NHS Greater Glasgow and Clyde

CLINICAL GUIDELINE

Opioid Prescribing for Chronic Non Malignant Pain – Medication Safety

A guideline is intended to assist healthcare professionals in the choice of disease-specific treatments.

Clinical judgement should be exercised on the applicability of any guideline, influenced by individual patient characteristics. Clinicians should be mindful of the potential for harmful polypharmacy and increased susceptibility to adverse drug reactions in patients with multiple morbidities or frailty.

If, after discussion with the patient or carer, there are good reasons for not following a guideline, it is good practice to record these and communicate them to others involved in the care of the patient.

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Important Note:

The Intranet version of this document is the only version that is maintained.
Any printed copies should therefore be viewed as 'Uncontrolled' and as such, may not necessarily contain the latest updates and amendments.

NHSGGC Guideline: Medication Safety in Opioid Prescribing for Chronic Non Malignant Pain

NHS Greater Glasgow and Clyde

Updates from last guideline:

Focus has changed from how to initiate opioids, to how to review, rationalise, reduce and stop opioids while supporting the patient

Patients prescribed high dose opioids ≥ 50mg daily morphine, or equivalent, should be reviewed at least annually, as the risk of harm significantly increases at this dose or above[4].

Pain specialist advice or review should be sought at doses >90 mg/day morphine equivalent.

Other changes are:-

- updates to the management of side effects
- new flare up management advice
- inclusion of a link to a calculator to aid tapering and stopping of strong opioids
- addition of advice on naloxone prescribing
- advice on monitoring for signs of adrenal suppression

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Key Messages

This document provides guidance for prescribers on the management of patients with chronic, non-malignant pain. It contains guidance when reviewing patients already on established/historic prescribed opioid medication and also when discussing with patients the possible initiation of opioid medication.

The maximum recommended daily dose of oral opioid morphine or equivalent remains at 90mg /24 hours.

Joint review between the patient and healthcare professional (HCP) is to ensure prescriptions are appropriate and safe, and to agree a treatment plan. Proactive reviews, when patients are not experiencing crises or acute illness, are just as important in ensuring appropriate opioid prescribing and use. The frequency of these reviews will vary with the patient and their needs.

The guideline highlights the Faculty of Pain Medicine advice against the use of the World Health Organisation (WHO) 3-Step 'Ladder' in non-cancer pain. Although a stepped approach is sensible, the benefits of opioid use should not be determined only by the patients reported pain intensity.

If initiating opioids, the suggested opioid trial period is 2 weeks, using immediate acting strong opioids instead of long acting opioids for this purpose (the advice to use long acting opioids for the longer term pain management remains the same as before within the reduced maximum daily dose as indicated above).

Whilst these recommendations are suitable for the majority of patients, prescribers should use their clinical judgement to optimise each patient's treatment.

This guidance should be used in conjunction with local and/or national guidance on the assessment and treatment of pain (e.g. guidelines produced by SIGN, NICE, the British Pain Society and the Faculty of Pain).

Users should also refer to local formulary and BNF to inform dosing and prescribing decisions for individual patients (taking into account any precautions, contraindications, dose adjustments and adverse effects of pharmacological treatment).

The guideline highlights the Faculty of Pain Medicine advice against the use of the World Health Organisation (WHO) 3-Step 'Ladder' in non-cancer pain. Although a stepped approach is sensible, the benefits of opioid use should not be determined only by the patients reported pain intensity.

Recommended named strong opioids for prescription have been removed to allow for flexibility and changes in local formulary advice. Other changes include updates to the management of side effects, new flare up management advice and inclusion of a link to a calculator to aid tapering and stopping of strong opioids.

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Do's and Do not's

DO:

- ✓ Manage chronic non-malignant pain using non pharmacologic therapy and non-opioid pharmacologic therapy before considering opioids
- ✓ Be aware that the evidence for use of opioids is mainly from use in acute pain and pain at the end of life, there is little evidence of benefit in long term use for chronic pain regardless of diagnosis
- ✓ Be aware that the risk of harm increases substantially at doses above oral morphine equivalent of 90mg/day (Oxycodone 45mg/24 hours and Transdermal fentanyl patch 25mcg/hr)
- ✓ Be aware that opioids are associated with significant respiratory depression. Opioids are relatively contraindicated in sleep apnoea and also concurrent benzodiazepine and gabapentinoid prescription
- ✓ Be aware that opioids are associated with common and significant side effects. These include nausea, vomiting, constipation, pruritus, dizziness, dry mouth and sedation
- ✓ Consider longer term side effects including endocrine suppression manifesting as reduced libido, erectile dysfunction, reduced fertility and osteoporotic fractures
- ✓ Adrenal insufficiency is a possible side effect of opioid prescription for more than 6 months. Routine testing is not recommended if the patient is well. However, if the patient has symptoms of adrenal insufficiency

(e.g. fatigue, weight loss, low blood pressure, fainting, increased thirst, low mood) then an early morning cortisol test is recommended, with referral to endocrinology if cortisol is low.'

