Basingstoke, Southampton and Winchester District Prescribing Committee

Chronic Pain Prescribing Guidelines

Guidelines for the pharmacological management of chronic, non-malignant, non-palliative pain in primary care / non-specialist centres

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Section 1: Introduction

Purpose

To facilitate appropriate prescribing in primary care for adults presenting with chronic (persistent), non-malignant, non-palliative pain.

Scope

All patients aged 18 years or over, with chronic, non-malignant, non-palliative pain.

For use by all non-specialist prescribers within primary and secondary care. (Pain specialists may, with justification provided, prescribe outside of these guidelines but in accordance with formulary agreements).

How to use these guidelines

This document is designed to guide prescribing for chronic pain.

When medicines are prescribed, they should be used in combination with other treatment approaches to support improved physical, psychological and social functioning.

The document is based on NICE guidance193, SIGN guideline 136, MHRA advice, the Royal College of Anaesthetists 'Opioids Aware' pages and established practice throughout the UK.

It is a guide and needs to be used in the context of the individual patient and the experience of the practitioner responsible for their care.

Introduction

Chronic pain is usually defined as pain that has lasted for more than three months. It sometimes begins with an injury, but the pain does not resolve as expected; sometimes it is not clear how a chronic pain has started. Chronic pain is usually not a sign of on-going tissue damage but may relate to changes in the peripheral and central nervous system that occur over time so that the pain signalling becomes self-sustaining over a prolonged period[1].

Chronic pain may be defined as secondary (i.e., due to an underlying condition) or primary (where there is no clear underlying condition or the symptoms seem to be out of proportion to the disease or injury)[2].

Chronic pain is difficult to treat, with most types of drug treatment helping only a small percentage of patients. Therefore, it is important to manage expectations[1].

If pharmacological treatment is prescribed, it should be considered a small part of a broader plan.

Section 2: Before Prescribing

Assessment

A comprehensive person-centred assessment is essential in order to consider the cause of the pain, the effect it has on the person and to agree a management plan. In addition to physiological investigations, assess emotional state and social circumstances, past and present. Investigate the impact of the pain on the person's life and explore the person's understanding of the meaning of the pain.

Further detail can be found at NICE NG193

Best practice when considering prescribing

- A good initial consultation gives the patient the best chance of positive outcomes.
- It is important to help patients to understand what chronic pain is.
- Promote self-management from the first appointment, regardless of other investigations or treatments. Self-management is important in order to live well with pain.
- Reassure patients that physical activity does not usually cause further tissue damage.
- If medication is prescribed, it should be considered a small part of a broader plan.
- The goals of pharmacological treatment should always be to manage symptoms sufficiently to enable patient to improve their social, emotional and physical functioning.
- Manage expectations and establish ground rules from the start.
- Good management of prescribing reduces chance of medicine related harm and other issues further down the line.
- It is important to carry out regular review and reassessment to determine that there is continued value from using a particular medication.

For further details see appendix: 'Best practice for opioid management'.

Section 3: Simple and topical analgesics

Paracetamol

- First line in osteoarthritis. Regular dosing may be required[5].
- Caution in low body weight (under 50 kg), malnutrition, dehydration, alcohol dependence, severe liver disease and in older people or in frailty. Consider a dose reduction in these groups[3].

NSAIDs

- First line for low back pain[4].
- Consider topical ahead of oral NSAIDs where feasible (e.g., hand/knee OA[5]).
- Use the lowest effective dose and the shortest duration of treatment necessary to control symptoms.
- Consider risk of gastrointestinal, renal and cardiovascular morbidity.
- Take account of drug interactions e.g., NSAIDs with ACE inhibitors or ARBs may pose particular risks to renal function, SSRIs increase GI bleed risk.
- Ibuprofen (1200mg a day or less) and naproxen (1000mg a day or less) are first line choices for safety reasons.
- Co-prescribe a proton pump inhibitor (PPI) with NSAIDs for people with osteoarthritis, rheumatoid arthritis and for people at risk (see NICE CKS topic on NSAIDs for further detail).
- For further guidance on prescribing NSAIDs, see appendix 'NSAID prescribing decision flowchart'.
- Medicines Safety Portal has a topic on NSAIDs and can be found here.

Topical capsaicin

- Consider topical capsaicin for knee or hand arthritis as an adjunct to core treatment[5] (250 micrograms per gram - Zacin 0.025%) - apply four times a day[6].

Section 4: Opioids

Opioids Aware Key Messages

1. Opioids are very good analgesics for acute pain and for pain at the end of life but there is little evidence that they are helpful for long term pain.

2. A small proportion of people may obtain good pain relief with opioids in the long term if the dose can be kept low and especially if use is intermittent (however it is difficult to identify these people at the point of initiation).

