\_Defi...isplay.cfm&ContentID=1728](http://iasp-pain.org/AM/Template.cfm?Section=Pain_Defi...isplay.cfm&ContentID=1728)
2. Pain: treatment and management. CPPE 2009.