- ✓ Do explain the reasons for your prescribing decisions to the person
- ✓ Do document all discussions carefully and give a copy to the person
- ✓ Taper and stop opioids in patients who are not benefiting from their use even if there is no other alternative effective treatment, as the continuing use of opioids can be harmful
- ✓ Offer the person a second opinion
- ✓ Use opioids in conjunction with non-medication therapies and self-management strategies
- ✓ Be aware of the potential for Opioid Induced Hyperalgesia (OIH) manifesting as a paradoxical worsening of pain with increasing opioid dose. NHS Ayrshire and Arran have an excellent video on hyperalgesia that is worth sharing with patients https://www.youtube.com/watch?v=pdpfFUAeTME&t=3s

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DO NOT:

- Do not prescribe a medicine if you don't think it is in their best interest
- Do not prescribe opioids for patients with concurrent significant mental health problems, drug dependency or addiction
- Do not prescribe opioids for patients with opioid insensitive pain e.g. no analgesia from weaker opioids
- Do not prescribe opioids for chronic primary pain. ICD-11 gives examples of chronic primary pain, including fibromyalgia (chronic widespread pain), complex regional pain syndrome, chronic primary headache and orofacial pain, chronic primary visceral pain and chronic primary musculoskeletal pain
- Do not prescribe opioids for patients currently taking benzodiazepines and other sedative medication
- Do not prescribe opioids for patients with active illicit drug abuse (including those of prescription drugs). There should be a collaborative approach to management between primary care, Addiction services and the Pain Management service.

When to refer to a pain clinic

Consider referring the following patients to the pain service for advice (please note that these patients should also fulfil the criteria for referral to the Pain service in the first instance). Referral Criteria: Pain Management Home (paindata.org)

Patients with problem prescription opioid drug use if willing to engage in drug reduction

Patients already in the process of weaning opioid medication but are having difficulty with it

Patients taking an oral morphine equivalent of >90mg per day

Switching opioids is complex and beyond this guideline for primary care management of opioids for non-malignant pain. Please seek specialist advice if considering an opioid switch.

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Supporting People already taking Opioids

For more information, see Overview | Medicines associated with dependence or withdrawal symptoms: safe prescribing and withdrawal management for adults | Guidance | NICE3

At all stages of prescribing and withdrawal management, aim to foster collaborative, trusting and supportive relationships with people taking an opioid.

Provide information on non pharmacological forms of pain management – see resources in Appendix 6

Follow the recommendations in the NICE guideline on patient experience in adult NHS services, particularly those relating to:

- continuity of care and relationships
- enabling patients to actively participate in their care
- tailoring healthcare services to each person.

Ask people whether they would like to have support during appointments from a family member, carer or other person close to them.

Review the decision to continue to prescribe opioids taking in to account individual risk factors

When making decisions about prescribing medicines, determine whether there are any factors that might increase the person's risk of developing problems associated with dependence, and discuss these with them.

Factors include:

- a comorbid mental health diagnosis
- a history of drug misuse
- not having a clear, defined diagnosis to support the prescription
- taking an opioid together with a benzodiazepine.

Use the NICE guideline on shared decision making to support people when making decisions. Overview | Shared decision making | Guidance | NICE

Recognise and acknowledge that decisions about medicines can be difficult for a person who is in distress. If a shared decision about continuing a medicine cannot be reached and the medicine is not in the person's best interests, follow the advice on 'handling patient requests for medicines you don't think will benefit them' in the General Medical Council guidance: good practice in prescribing and managing medicines and devices. Good practice in prescribing and managing medicines and devices - ethical guidance summary - GMC (gmc-uk.org)

Opioid information leaflets and tapering pack are available in the Resources section at the end of this guideline.

