Please note, this page contains supplementary information and is not a component of the eLearning course.

Non-opioid pain medicines: Considering alternatives and deprescribing

Many patients taking opioids also regularly take one or more non-opioid pain medicines. This supplementary information outlines indications for considering non-opioid pain medicines and guidance on tapering.

What else is there to treat persistent pain?

Whilst patients may be willing to consider reducing ineffective opioids, they may expect to be offered an alternative medicine for their pain. Recent clinical guidance[1] has moved away from recommending the prescription of pain medicines to patients with persistent pain and does recommend supporting patients to self-manage pain.

For most patients with persistent pain, and especially those who have already been prescribed regular opioids, it is unlikely that there will be an appropriate non-opioid pain medicine you can prescribe as an alternative.

Therefore, it is anticipated that the plan for the majority of patients attending pain reviews will not include a prescription of an alternative pain medicine.

It makes sense to review the effects of any non-opioid pain medicines a patient takes at the same time as reviewing the opioids. In doing so, you are:

- acknowledging the understandable and natural desire patients have to find a medicine to reduce their pain (“what else is there for my pain”?)
- providing an opportunity to explore what they have tried in the past and the response, so that patients can reflect on how well (or not) taking pain medicines has worked for them so far,
- gathering all the information you need to advise on whether there are any other options they could try and,
- creating an opportunity to address co-prescribing that is a cause for concern, for example opioids combined with gabapentinoids and/or benzodiazepines, and continued use of other ineffective pain medicines

Considering alternative non-opioid analgesics

Most pain medicines don’t work for most patients with persistent pain, a few work for some patients. Prescribing for persistent pain should therefore be evidence based for the type of

persistent pain problem the patient has. The indications for prescribing various groups of pain medicines are outlined below.

Paracetamol

Paracetamol is an effective analgesic for mild to moderate acute pain. It has a synergistic effect with opioids in the management of acute pain and therefore is often used in combination with opioids for its 'opioid-sparing' effect.

Current clinical guidelines consistently recommend paracetamol as the first-line analgesic medicine for pain associated with osteoarthritis, given its low risk of substantive harm[2]. However, paracetamol provides only minimal improvements in pain and function for people with hip or knee osteoarthritis[3].There is little evidence to suggest that paracetamol is effective for other types of persistent pain and neither is there evidence that it is ineffective. However, there are concerns regarding side effects[4], which need to be balanced against benefit on an individual basis.

If patients are already taking paracetamol, within recommended dose limits, and feel that they benefit from it then there is no reason to change this, but it should not be continued if there is no evidence of benefit[1] due to the possibility of causing harm.

Topical Treatments

Topical NSAIDs should only be considered for localised joint pain and if the patient has

(a) not tried them already and

(b) isn't also taking an oral NSAID.

There is no evidence to support the use of topical NSAIDs in other persistent pain conditions.

Topical capsaicin may be considered for knee or hand osteoarthritis[2] and for localised neuropathic pain[5].

Oral NSAIDs

NSAIDs may be useful for acute pain and some patients may benefit from NSAIDs for persistent musculoskeletal pain[2,6]. There is no evidence that NSAIDs are effective for other types of persistent pain[1].

The guidance regarding NSAIDs will be familiar: NSAIDs should be prescribed at the lowest effective dose for the shortest possible period of time, taking into account potential differences in gastrointestinal, liver and cardio-renal toxicity, and the patient's risk factors, including age. A plan for ongoing monitoring of risk factors should be in place, and the use of gastroprotective treatment (PPI) considered, even for short-term use and particularly in people aged over 65.

Antidepressants

There is evidence indicating that antidepressants (duloxetine, amitriptyline and the SSRIs fluoxetine, paroxetine, citalopram and sertraline) may improve quality of life, pain and psychological distress in some people with persistent pain, although the body of evidence is small[1].This is an unlicensed use of antidepressants and should not be considered except following discussion with a GP at the practice and/or on specialist recommendation.

When prescribed for persistent pain, a two-month trial of SSRI's and SNRI's (e.g. duloxetine) is usually required before deciding on effectiveness. Beyond that these drugs should only be continued for persistent pain if there is clear evidence of benefit. If antidepressants are prescribed for low mood, then different considerations may apply.

For recommendations on stopping or reducing antidepressants, **see section on deprescribing below**.

Gabapentinoids

Gabapentin and pregabalin (gabapentinoids) should only be prescribed for diagnosed neuropathic pain conditions and not for conditions such as chronic back pain and osteoarthritis. They are recommended in clinical guidance[5] but it is worth noting that most of the evidence for their effectiveness is derived from populations with either painful diabetic neuropathic pain (PDNP) and post-herpetic neuralgia (PHN). Their effectiveness outside of these clearly defined neuropathic pain conditions is less certain and evidence suggests they are not effective for sciatica[6].