3. The risk of harm increases substantially at doses above an oral morphine equivalent of 120mg/day, but there is no increased benefit.

4. If a patient is using opioids but is still in pain, the opioids are not effective and should be discontinued, even if no other treatment is available.

5. Chronic pain is very complex and if patients have refractory and disabling symptoms, particularly if they are on high opioid doses, a very detailed assessment of the many emotional influences on their pain is essential.

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 the Office for Health Improvement and Disparities (formerly Public Health England).

Duration of treatment

Opioids should be considered for **short- to medium-term** treatment (usually less than 12 weeks) of carefully selected patients with chronic non-malignant pain, for whom other therapies have been insufficient, and the benefits may outweigh the risks of serious harms such as addiction, overdose and death.

SIGN. (2013) Management of Chronic Pain. [Online] Available at: https://www.sign.ac.uk/our-guidelines/management-of-chronic-pain/ *(Accessed: 15 December 2021)*

Additional Best Practice Messages

- Before initiating an opioid, **Best Practice for Opioid Management** should be considered (see appendix).
- **Always start with a plan to stop**.
- Oral route is the preferred route of administration.
- **Do not** use opioids for chronic low back pain, sciatica, headaches, fibromyalgia or chronic primary pain.
- **If an opioid is ineffective DISCONTINUE.**
- **Do not mix opioids, choose one.** Prescribing a combination of opioids is not recommended, there is no analgesic benefit but increases the risk of side effects and of accidental overdose. Research has shown that no improvement in pain relief was found by adding short-acting opioids as rescue use medication for patients using long term opioids (SIGN, 2013).
- Opioids vary in potency. Consider the total daily morphine equivalent dose of the overall amount of opioid being given. See appendix: Morphine Dose Equivalence Tables.
- It is important to carry out **regular reviews.** New opioids should be reviewed within 4 weeks. If stable, reviews should be at least 6 monthly to determine if there is continued benefit from using a particular medication and if the benefit outweighs the side effects, risks and harms.

Cautions

- Use with caution in convulsive disorders, impaired respiratory function (avoid in COPD), inflammatory and obstructive bowel disorders, sleep apnoea, hypotension, current or history of mental health disorder, current or history of substance misuse. For full list of cautions and contra-indications, see BNF.
- The MHRA have warned there is a potentially fatal risk of respiratory depression when used in combination with benzodiazepines or pregabalin.
- Prolonged use of opioids, even at therapeutic doses, may lead to dependence and addiction (see MHRA advice for more information, including information for patients).
- Dose adjustments may need to be made in renal or hepatic impairment. It may be necessary to seek specialist prescribing advice.

Adverse Effects

- Common side effects include nausea, vomiting, constipation, pruritus, dizziness, dry mouth and sedation.
- Long term harms include falls and fractures, endocrine abnormalities (including sexual dysfunction, depression and fatigue), immunosuppression and hyperalgesia.
- Opioids have multiple effects on respiratory physiology.
- Respiratory depression is a much-feared harm associated with the use of opioids. It is most likely to be a potential problem if there has been a large, often unintended dose increase, or changes in formulation or route of administration. The risk is increased when other CNS depressants are concomitantly prescribed (e.g. pregabalin, gabapentin, diazepam).
- Older people are more susceptible to the adverse effects of opioids.
- Driving impairment: It is an offence to drive whilst impaired due to taking drugs (prescribed or not). For further information see: https://www.gov.uk/drug-driving-law. A patient information leaflet can be found here.
- Information for patients about opioid medication can be found at Opioids Aware, Pain Concern and Live Well With Pain.

Codeine, Dihydrocodeine and Tramadol

- For the treatment of mild-to-moderate pain in people who have an inadequate response to paracetamol and/or a non-steroidal anti-inflammatory drug.
- See NICE CKS Analgesia Mild to Moderate for further information on dosages and cautions.
- Tramadol is an opioid and also inhibits the uptake of serotonin and norepinephrine. When starting with a plan to stop, consider that tramadol can be difficult to taper due to withdrawal from two systems. Consider risk of serotonin syndrome when prescribed in conjunction with other serotinergic drugs (e.g. antidepressants). Avoid combination if possible and consider alternative opioids or counsel patient on potential symptoms. More information can be found here.
- Tramadol should be avoided in epilepsy as it lowers seizure threshold.