DEPRESCRIBING: HOW TO TAPER AND STOPPING OPIOIDS

Indications for Stopping or Tapering (Weaning) Opioids:-

- Patient request
- No benefit (this means less than 30% pain reduction and/or no meaningful functional improvement)
- Opioid trial goals not achieved
- Pain resolves or remains stable for > 3 months
- Intolerable, adverse or harmful side effects
- Patient receives other, definitive treatment for pain
- Intolerable, adverse or harmful side effects
- Overdose risk increased e.g. deteriorating medical complication, polypharmacy with other CNS depressants such as benzodiazepines, gabapentinoids, hypnotics, sedating antidepressants, alcohol or illicit drugs
- Aberrant behaviour with opioids
- Morphine equivalent doses above 90mg/day (please see table for opioid conversion examples) or visit Pain Management Opioid Dose Converter (paindata.org)

Step 1: Assess risk Consider seeking advice if patients have one or more of the following:-

- History of mental health including depression and anxiety
- History of substance, alcohol or prescription drug overuse
- Multiple opioids or multiple formulations of opioids
- Polypharmacy with other CNS depressants
- High doses (morphine equivalent > 90mg/day) or more potent opioids. Conversion calculator for morphine equivalent doses of other opioids Pain Management Opioid Dose Converter (paindata.org)
- PADT is a useful patient review tool: PainAssessmentandDocumentationTool.pdf (krhamaine.com)

Consider referral at any stage to Pain Services for optimisation of non-pharmacological pain management strategies and /or education & support for opioid tapering

Step 2: Prepare patient

- Discuss risks of long term opioids and benefits of tapering
- Discuss possibility of mild opioid withdrawal symptoms (including increased pain) but reassure these are transient and can often be managed symptomatically if required
- Discuss tapering goals and plan frequency of review
- Agree dispensing intervals
- Where possible, consolidate all opioids into one single modified release preparation
- Do not prescribe PRN doses
- Optimise non-opioid and self-management elements of pain management
- Provide written information on opioid tapering e.g.
- opioid-tapering-v0-12.pdf (mcmaster.ca)
- https://www.therapeutics.scot.nhs.uk/wp-content/uploads/2021/12/Opioid-Medication-Leaflet-Digital..pdf

Step 3: Plan taper

- Document decision to taper/stop and agree taper schedule
- In most cases, reasonable to reduce by 10% of original dose every 1-2 weeks as tolerated (higher risk patients may require smaller decrements or longer intervals between dose reductions). Use taper calculator if required: https://www.paindata.org/taper.php
- There should be planning for short term pain flares and for any opioid withdrawal effects
- Emotional impact: it is helpful for the patient to be aware that anxiety is to be expected during opioid reduction, and that this can be managed together. Resources such as patient information leaflets and those found on NHS inform https://www.nhsinform.scot/illnesses-and-conditions/mental-health/anxiety can be useful to help individuals manage these symptoms
- Monitor patient during taper. If experiencing withdrawal effects then rate of reduction should be slowed down.
- Consider additional support e.g. psychological, drug support service, alcohol service
- Non-pharmaceutical approaches should be encouraged, either alone or in conjunction with medicines as agreed with the individual and as part of their overall treatment plan
- A list of helpful patient resources can be found at the end of this document
- Tapering and stopping high dose opioids e.g. morphine equivalent of >300mg/day, long term opioids e.g. > 10 years or very potent opioids e.g. Fentanyl patches may require slower tapers and additional support from a combination of specialist services

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Step 4: Review

- Frequency of review depends on rate of taper and degree of support required e.g. if reducing every 1-2 weeks, monthly review may be appropriate
- Ideally, same clinician will review patient each time prior to next reduction
- Ask about improvement in function and reduction of side effects as well as pain and withdrawal symptoms
- Ask about mental health symptoms

Trouble shooting

- If mood deteriorates, anxiety increases or pain escalates, hold the current opioid dose for a further 3-4 weeks. Avoid reversing the taper or adding in PRN opioids or sedatives. Instead, work with them closely to manage their pain and mood using non-drug related strategies, or consider adjuvant treatments such as antidepressants
- If withdrawal symptoms are evident, hold the current opioid dose until completely settled. Most symptoms settle within a couple of weeks but some can persist for several months. Reassure patient that although uncomfortable, these are rarely medically serious. Consider prescribing symptomatically e.g. smooth muscle relaxants, anti-diarrhoeal, anti-emetic, paracetamol or NSAIDs
- Unsuccessful taper (patient defaults from treatment plan or tapering becomes clinically inappropriate). Stabilise on lowest appropriate maintenance dose and revisit in 3-6 months.