Even for patients with neuropathic pain, gabapentinoids help only around 1 in every 4 or 5 patients. As with opioids, there has been a dramatic increase in prescribing of these drugs and this has been accompanied by a growing evidence of their potential for harm including overdose, dependence and misuse, as well as side effects of tiredness, nausea and mood changes. As a result, from April 2019 gabapentin and pregabalin have been designated Schedule 3 controlled drugs under the Misuse of Drugs Regulations 2001, and Class C of the Misuse of Drugs Act 1971.

If you feel that a patient has clear neuropathic pain symptoms, has not yet tried gabapentinoids and wishes to do so then it is recommended that you discuss this with a GP at the practice before a decision on prescribing is made. Combining opioids and gabapentinoids increases the risk of harm and therefore decisions about gabapentinoid prescribing needs to also take into account the patient's readiness to reduce opioids.

A more likely scenario is that you identify patients who are continuing on gabapentinoids without benefit. In these circumstances it is appropriate to consider tapering these drugs at some point, **see section on deprescribing below.**

Benzodiazepines and other muscle relaxants

Guidelines from many countries have said that muscle relaxants should be considered for short-term use. The evidence for this mainly came from studies on medications that are not licensed for this use in the UK. The 2009 NICE guideline on low back pain recommended considering diazepam as a muscle relaxant for short term use in people with low back pain when the paraspinal muscles are in spasm. This practice continues to some extent but the evidence base to support this particular use of diazepam is extremely small and in 2016 NICE made a research recommendation to find out if diazepam is clinically beneficial and cost effective in the management of acute low back pain. Since then, a randomised controlled trial, reported no additional benefit of adding diazepam to NSAID therapy for acute back pain[7].

Benzodiazepines are not recommended for sciatica as there is evidence that they do not help this condition. Neither is there any evidence that other muscle relaxants such as Baclofen are effective[6].

Benzodiazepines and other muscle relaxants are not recommended for long-term use or for persistent pain[1].Nevertheless, it is not uncommon to encounter patients prescribed both opioids and benzodiazepines long-term. In these circumstances, it is appropriate to consider tapering benzodiazepines at some point, **see section on deprescribing below.**

Cannabis-based products

Cannabis-based medicines are currently not recommended for persistent pain due to a lack of evidence supporting their use, and should not be prescribed. Where trials have demonstrated benefits of cannabis-derived medicines for persistent pain, the effects were comparatively small and not cost effective; importantly no reduction in opioid use as a result was found[8]. These products are not currently prescribed in primary care or in specialist pain services.

Some cannabis-based products that might claim to be medical cannabis, such as "CBD oil" or hemp oil, are available to buy legally as food supplements from health stores. At the moment these products are not regulated as medicines so their quality and content is not known. Some products bought online may be illegal and potentially dangerous. There is no guarantee that cannabis-based products are of good quality or provide any health benefits.

Deprescribing non-opioid analgesics

Patients with persistent pain often take several medicines for pain, which may also be ineffective and /or potentially harmful. Of particular concern is co-prescribing of other potentially sedating medicines such as gabapentinoids, benzodiazepines, Z-drugs for pain and/or mood/ sleep. This increases the risk of opioid-related harm considerably and increases the likelihood of opioid misuse.

It is recommended that only one change to pain medicines is made at a time. The first priority of a pain review is opioid tapering, in patients who agree to this. For these patients changes to non-opioid medicines can be added to the plan at a later stage.

Where patients are not ready to reduce opioids, or where this does not seem necessary (i.e. low dose, functional benefits outweighing any adverse effects/ risk) then deprescribing of other ineffective/ potential harmful pain medicines can be considered at an earlier stage.

As with opioids, benzodiazepines and gabapentinoids should not be stopped abruptly or reduced too quickly as this may precipitate withdrawal symptoms. Some patients may also experience withdrawal effects when coming off antidepressants. For this reason, gradual reduction (tapering) is recommended whenever a plan to come off gabapentinoids, benzodiazepines and antidepressants is agreed.

Gradual reduction of any potentially ineffective pain medicines is also recommended to allow for any previously unnoticed benefits to emerge. This approach also offers the opportunity to continue at the lowest effective dose, if it transpires that there is some benefit.