Morphine

- Oral morphine is first line choice.
- Initially supply one to two weeks of immediate release morphine 5-10mg prn.
- The patient should keep a diary reporting on all doses taken, pain intensity, activity levels, sleep and side effects.
- It is usually expected that pain reduction of at least 30% should be achieved in order to continue prescribing. Functional goals should also be agreed.
- A successful short-term trial does not predict long term efficacy.
- Continuing on immediate release preparations may be most appropriate when the pain is intermittent or variable, switching to MR preparations may be most appropriate for persistent pain through the day and night.
- A trial using fixed doses of MR preparations may be tried, but there may need to be one or more upward dose escalations and therefore the trial would take three weeks or more.
- Agree arrangements for review with patients.
- Best practice is to keep the opioid dose as low as possible.
- Oral liquid morphine is ONLY suitable for short term use. Doses can unintentionally escalate quickly, and it is often difficult to monitor how much a person is taking on a regular basis. If an immediate release morphine preparation is required, tablets (Sevredol) are the preferred option[7].

Buprenorphine Patches

- Should be reserved for patients who have difficulty swallowing, renal impairment, compliance issues or who are unable to tolerate the side-effects of oral morphine. This is due to higher acquisition cost.
- Skin irritation is very common.
- When ‘starting with a plan to stop’, consider that patches may be more difficult to taper than oral preparations.

Fentanyl patches

- Fentanyl is a potent opioid.
- Not to be used in opioid naïve patients.
- When starting with a plan to stop, remember that steps between available strengths are large and tapering is difficult.
- The MHRA have issued this safety warning regarding serious harm associated with fentanyl patches.

Other Opioids

- There is little evidence that one opioid is more effective or associated with fewer side effects than others. Therefore, oral morphine is the first line choice.
- Oxycodone may be used if morphine has been tried but side effects were intolerable, or if there is renal impairment.
- There is no place for rapid onset drugs such as pethidine, transmucosal/sublingual fentanyl or injectable opioids in the management of persistent non-cancer pain.

Tapering and Stopping Opioids

All drugs prescribed for pain should be subject to regular review to evaluate continued efficacy, and periodic dose tapering is necessary to evaluate on-going need for treatment. See appendix ‘Opioid Tapering Guide’.

Summary

- Self-management is important - medication should be considered a small part of a broader plan.
- Consider best practice before prescribing.
- The ‘pain ladder’ is not appropriate for treating chronic pain – do not escalate doses or ‘move upwards’ though more potent opioids.
- Never exceed 120mg morphine equivalent a day.
- Opioids should not be prescribed for chronic primary pain (e.g. Fibromyalgia, chronic primary headache and orofacial pain, chronic primary musculoskeletal pain, chronic primary visceral pain).

Section 5: Antidepressants

- Consider prescribing an antidepressant for chronic primary pain (pain with no clear underlying cause, or pain (or its impact) that is out of proportion to any observable injury or disease).
- These medicines may help with quality of life, pain, sleep and psychological distress – even in the absence of depression. This is off licence use.
- The choice of antidepressants recommended by NICE for this purpose is amitriptyline, citalopram, duloxetine, fluoxetine, paroxetine or sertraline.
- When choosing which antidepressant is most appropriate to use, it is important to consider the individual, the key features of their presentation, any co-morbidities and other prescribed medication.

Section 6: Neuropathic Agents

Introduction

Neuropathic pain is a clinical description (and not a diagnosis) which requires there to be a **lesion or a disease of the nervous system**. This may be established by diagnostic investigations or by knowledge of an underlying disease (e.g., stroke, diabetes mellitus). There are validated tools (e.g., Pain Detect) that indicate the *likelihood* of neuropathy.

NICE recommends that a choice is offered of amitriptyline, duloxetine, gabapentin or pregabalin as initial treatment for neuropathic pain (except trigeminal neuralgia). If the initial treatment is not effective or is not tolerated, offer one of the remaining 3 drugs, and consider switching again if the second and third drugs tried are also not effective or not tolerated. (See NICE CG 173 Neuropathic pain in adults for further guidance).

When choosing which drug is most appropriate to use, it is important to consider the individual, the underlying cause of the pain, any co-morbidities, other prescribed medication and risk factors for dependence.

A 30% reduction in pain symptoms and an improvement in ability to carry out daily activities would indicate a successful trial.

Tramadol is not a first line treatment. Therefore, it should only be considered following advice and guidance from a specialist.

Morphine and other opioids are NOT recommended

NB: Pregabalin and gabapentin are Schedule 3 Controlled Drugs. They both carry a risk of dependence and may be misused or diverted (Advice for prescribers on the risk of the misuse of pregabalin and gabapentin)

Amitriptyline

- 10mg in the evening, increased gradually according to response.
- Usual dose 25-75mg in the evening.