Guidance if deciding to initiate an opioid in a patient not already prescribed strong opioids

Before Opioid Trial

Step 1: Biopsychosocial assessment of diagnosis, pain and function

- Avoid strong opioids in chronic primary pain, low back pain, headache and fibromyalgia, and in cases where there is no specific diagnosis 2
- Assess baseline pain and function using, for example, the Brief Pain Inventory
- This includes screening for major medical co-morbidities and psychosocial factors 1

Step 2: Consider Non-Opioid Therapies

- Non opioid medication including topical therapies, graded exercise, and psychological support strategies – see Appendix 6 Resources section
- If neuropathic pain is present, consider neuropathic pain treatment or refer to GGC Neuropathic Pain Guidelines: ggc-neuropathic pain guideline.pdf (paindata.org)

Step 3: Assess Risk of Harm of Misuse from Using Opioids

- Individuals at increased risk of misuse BEFORE starting opioids are those who:
- Have a history of recreational drug misuse or alcohol dependence.
- Have a history of, or are currently experiencing, mental health problems.
- Have a history of preadolescent sexual abuse.
- Consider risk factors for misuse and assess using a validated scoring tool such as The Opioid Risk Tool: https://www.drugabuse.gov/sites/default/files/files/OpioidRiskTool.pdf

Step 4: Talk to Patient About Treatment Plan

- Set realistic goals for pain reduction typically aim for approximately 30% pain reduction with functional improvement, or pain intensity rating to justify ongoing opioid use
- Discuss benefits, side effects and risks of strong opioids and provide information Opioid-Medication-Leaflet-Digital..pdf (scot.nhs.uk)
- Describe the opioid trial including upper limit of dosing
- Set criteria for stopping opioid such as failure to meet goals, no clear evidence of a dose response, or rapid development of tolerance requiring higher doses of opioids
- Plan review appointments, initial assessment should be 1-2 weeks from starting opioid, thereafter at appropriate regular intervals
- Document details of discussion with patient, including acceptable behaviour in relation to medication use as well as driving (see Appendix 2)

- Check patient understands treatment plan
- Ensure patient understands safe storage of medication.

Starting an Opioid Trial

Remember: when prescribing, start low, go slow

Trial period should be limited to 2 weeks if possible with review by prescriber or delegated member of team

- Continue with analgesia such as paracetamol/NSAIDs if appropriate
- For patients currently on analgesia containing codeine or dihydrocodeine, discontinue, and prescribe immediate release **oral morphine equivalent** at the lowest effective dose e.g. **morphine 5- 10mg** (max 4 hourly). *** MORPHINE is usually the first strong opioid of choice**
- For patients currently on tramadol, wean off, and prescribe immediate release **oral morphine equivalent** at the lowest effective dose e.g. morphine 5- 10mg (max 4 hourly)
- Prescribe a limited (e.g. 1-2 week) supply of immediate release **oral morphine equivalent** tablets initially
- Use immediate release preparations for the trial to determine the dose range, then convert to equivalent long-acting preparation as soon as possible at end of trial.
- In patients with significant renal dysfunction, refer to Appendix 3 for dose adjustments
- **In frail or elderly patients, dosage should be guided by individual circumstances and co-morbidities, and not by guideline dose recommendation**

During Opioid Trial

- Encourage the patient to keep a diary during the opioid trial
- Assess within 1-2 weeks of starting trial using, for example, using the PADT tool: PainAssessmentandDocumentationTool.pdf (krhamaine.com)
- Assess pain and function compared to baseline at 2 weeks
- If morphine is not tolerated despite treatment of side effects, recommence trial using an alternative immediate release oral morphine equivalent as per local formulary recommendations
- Observe for signs of aberrant behaviour, drug misuse and addiction using the PADT tool. If suspicious, urine screen for relevant substances can be done. PainAssessmentandDocumentationTool.pdf (krhamaine.com)
- In our clinical experience, if no clinically meaningful improvement in pain and function at a dose of 40mg oral morphine equivalent in 24 hours then it is very unlikely that continuing opioid therapy will be helpful. It is also unlikely that an alternative opioid will be effective. See Faculty of Pain advice5. Wean and discontinue the opioid medication. Refer to Deprescribing Advice for advice on tapering.
- Do not continue prescribing opioids if the trial has failed even if there is no alternative analgesic
- If there is improvement in pain symptoms and/or function, patients could be considered for continuing opioid prescription, for a planned period of time.

Continuing Opioid Prescribing (After a Successful Trial)

Aim to establish the patient on a long-acting opioid with no immediate release preparation for stable chronic pain. For those patients with mild breakthrough pain consider non opioids and weak opioids.