Gabapentinoids

- Discuss the rationale for deprescribing e.g. lack of effectiveness and/or potential risks of continued use including sedation and increased risk of falls or accidents, risk of dependence/addiction and risk of overdose (unintentional / intentional) especially in combination with opioids. Emphasise potential benefits of reducing / stopping e.g. improved alertness, concentration & memory and less prone to falls

- Discuss withdrawal symptoms and how the risk of these will be managed:

  If gabapentinoids are reduced suddenly or stopped abruptly patients may experience withdrawal symptoms including: nausea, dizziness, headaches, insomnia, restlessness and anxiety.

  Bear in mind that the patient may have experienced these in the past due to stopping the drug or missing doses (intentionally or unintentionally) and it is useful to enquire about this.

  Explain that withdrawal symptoms are unlikely to occur with gradual tapering.

- Agree a tapering plan

  The product characteristics of gabapentinoids suggest they can be reduced fairly quickly, For example:

  Pregabalin: reduce the daily dose at a *maximum* of 50-100mg/week.

  Gabapentin: reduce the daily dose at a *maximum* rate of 300mg every four days or so.

In practice, a slower taper is often of benefit to patient and may help to sustain a meaningful reduction.

Benzodiazepines

For patients who have been prescribed benzodiazepines long-term, it is recommended that you liaise with the patient's GP before commencing deprescribing. Otherwise, the principles are similar to those for other potentially dependence-forming prescription medicines.

- Discuss the rationale for deprescribing including lack of long-term efficacy and potential risks of continued use including daytime sedation, falls and accidents, physical dependence, memory disorder. Risks increase in older people. Emphasise potential benefits of reducing / stopping e.g. improved alertness, concentration & memory and less prone to falls.

- Discuss withdrawal symptoms and how the risk of these will be managed:

  Possible benzodiazepine withdrawal symptoms include insomnia, anxiety, irritability, sweating and gastrointestinal symptoms such as diarrhoea. Reassure that these are temporary, lasting for days to a few weeks, and are usually mild. Explain that the dose will be tapered gradually to reduce the risk of causing withdrawal symptoms.

- Agree a tapering plan: Have a look at the algorithm for benzodiazepines and Z-drugs that has been approved by NICE. In summary this recommends a slow taper, reducing the dose by approximately 25% every 2 weeks and slowing to a roughly 12.5% reduction, if possible, and/or introducing drug-free days towards the end. In practice, and along with tapering other medicines, a slower reduction may be more achievable long term.

Antidepressants

It is now recommended that people on antidepressants are advised that if they stop taking antidepressant medication abruptly, miss doses or do not take a full dose, they may experience discontinuation symptoms such as restlessness, insomnia, unsteadiness, sweating, abdominal symptoms, irritability, anxiety, confusion and altered sensations. The severity and duration is very variable from no or mild/ self-limiting symptoms to severe long-lasting symptoms.

NICE recommends gradually reducing the dose of antidepressants, normally over a 4-week period, although some people may require longer periods, particularly for drugs with a shorter half-life (such as paroxetine and venlafaxine). This may not be required with fluoxetine because of its long half-life.

For patients who have been prescribed antidepressants for depression, factors such as the number of previous depressive episodes and severity are worth considering before deciding whether or not to stop. A discussion with a GP is recommended.

References

1. NICE Guideline, 2021. Chronic pain (primary and secondary) in over 16s: assessment of all chronic pain and management of chronic primary pain. [Online]. Available at: https://www.nice.org.uk/guidance/ng193 [Accessed April 2022].

2. NICE Guidance, 2014. *Osteoarthritis: care and management.* [Online] Available at: https://www.nice.org.uk/guidance/cg177 [Accessed September 2020].

3. Leopoldino, A. O. et al., 2019. *Paracetamol for treating people with hip or knee osteoarthritis,* s.l.: Cochrane Database of Systematic Reviews.

4. Robert, E. et al., 2015. Paracetamol: not as safe as we thought? A systematic literature review of observational studies. *Annals of the Rheumatic Diseases,* 75(3), pp. 552-559.

5. NICE Guidance, 2013. *Neuropathic pain in adults: pharmacological management in non-specialist settings.* [Online] Available at: https://www.nice.org.uk/guidance/cg173 [Accessed September 2020].

6. Nice Guidance, 2016. *Low back pain and sciatica in over 16s: assessment and management.* [Online] Available at: https://www.nice.org.uk/guidance/ng59 [Accessed September 2020].

7. Friedman, B. W. et al., 2017. Diazepam is No Better Than Placebo When Added to Naproxen for Acute Low Back Pain. *Annals of Emergency Medicine,* 70(2), pp. 169-176.

8. NICE Guidance, 2019. *Cannabis-based medicinal products.* [Online] Available at: https://www.nice.org.uk/guidance/ng144. [Accessed September 2020].