Gabapentin

- Titration to an effective dose can be accomplished over a few days e.g., Day 1: 300mg once a day, day 2: 300mg twice a day, day 3: 300mg three times a day. Continue to increase using increments of 300mg per day given in three divided doses.
- Titrations can be done more slowly and treatment is more likely to succeed if patient led, stopping at the point where the benefits outweigh the side effects.
- Usual total daily dose 900mg to 3600mg in three divided doses.
- MHRA advice (October 2017): 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 and dose adjustments may be necessary in these patients.

Pregabalin

- Initially 150 mg daily in divided doses then increased if necessary after 3–7 days to 300 mg daily in divided doses. Can be further increased after intervals of 3-7 days according to response and tolerability.
- Titrations can be done more slowly, and treatment is more likely to succeed if patient led, stopping at the point where the benefits outweigh the side effects.
- Usual dose from 75mg twice a day (total 150mg daily) to a maximum of 300mg twice a day (total 600mg daily).
- MHRA advice (February 2021): Pregabalin has been associated with reports of respiratory depression, in some cases without concomitant opioid treatment. People at higher risk include those with compromised respiratory function, respiratory or neurological disease, or renal impairment; people taking other CNS depressants (including opioid-containing medicines) and people aged older than 65 years.
- MHRA advice (April 2022): Pregabalin used in the first trimester of pregnancy is associated with a slightly increased risk of major congenital malformations. Therefore, it should be avoided unless clearly necessary, and only if the benefit to the patient outweighs the risk to the foetus. Information for patients can be found here.

Duloxetine

- Usual dose 60mg once daily.
- To reduce nausea and vomiting, can be initiated at 30mg once daily, increasing to 60mg after 2 weeks.

Carbamazepine (Trigeminal Neuralgia only)

- Carbamazepine: Initially 100 mg 1–2 times a day, some patients may require higher initial dose, increase gradually according to response; usual dose 200 mg 3–4 times a day, increased if necessary up to 1.6 g daily.

Lidocaine Plasters

- NHS England have categorised lidocaine plasters as an item which should not routinely be prescribed in primary care due to low clinical effectiveness.

- **Only** to be initiated in primary care for patients with previous herpes zoster infection (post-herpetic neuralgia) who have been treated in line with NICE CG173: Neuropathic pain but are still experiencing pain associated with it.

- May be prescribed in a co-operation arrangement with a pain specialist **in exceptional circumstances** (e.g., other treatment options have failed or cannot be used due to co-morbidities) for chronic localised neuropathic pain.

[1] Faculty of Pain Medicine. (No date) *Opioids Aware*. [Online] Available at: https://fpm.ac.uk/opioids-aware-understanding-pain-medicines-pain/about-pain (Accessed: 15 December 2021)

[2] NICE. (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/chapter/Context (Accessed: 15 December 2021)

[3] NICE. (2020) Analgesia - mild-to-moderate pain. [Online] Available at: https://cks.nice.org.uk/topics/analgesia-mild-to-moderate-pain/management/paracetamol/ (Accessed: 15 December 2021)

[4] NICE. (2020) Low back pain and sciatica in over 16s: assessment and management. [Online] Available at: https://www.nice.org.uk/guidance/NG59/chapter/Recommendations#non-invasive-treatments-for-low-back-pain-and-sciatica (Accessed: 15 December 2021)

[5] NICE. (2020) Osteoarthritis: care and management. [Online] Available at: https://www.nice.org.uk/guidance/cg177/chapter/1-Recommendations#pharmacological-management (Accessed: 15 December 2021)

[6] Joint Formulary Committee. (2021) *British National Formulary*. [Online] Available at: https://bnf.nice.org.uk/drug/capsaicin.html (Accessed: 15 December 2021)

[7] Wickware C, Investigation: should liquid morphine be reclassified? *The Pharmaceutical Journal.* [Online] Available at: https://pharmaceutical-journal.com/article/feature/investigation-should-liquid-morphine-be-reclassified (Accessed: 15 December 2021)

Best Practice in Opioid Management

- ✓ **Consider the individual and the influences on their pain.**

Pain is a complex biopsychosocial phenomenon. In addition to physiological investigations, assess emotional state and social circumstances, past and present. Refer patient to physiotherapy or to psychological therapies if appropriate and make use of social prescribing initiatives.

- ✓ **Encourage engagement in self-management.**

Self-management is important in order to live well with pain – it is helpful to promote self-management from the first appointment, regardless of other investigations or treatments. If medication is prescribed, it should be considered a small part of a broader plan. Reassure patients that physical activity does not usually cause further tissue damage. See https://www.solent.nhs.uk/msk/self-help/ for ideas, videos, leaflets and local/national support groups.

- ✓ **Consider whether opioids are appropriate for the diagnosis and in line with NICE guidelines.**

Do not prescribe opioids for persistent low back pain, sciatica, headaches, fibromyalgia or chronic primary pain.