- Use oral route; do not initiate subcutaneous, intravenous or any parenteral route of administration
- Use the lowest possible dose. Avoid doses >90mg/day morphine equivalent (specialist advice required if doses are escalated beyond this threshold)
- There are no high quality randomised controlled trials to suggest that one opioid is more effective than another. **If there is NO clinical benefit with a full trial of one opioid, we would not encourage further opioid trials in primary care – seek expert advice.**
- Arrange regular review e.g.3-6 monthly, ideally with a single prescriber. Consider using the PADT tool: PainAssessmentandDocumentationTool.pdf (krhamaine.com)
- At each review, aim for use of the lowest possible dose and consider tapering if possible
- Agree a plan with the patient to manage flare ups. See Appendix 1.
- Be aware of side effects resulting from continuing use of opioids. These include tolerance, withdrawal, cognitive impairment, weight change, reduced fertility and irregular periods, erectile dysfunction, hyperalgesia, depression, dependence, addiction, reduced immunity, osteoporosis and constipation
- Follow this link for further information on dependence and addiction: drugs-opioids.pdf (paindata.org)

- If hypogonadism is suspected: consider measuring sex hormones. If abnormal seek advice from your local endocrine clinic and discuss tapering of the causative drug.
- Adrenal insufficiency is a possible side effect of opioid prescription for more than 6 months. Routine testing is not recommended if the patient is well. However, if the patient has symptoms of adrenal insufficiency (e.g. fatigue, weight loss, low blood pressure, fainting, increased thirst, low mood) then an early morning cortisol test is recommended, with referral to endocrinology if cortisol is low.
- Consider prescription of naloxone. See Appendix 5.

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APPENDICES

Appendix 1 - Flare-up Management

Flare ups are common in people with chronic pain. Although flare ups are often distressing and frightening, they rarely indicate new damage.

- Advise patient to continue taking medication as prescribed.
- If short term changes to the patient's medication are required, then a management plan needs to be agreed between patient and the healthcare provider and be adhered to. Return to normal medication when flare up has settled.
- Reduce exercise and normal activity, but maintaining some gentle activity as this is important.
- Suggest patient ask others to help during the flare up and gradually get back to usual levels of activity.
- Advise patient to learn deep breathing exercises and relaxation techniques. Check for negative thoughts and "catastrophic" thinking. Hot water bottles, heat packs, electric blankets, warm baths or Jacuzzis can sometimes help.
- Encourage the patient to eat regularly and have a few meals in the freezer that can be heated up.
- Distraction is often helpful – TV, reading, having someone to talk to etc.
- Return to normal activities and exercise when flare up has settled.

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- Encourage patient to develop a flare up management plan that works for them. They should start the plan as soon as the flare up begins.

  https://paindata.org/documents/self-management-persistent%20pain%20english.pdf

  https://www.nhsinform.scot/illnesses-and-conditions/mental-health/mental-health-self-help-guides/chronic-pain-self-help-guide

  https://painconcern.org.uk/wp-content/uploads/2020/09/Manage-Your-Pain-English-v.2.pdf

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Appendix 2 - Driving

Information on prescribed medications and driving can be found at:-
https://www.gov.uk/drug-driving-law

https://www.gov.uk/government/collections/drug-driving#table-of-drugs-and-limits

Here is a useful guide for health care professionals:

Drug+driving+-+guidance+for+healthcare+professionals (paindata.org)

Here is the GG&C Patient Information leaflet for Opioids which has a section on driving:

drugs-opioids.pdf (paindata.org)

Appendix 3 - Opioids & Renal Impairment

For those patients with moderate to severe renal impairment (see table) the likelihood of opioid toxicity with any opioid increases. In general, the following guiding principles should be followed:

- Use all opioids with extreme caution as accumulation may occur.[1]
- Use the smallest effective dose and lengthen the dosing frequency.[1]
- Titrate cautiously from the lowest possible dose every 3-4 days using immediate release preparations.[1]
- Consult the renal team or pain team for specialist guidance.
- Consider prescribing naloxone[1] (see Appendix 5)

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Renal Function GFR mL/min [CKD Stage] [1, 2]

Opioid	>50[1-2]	20-50 [3A/B]	10-20 [4]	<10 [5]
Codeine	30 – 60 mg up to 4 -6 hourly [1, 2, 3] Maximum daily dose of codeine should not exceed 240mg [2, 3]		Start at 50% of normal dose, titrate cautiously [1]	Start at 50% of normal dose and extend dosing interval to 6 hourly, titrate cautiously [1]
Dihydrocodeine	30 mg up to 4 -6 hourly [1, 2, 4] Maximum dose in 24 hours 180mg (6 tablets) [2, 4]		Start at a small dose and titrate cautiously [1]	Start at a small dose and titrate cautiously [1]
Tramadol	50–100 mg up to 4 hourly; maximum 400 mg daily [1, 2, 5]		50–100 mg every 8 hours initially and titrate dose as tolerated [1]	50 mg every 8 hours initially and titrate dose as tolerated [1] NB: Manufacturer does not recommended in severe renal [2, 5]