- ✓ **Manage expectations.**

Opioids may be useful for acute pain and cancer pain over a period of days or weeks. However, they are poorly effective in the long-term, helping only a small percentage of patients. Complete relief from pain is not realistic. Persistent pain is not usually a sign of on-going tissue damage but may indicate a hypersensitive nervous system. Information leaflets, YouTube videos and websites are available to help to explain this to patients.

- ✓ **Agree functional goals.**

The goals of treatment should be to manage symptoms sufficiently to enable patient to improve their social, emotional and physical functioning.

- ✓ **Make a shared decision.**

Agree with the patient whether or not prescribing medication is the best course of action. This decision does not have to happen on the first consultation and the patient may need time to think about it and discuss with family/friend. Patients should understand the potential side effects of the medication, including long term harms of opioids. Patient information leaflets may be useful to support this discussion (e.g. Opioids Aware or Pain Concern).

- ✓ **Consider cautions and risk factors of prescribing opioids.**

Consider co-morbidities and risk factors that may affect the prescribing decision or the dose to be prescribed (e.g. elderly, impaired renal/liver function, COPD, epilepsy). Also consider risk factors for dependence. Look out for drug interactions, particularly with other CNS depressants. There is a risk of respiratory failure, coma and death when opioids are prescribed with benzodiazepines or gabapentin/pregabalin. There is a risk of serotonin syndrome when tramadol is prescribed with an SSRI.

- ✓ **Clinical Records.**

Record the rationale for prescribing, information given to patients, agreed goals of treatment and arrangements for review.

- ✓ **Start low, go slow.**

A small proportion of people may obtain good pain relief with opioids in the long term if the dose can be kept low and especially if use is intermittent. Start with a trial and review after 1-2 weeks to establish if the pain is opioid responsive. One or two dose increases may be appropriate. See Opioids Aware for further detail.

- ✓ **Start with a plan to stop.**

Explain the arrangements for review and circumstances under which the treatment will be discontinued. One prescriber should be responsible for prescribing opioids for the patient where possible. Issue prescriptions as 'acute' and only put onto repeat if functional goals are clearly met. For some patients, a written 'Patient Agreement' may be useful.

- ✓ **Review at least 6 monthly.**

It is important to carry out regular reviews to determine if there is continued benefit from using a particular medication and if the benefit outweighs the side effects, risks and harms. Remember to review functional goals and to enquire about self-management.

References:

Faculty of Pain Medicine. (No date) *Opioids Aware*. URL: https://fpm.ac.uk/opioids-aware [Accessed 15 March 2021]

MHRA. (2020) *Opioids: risk of dependence and addiction*. URL: https://www.gov.uk/drug-safety-update/opioids-risk-of-dependence-and-addiction [Accessed 15 March 2021]

MHRA. (2021) *Pregabalin (Lyrica): reports of severe respiratory depression*. URL: https://www.gov.uk/drug-safety-update/pregabalin-lyrica-reports-of-severe-respiratory-depression [Accessed 15 March 2021]

MHRA. (2020) *Benzodiazepines and opioids: reminder of risk of potentially fatal respiratory depression*. URL: https://www.gov.uk/drug-safety-update/benzodiazepines-and-opioids-reminder-of-risk-of-potentially-fatal-respiratory-depression [Accessed 15 March 2021]

Acknowledgement: Southampton City CCG Medicines Management Team, approved by GP Prescribing Lead March 2021.

NSAID Prescribing Decision Flowchart

Establish need for NSAID.

- NICE guidelines that recommend NSAIDs include: CG177 Osteoarthritis, NG100 Rheumatoid arthritis, NG59 Low back pain and sciatica, NG65 Spondyloarthritis, NG73 Endometriosis, NG88 Heavy menstrual bleeding.
- Consider alternatives such as topical NSAIDs, physiotherapy or an alternative analgesic such as paracetamol.
- Check if the person already takes an NSAID either prescribed or purchased OTC.

Contra indications

- History of hypersensitivity/severe allergic reaction to an NSAID (including aspirin).
- Severe heart failure – NSAIDs may impair renal function.
- Severe renal failure eGFR < 30ml/min/1.73m^2.
- Severe hepatic impairment, liver fibrosis, cirrhosis, or acute liver failure.
- Current treatment for GI bleeding, symptomatic peptic ulcer, or GI perforation/obstruction.
- COX-2s and diclofenac are also contraindicated in people with ischaemic heart disease, cerebrovascular disease, peripheral arterial disease, mild to severe heart failure.

Cautions

- The elderly (increased risk of serious adverse effects).
- History of peptic ulceration (standard NSAIDs contraindicated).
- Inflammatory bowel disease – may increase risk of developing or cause exacerbations of ulcerative colitis or Crohn's disease).
- Renal impairment – avoid if possible.
- Heart failure or hypertension – NSAIDs may impair renal function.
- Hepatitis or cholestasis.
- Women trying to conceive (may impair fertility).

Assess GI and CV Risks (see guidance notes 2 and 3)
Consider if potential benefit of NSAID/COX-2 treatment outweighs risk

No GI or CV risk factors

First line: Ibuprofen up to 1200mg/day **OR** naproxen up to 1000 mg/day
2nd line: celecoxib (if in accordance with NICE)

Add PPI for prolonged use (e.g. osteoarthritis, rheumatoid arthritis, chronic low back pain) and in older people.

GI risk factors

Moderate risk :
Ibuprofen 1200mg per day plus PPI
OR naproxen 1000mg per day plus PPI
OR celecoxib alone

High risk:
Celecoxib plus PPI

CV risk factors

Ibuprofen up to 1200mg per day
OR naproxen up to 1000 mg per day

Do not prescribe NSAIDs in severe heart failure

Ideally avoid NSAIDs in severe renal impairment (eGFR < 30 ml/mi/1.73m^2)

Avoid etoricoxib in uncontrolled hypertension

Avoid long term use where possible and always aim to use lowest effective dose for shortest possible duration

Guidance Notes

1) NSAID Selectivity and Local Formulary NSAIDs

- NSAIDs work by inhibiting cyclo-oxygenase enzymes (COX-1 and COX-2) which then inhibits prostaglandin synthesis.
- COX-1 produces prostaglandins that help to maintain gastric mucosal integrity and platelet-initiated blood clotting. Inhibition of COX-1 is thought to be responsible for GI toxicity.
- COX-2 produces prostaglandins that mediate pain and inflammation. Inhibition is thought to be responsible for anti-inflammatory actions. Inhibition also suppresses prostacyclin – prostacyclin protects endothelial cells, produces vasodilation and interacts with platelets to antagonise aggregation.
- Selective COX-2 shifts the prothrombotic/antithrombotic balance in favour of thrombosis, presenting a CV risk.
- NSAIDs vary in how selective they are for COX-1 and COX-2 pathways.
    - **Non-selective (standard) NSAIDs**: ibuprofen (up to 1200mg per day), naproxen, indomethacin, mefenamic acid.
    - **Non-selective with preference to COX-2**: diclofenac, meloxicam, nabumetone, high dose ibuprofen (2400mg per day).
    - **COX-2 specific**: celecoxib, etoricoxib (amber).
- Ibuprofen (1200mg a day or less) and naproxen (1000mg a day or less) are the preferred choices for safety reasons.
- COX-2 have greater anti-inflammatory action but less favourable safety profiles.
- About 60% of patients will respond to any NSAID; of the others, those who do not respond to one may well respond to another. Therefore, it may be necessary for more than one NSAID to be tried in an individual patient[1].

2) GI Risk Factors

People are at **moderate risk** of GI adverse events if they have 1-2 risk factors.
People are at **high risk** if they have more than 2 risk factors or a history of previously complicated ulcer.

- High dose of an NSAID
- Aged over 65
- History of gastroduodenal ulcer, GI bleeding or gastroduodenal perforation
- Concomitant use of medications that are known to increase likelihood of upper GI adverse events (e.g. anticoagulants, corticosteroids, SSRIs/SNRIs.
- Serious comorbidity such as CV disease, hepatic or renal impairment (including dehydration), diabetes or hypertension.
- Heavy smoking
- Excessive alcohol consumption
- H Pylori infection
- Requirement for prolonged NSAID use

3) Risk Factors for Cardiovascular or Renal Complications (including MI, heart failure, hypertension, renal failure)

- Cerebrovascular disease
- Heart failure
- Ischaemic heart disease
- Peripheral arterial disease
- Renal impairment
- People with risk factors for CV disease (e.g. hypertension, hyperlipidaemia, diabetes, smoking)
- Aged over 65

4) Monitoring

Review regularly

- is it still needed? Can the dose be reduced? Ask about and manage adverse effects.

Monitor blood pressure

- in the elderly, people taking COX-2s and people with hypertension.
- before starting, two weeks after starting treatment, periodically during treatment and after any dose increases.

Monitor renal function

- at least annually.
- for people with renal impairment – 1-2 weeks after starting treatment or increasing the dose.

Monitor liver function

- for those with hepatic impairment or on long-term NSAIDs.

Monitor haemoglobin levels

- in people at high risk of GI adverse effects 1-2 weeks after treatment started.