Morphine	IR: 5–20 mg every 4 hours [1]	75% of normal dose [1]	Use small doses (50% of dose), e.g. 2.5–5 mg and extended dosing intervals. Titrate according to response [1]	Use small doses (25% of dose), e.g. 1.25–2.5 mg and extended dosing intervals. Titrate according to response [1]
	MR: according to preparation every 12 or 24 hours [1]	Avoid slow release oral preparations in severe renal disease as any side effects may be prolonged [1]		
Oxycodone Limited accumulation of metabolites in renal failure compared with morphine [1]	IR: 5 mg 4–6 hourly MR: 10 mg 12 hourly	Start at 75% of normal dose, titrate cautiously[1]		Start with small doses e.g. 1.25 mg and titrate cautiously [1]

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Opioid	>50[1-2]	20-50 [3A/B]	10-20 [4]	<10 [5]
Fentanyl (Topical) NB: Not recommended in opioid-naïve patients [6]	Initially 12–25 mcg/ hour, patches changed every 72 hours increased according to response.[1]	50 - 75% of normal dose e.g. 12 mcg[1] Observe carefully for signs of toxicity [2, 6]		50% of normal dose e.g.: 12 mcg [1] Observe carefully for signs of toxicity [2, 6]
Hydromor-phone *Licenced only for severe cancer pain [7]	IR: 1.3 mg 4 hourly, increas-ing dose as required [1, 2, 7] MR: 4 mg 12 hourly, increas-ing dose as required [1]	Start at lowest possible dose and titrate cautiously with IR capsules [1, 2, 7]		
Tapentadol *Only MR preparation SMC licensed for chronic pain. IR licenced only for moderate to severe acute pain [2, 8]	Normal dosing IR: 50 mg every 4–6 hours, maximum dose 600 mg daily [1] MR: Initially 50 mg twice daily, maximum 500 mg daily [1]			Start at lowest possible dose and titrate cautiously [1] Not recommended by manufacturer in severe renal impairment due to lack of studies [1, 2, 8]

Buprenorphine *Transtec not SMC approved	Transdermal: • Transtec: 35–140 mcg/hour every 96 hours[1] • Butrans: 5–40 mcg/hour, change patch every 7 days [1]
	• In opiate naïve patients start with the lowest patch size and increase cautiously [1]
Alfentanil/ Pethadine/ Diamorphine	Not recommended for chronic non-malignant pain.

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Renal Appendix References:

1. The Renal Drug Database [Internet]. Renaldrugdatabase.com. 2021 [cited 18 August 2021]. Available from: https://renaldrugdatabase.com/
2. Individual drug monographs - electronic medicines compendium (emc) [Internet]. Medicines.org.uk. [cited 18 August 2021]. Available via: https://www.medicines.org.uk/emc/
3. Alternatively follow the links directly:
4. Codeine Phosphate 30mg Tablets - Summary of Product Characteristics (SmPC) - (emc) (medicines.org.uk)
5. Dihydrocodeine 30mg Tablets - Summary of Product Characteristics (SmPC) - (emc) (medicines.org.uk)
6. Tramadol 50 mg capsules - Summary of Product Characteristics (SmPC) - (emc) (medicines.org.uk)
7. Matrifen 12 micrograms/hour Transdermal patch - Summary of Product Characteristics (SmPC) - (emc) (medicines.org.uk)
8. Palladone capsules 1.3 mg - Summary of Product Characteristics (SmPC) - (emc) (medicines.org.uk)
9. Palexia 50 mg film-coated tablets - Summary of Product Characteristics (SmPC) - (emc) (medicines.org.uk)
10. Temgesic 200 microgram Sublingual tablets - Summary of Product Characteristics (SmPC) - (emc) (medicines.org.uk)

Appendix 4 - How To Manage Common Side Effects

Opioid-associated side effects should be anticipated and appropriate counselling about common side effects and their management should be provided to patients before the first prescription.

The PADT tool can be used to assess incidence of side effects such as nausea, constipation, itch, mental cloudiness and fatigue.
PainAssessmentandDocumentationTool.pdf (krhamaine.com)

Patients should be warned of the likelihood of enhanced effects and risks associated with concomitant use of other medicines and substances with sedative properties, including alcohol.

Constipation

Dietary advice should include general recommendations such as sufficient fluid intake, physical activity, and regular intake of dietary fibre. The majority of patients taking opioids for moderate to severe pain will develop opioid induced constipation. Tolerance does not develop to this side effect and constipation tends to persist throughout treatment and may require long-term management.