Consider monitoring blood pressure, renal function and features of heart failure for those with CV risk factors

- 1-2 weeks after starting or increasing the dose and regularly thereafter.

5) Common Drug Interactions

- **Alendronate** – increased risk of upper GI adverse effects
- **ACE inhibitors or A11RAs** – may increase blood pressure, risk of renal impairment ant rarely hypokalaemia.
- **Anticoagulants** – worsening of any bleeding event – avoid NSAIDs if possible (add PPI if unavoidable)
- **Antiplatelets** – increased risk of bleed
- **Corticosteroid** – increased risk of ulceration and/or GI bleed (add PPI).
- **Diuretics** – reduced antihypertensive effects of loop diuretics and exacerbation of congestive heart failure (avoid if possible, monitor if essential), acute renal impairment reported with potassium sparing diuretics (avoid) and reduced antihypertensive effect of thiazides (monitor BP regularly).
- **Fluconazole** – increased peak plasma level of NSAID and therefore higher risk of adverse effects.
- **Lithium** – increased risk of lithium toxicity (avoid if possible).
- **Methotrexate** – increased risk of methotrexate toxicity. Advise reporting of symptoms such as sore throat, dyspnoea or cough.
- **Quinolones** (e.g. ciprofloxacin) – avoid concomitant use in epilepsy or predisposition to convulsions.
- **SSRI/SNRIs** – Increased risk of upper GI bleed (add PPI if concomitant use necessary).

NB: Significant risk of AKI with 'triple whammy' treatment – NSAID + ACE inhibitor/A11RA + diuretic. Avoid if possible.

References and acknowledgements:
[1]Joint Formulary Committee. British National Formulary (online) London: BMJ Group and Pharmaceutical Press www.medicinescomplete.com
All other information taken from:
NICE CKS. NSAIDs – Prescribing Issues. Last updated April 2020. Available at NSAIDs - prescribing issues | Health topics A to Z | CKS | NICE
Adapted from Wirral CCG document with kind permission.

Approximate Equivalent Doses for Oral Opioids and Transdermal Patches.

This guide is intended to **illustrate relative opioid potencies** *and is* **NOT a switching guide.** *If switching advice is needed, see the Faculty of Pain guidance using the link below.*

Potency Ratio: To calculate the daily oral morphine equivalent dose (MED), multiply the dose of opioid by the potency ratio. NB if multiple opioids are taken, the MED is cumulative i.e. the figures are added together to get a total MED.

Drug (oral)	Potency ratio with oral morphine	Oral morphine daily equivalent dose (mg)	
Codeine	0.1	Codeine 30mg	3
		Codeine 240mg	24
Dihydrocodeine	0.1	Dihydrocodeine 30mg	3
		Dihydrocodeine 240mg	24
Tramadol	0.1	Tramadol 50mg	5
		Tramadol 400mg	40
Tapentadol	0.4	Tapentadol 50mg	20
		Tapentadol 400mg	160
Oxycodone	1.5	Oxycodone 10mg	15
		Oxycodone 200mg	300

	Changed weekly			Changed every 3-4 days		
Buprenorphine patch (mcg/hour)	5	10	20	35	52.5	70
Oral morphine equivalent dose (mg/day)	12	24	48	84	126	168

Fentanyl patch strength (mcg/hour)	12	25	50	75	100
Oral morphine equivalent dose (mg/day)	30	60	120	180	240

Values are approximate due to significant inter-individual variation and lack of comprehensive data. All values are taken from Faculty of Pain website: *Opioids Aware. Dose Equivalents and Changing Opioids. Retrieved from* https://fpm.ac.uk/opioids-aware-structured-approach-opioid-prescribing/dose-equivalents-and-changing-opioids

Opioid Tapering Guide

Non-malignant, Non-palliative Chronic Pain

Key Message: If a medication is not providing useful pain relief, it should be tapered or stopped, even if no other treatment is available.

Other indications for opioid tapering/discontinuation:

- Patient request
- >120mg oral morphine equivalent per day
- Opioid trial goal not met
- Opioids not indicated
- Indicators for dependence*
- Underlying condition resolves
- s/e intolerable or impairing function
- Patient receives definite pain relieving intervention
- Strong evidence patient is diverting medication

Precautions:

Pregnancy: Acute opioid withdrawal has been associated with premature labour and spontaneous abortion.

Unstable psychiatric or medical conditions: Although withdrawal does not have serious medical consequences, it can cause significant anxiety and insomnia.

Opioid addiction: Patient may be accessing opioids from other sources, i.e. multiple doctors, 'street'. Referral to drug addiction services may be required.