Refer to local formularies and prescribe a stimulant laxative with a stool softener. In refractory cases, if a patient has failed to respond to adequate trials of two classes of laxatives, consider a peripheral acting opioid antagonist[6].

Nausea & Vomiting

Nausea and vomiting are common when starting on opioids but generally tolerance develops after 5-10 days[1]. It is recommended that patients commencing on an opioid for moderate to severe pain should have access to prophylactic anti-emetics to be taken if required. Refer to local formularies for treatment of choice[7].

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Itch & Sweating

Pruritus occurs infrequently in patients who receive systemic opioids and is thought to be caused by either a central mechanisms or by cutaneous histamine release. Therefore consider antihistamines. If dry skin is also a problem, consider emollients.

If in initial opioid trial itch is an issue, consider an opioid rotation or a reduction in dose if the itch persists.

Hyperhidrosis can occur with opioids. Review concurrent medications and consider dose reduction or rotation where possible. Anecdotal evidence exists for the use of oral anti-cholinergic, clonidine or anti-histamine medication trials in cases where the opioid cannot be reduced or stopped8.

Appetite

Clinical experience suggests that continuing use of opioids may be associated with loss of appetite and hence weight loss. If it is suspected that those symptoms are solely related to opioid therapy then consider weaning the opioid medication.

Withdrawal

Opioid withdrawal symptoms are well known and include:

- Low energy, Irritability, Anxiety, Agitation, Insomnia.
- Runny nose, Teary eyes. Hot and cold sweats, Goose bumps.
- Muscle aches and pains.
- Abdominal cramping, Nausea, Vomiting, Diarrhoea.

The patient may require further information, support and advice. If withdrawal symptoms are induced by weaning/taper then consider reducing taper % or make slower adjustments to allow symptoms to subside.

Respiratory Depression

Respiratory depression is a much-feared harm associated with the use of opioids9. It is mostly a concern in acute pain management where patients have not developed tolerance. For persistent pain 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.

Fatalities have been reported in patients with obstructive sleep apnoea who are prescribed opioids and sleep apnoea may be a relative contraindication to opioid therapy. This is particularly important if patients are taking other central respiratory depressants such as benzodiazepines.

If opioids are prescribed to patients with obstructive sleep apnoea they will need up to date assessment of nocturnal respiratory function and should be compliant with therapy for this e.g., continuous positive airway pressure.

Patients with sleep apnoea being prescribed opioids will need regular and detailed assessment of treatment.

Appendix 5 - Naloxone Co-Prescription

Background	• Use of opioid pain medication can present a risk of serious adverse effects including death by opioid overdose. • Naloxone is a non-selective, centrally-acting opioid antagonist indicated for use in an emergency to reverse severe respiratory depression induced by opioids. It can be administered by anyone witnessing an opioid overdose for the purpose of saving life. • Consideration should be given to prescribing naloxone to any patient at risk of opioid overdose. • Before prescribing naloxone patients and/or their families/care providers should be given detailed information on the symptoms of opioid overdose, how to respond if overdose is suspected and how to use the prescribed formulation of naloxone
Risk Factors	• Prescribed doses > 50mg morphine equivalence/day. • Using other sedating medication/substances e.g. benzodiazepines, gabapentinoids, z-drugs, anti-depressants, alcohol and illicit drugs. • Co-existing medical conditions such as hepatic, renal or respiratory disease, sleep apnoea, HIV, obesity and those with depression, anxiety or prior history of non-fatal overdose. • Aged > 65 years • Suspected of not taking their medication as prescribed. This could include those who frequently request to increase doses or over-ordering of prescriptions.

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Exclusions	• Palliative care • Lives alone – this may not be an exclusion as may have family, friends or carers available.
Potential Conversation Starters	• "Do you have any concerns about the amount of pain medicine you are taking?" • "What does the word overdose mean to you?" - allows you to explore the difference between accidental and deliberate • "Have you heard of naloxone?" - This may give you an idea of their baseline knowledge and any beliefs associated with naloxone/patient group.

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Provide information about naloxone (with their permission)

Elicit/Provide/ Elicit technique may be useful

- Explain their personal risk of accidental overdose.
- Explain how naloxone works (blocks the opioid receptors in the brain for about 20-30mins. Doesn't remove opioids out the body).
- Explain that you want to make them as safe as possible. This can be done by a medication review, support to explore a gradual slow opioid reduction (or other medicines that increase risk).
- Normalise it – e.g. "America and other places in Scotland the co-prescription is already being done. This is not new." "It's like using a seatbelt – we put one on every time we drive in a car to reduce risk if we crash. Doesn't mean we are going to crash."
- Naloxone is available in a choice of two formulations for administration in non-medical settings:
- Prenoxad® 1mg/ml solution for injection in a prefilled syringe, administered as an intramuscular injection
- Nyxoid® 1.8mg nasal spray solution in a single dose container (Nyxoid is restricted to use in accordance with NHSGGC Take-Home Naloxone programme, only when the use of naloxone injection is inappropriate)
- Before prescribing naloxone patients and/or their families/care providers should be given detailed information on the symptoms of opioid overdose, how to respond if overdose is suspected and how to use the prescribed formulation of naloxone.
- Supporting information for both clinicians and patients, such as detailed training videos and printable patient information leaflets (PILs) are available via the manufacturers' websites
- For Nyxoid: www.nyxoid.com (please copy and paste into browser)
- For Prenoxad: http://www.prenoxadinjection.com/

Overdose identification and administration of naloxone **Use "teach back"** or **"chunk and check" method**	• How to identify overdose: • UNCONSCIOUS OR NOT RESPONDING: Not waking up or responding to voice commends or touch. Shake shoulders. Speak clearly in both ears • APPEARANCE: Blue/grey skin and lips. Clammy. Very small/ pinpoint pupils • BREATH: Very slow or irregular breathing or no breathing at all. May also be a rasping or snoring sound • How to respond to overdose: • A patient information card can be accessed at www.nyxoid.com • When and how to give Prenoxad Injection - Client). • Inform them that naloxone is not a substitute for emergency care • Provide them with a printed patient information leaflet • Inform them that, if needed, their family member/friend/care provider can make contact if need counselled on administration. • Remind them to store naloxone out of reach of children and to request new prescription for it when it goes out of date.
Supplementary training materials	• Nyxoid training videos can be accessed at www.nyxoid.com • Prenoxad http://www.prenoxadinjection.com/medical/how-to.html

Resources and References

Useful Resources

- Chronic Pain - NHSGGC
- Pain Management Home (paindata.org)
- https://www.fpm.ac.uk/faculty-of-pain-medicine/opioids-aware
- Opioid tapering resource pack Opioids and chronic pain - Oxford University Hospitals (ouh.nhs.uk)
- Opioid Medication Leaflet: Opioid-Medication-Leaflet-Digital..pdf (scot.nhs.uk)
- Useful links – Lothian Chronic Pain Service (nhslothian.scot)
- Home - Flippin' Pain
- Ten Footsteps to Living Well with Pain - Live Well with Pain

Other useful guidelines

- Dowell D, Haegerich TM, Chou R. CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016. MMWR Recomm Rep 2016;65(No. RR-1):1–49. DOI: http://dx.doi.org/10.15585/mmwr.rr6501e1
- Strategy-Chronic-Pain-Quality-Prescribing-for-Chronic-Pain-2018.pdf (scot.nhs.uk)
- https://www.therapeutics.scot.nhs.uk/wp-content/uploads/2018/04/Polypharmacy-Guidance-2018.pdf

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3. Medicines associated with dependence or withdrawal symptoms: safe prescribing and withdrawal management for adults | Guidance | Overview | Medicines associated with dependence or withdrawal symptoms: safe prescribing and withdrawal management for adults | Guidance | NICE
4. https://www.therapeutics.scot.nhs.uk/wp-content/uploads/2021/12/Draft-Opioid-Guide.pdf
5. https://fpm.ac.uk/opioids-aware-structured-approach-opioid-prescribing/opioid-trial
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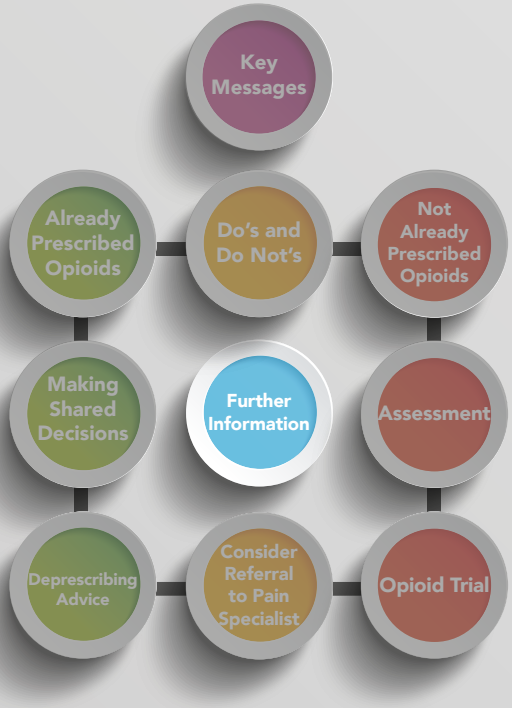

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