***** e.g. refusal to explore other treatments, failure to attend appointments for review, early/repeated requests for prescriptions, lost medication, seeking opioids from other prescribers and services, resisting referrals to specialist services, deteriorating social function, alcohol abuse or use of illicit/OTC/internet drugs.

Step 1: Discuss with patient

Explain the reasons for tapering opioids:

Side effects of opioids include constipation, itchy skin, breathing problems, unable to think clearly, low mood, tiredness, low libido, risk of falls and fractures

The level of pain relief from opioids becomes less over time due to tolerance

Opioids increases the risk and the incidence of falls and fractures by over a third

Sometimes opioids can cause your pain to get worse. This is called 'opioid induced

Gradually tapering doses may result in less pain and better mood, function and overall QOL

Written information is available to give to patients – ***'Why does my GP want to reduce my pain killers?'***

Enlist support and understanding from friends and family.

Learn and practice self-management strategies.

What to expect:

- Increased pain and/or joint and muscle aches is associated with withdrawal. This generally subsides within a few days and is lessened if doses are tapered slowly.
- Other withdrawal symptoms – Flu-like symptoms i.e. sweats, chills, headache, joint and muscle pains, diarrhoea, fatigue, anxiety, insomnia, can occur with stopping opioids suddenly. Therefore it is best to decrease slowly over weeks or months.

What if the patient isn't keen? GMC guidance is that doctors have to act in the patients best interests – this may involve reducing an opioid against a patient's wishes. Ensure your reasons are documented.

Step 2: Start the tapering process

Give the patient as much choice as possible over how the opioid reduction is achieved. This gives more ownership and improves engagement and is therefore more likely to succeed.

- The long term goal is to improve pain control and quality of life whilst reducing adverse effects.
- Make it clear that once the opioid dose is reduced, it will NOT be increased.
- There is a risk of overdose if a higher dose of opioid is taken following tapering as tolerance is reduced.

Mixed opioids:	Reduce one at a time
Immediate release or prn doses:	Either keep the frequency the same (e.g. 4 times a day) and reduce the dose each week or maintain the dose and decrease the frequency each week.
MR doses:	A decrease of 10% of the original dose every 1-2 weeks is usually well tolerated.
Slower tapering	Use smaller of reductions (5%) or increase the interval of dose reductions. May be more effective for people who are anxious or psychologically dependent. Also more practical to manage if patient has monthly scripts.
Faster tapering	May be indicated for patients experiencing significant adverse effects or displaying aberrant drug taking or drug seeking behaviours.
Patches:	Reductions in doses of patches are dictated by available strengths and are therefore larger than the other opioids.

The tapers may need to be slowed as the reductions become a higher proportion of the overall dose.

Anxiety and depression often worsen during an opioid reduction as emotions that may have been suppressed start to emerge. Be prepared to manage this if necessary.

Do not treat withdrawal with more opioids or benzodiazepines.

Step 4: Follow-up and review

Review regularly: Ideally before each dose reduction (telephone or face to face). Ask about reduction in side effects, improvement in alertness, mobility, functional goals and emotional wellbeing as well as withdrawal symptoms and pain.

Worsening pain or mood:	Hold the tapering dose. Do not add prn opioids, sedatives or hypnotics.
Withdrawal symptoms:	Hold the tapering dose and consider if the rate need to be slowed.

It may be clinically appropriate to maintain a patient on a reduced dose rather than a complete taper if pain and functional goals are met in line with treatment plan. Review after 3-6 months.

Depression and Anxiety
Steps to Wellbeing: https://www.steps2wellbeing.co.uk/
iTalk: https://www.italk.org.uk

Pain Medicines Management Advice
Vicki Rowell (Pharmacist) – Southampton
vicki.rowell@nhs.net

Drug Abuse and Addiction
Southampton Drug and Alcohol Recovery Service: https://www.changegrowlive.org/content/southampton-drug-and-alcohol-recovery-service-dars
Inclusion Recovery Hampshire: https://www.inclusionhants.org

Other
Live Well With Pain: https://livewellwithpain.co.uk
Opioids Aware: https://www.rcoa.ac.uk/faculty-of-pain-medicine/opioids-aware
'Brainman Stops His Opioids' YouTube Video: https://www.youtube.com/watch?v=MI1myFQPdCE

References: Faculty of Pain Medicine. (No date) *Opioids Aware*. URL: https://fpm.ac.uk/opioids-aware [24 February 2021]
Oxford University Hospitals. (2017) *Guidance for opioid reduction in primary care.* URL: https://www.ouh.nhs.uk/services/referrals/pain/documents/gp-guidance-opioid-reduction.pdf [24 February 2021]. *Adapted from Anglia Medicines Optimisation Team: Tapering Opioids for Non-Malignant, Chronic Pain*