DERBYSHIRE JOINT AREA PRESCRIBING COMMITTEE (JAPC)

MANAGEMENT OF NON-MALIGNANT CHRONIC PAIN IN PRIMARY CARE

- Chronic pain refers to pain that exists beyond the expected time of healing usually taken as three months or more. It is recognised as a long term condition in its own right.
- Medications should usually be a small part of the pain management plan and should be used in conjunction with non-pharmacological interventions, such as advice regarding activity, physiotherapy and an explanation that pain may be resistant to medication and that complete relief of symptoms may not be a goal of therapy.
- Unlike acute pain and cancer pain at the end of life, persistent pain not associated with cancer has an unpredictable course and may continue for many years: substantial reduction in pain intensity using medication alone is rarely an achievable goal. Thus, it is often better to have interventions targeted at increased pain management skills together with enhanced understanding about how pain works.
- Based on advice from the Faculty of Pain Medicine, JAPC does not support the World Health Organisation (WHO) 3-step "Ladder" approach to manage pain in non-cancer patients. It may be rational to use a stepped approach but this should not be determined by reported pain intensity (which is the principle of the analgesic ladder).
- JAPC advise that patients receiving opioid doses of >50mg/day morphine equivalent should be reviewed regularly (at least annually). Clinicians may seek specialist advice for doses >90mg/day morphine equivalent.
- Referral to a pain clinic should be carefully considered before starting patients on strong opioids such as morphine. Current recommendations are that no patients should exceed the equivalent of 120mg per day of oral morphine. If a patient exceeds this dosage then efforts should be made to reduce the opiate to 120mg/day of oral morphine equivalent or less.
- Long-term (>3months) use of opioids in non-cancer pain, even at therapeutic doses, carries an increased risk of dependence and addiction. Before prescribing opioids, discuss with the patient the risks and features of tolerance, dependence, and addiction, and agree together a treatment strategy and plan for end of treatment. See MHRA September 2020
- See appendix 1 for the safe prescribing of strong opioid painkillers which are often ineffective for long term pain and has the risk of unintentional overdose, addiction and death.
- In the management of osteoarthritis JAPC advises that the best way to reduce harms of oral NSAIDs is to avoid their use altogether by using alternative pain management strategies. The effectiveness of paracetamol for some types of pain has been questioned. However they are relatively safe and remain viable options before moving on to oral NSAIDs
- For the management of neuropathic pain or back pain & sciatica see separate JAPC guidance. For the treatment of migraine see Derbyshire Medicines Management Formulary.
- There is a lack of evidence in the literature to support combination treatments. However local consultant opinion supports the notion of synergy between drugs of different classes and provides a useful strategy, for example tricyclic antidepressants and anti-convulsants, before patients' progress to morphine. There appears to be little logic to combine drugs of the same class e.g. codeine and morphine and codeine and tramadol.
- If a medicine after a suitable trial does not work for the patient it should be stopped, the dose should not be increased.
- For patients where pain is having a significant effect on physical functioning and mood who can engage with groups, consider referral to a pain management programme (covering parts of Derbyshire formerly under North Derbyshire and Hardwick CCGs); for patients with significant mood issues

reactive to management of and adjustment to chronic pain, consider referral to Health Psychology Service (covering parts of Derbyshire formerly under North Derbyshire and Hardwick CCGs); for patients in Southern Derbyshire, access to specialist psychological and physiotherapy services is available through Derby Royal Hospital Pain Management Clinic.

Table of Contents

1. Introduction

The purpose of this document is to produce a unified guideline for clinicians in primary care for pain management with most attention on recommendations for prescribed medication. The guidelines are based on best available evidence to improve patient's quality of life, reduce prescribing costs and reduce the need for unnecessary hospital referrals and/or admissions.

2. Non-pharmacological management of chronic non-malignant pain

Non-pharmacological methods are the mainstay in the management of chronic pain. The general principles include:

1. **Activity:** the evidence shows that keeping active improves both physical and mental well-being. Being active when in pain can be a challenge and it is therefore important for patients to know that it is safe to be active in spite of pain; provide reassurance that pain does not always indicate harm especially when pain persists for a long time. For some patients, weight loss may improve outcomes; support for assistance with weight loss efforts is available from: https://www.livelifebetterderbyshire.org.uk/

2. **Psychological approaches:** the evidence shows that pain is associated with anxiety and stress; therefore it may be helpful to use relaxation techniques and/or psychological approaches (such as cognitive behavioural therapy) to help to manage the pain. High levels of anxiety, stress and pain may lead to sleep disturbance; hence, sleep restoration strategies may also be helpful,

3. **Encourage self-management:** for the control of pain in all clinical and non-clinical settings. This includes ensuring a good understanding of medication and being able to use it both wisely and flexibly as well as using non-pharmacological options.

4. **Understanding pain:** Psychoeducation around pain mechanisms can help to reduce the experience of psychological threat. Fear is a major driver that can contribute to persistent pain. Education helps reduce fear, promote understanding and resilience and enable recovery of confidence and activity. Every clinical interaction has the potential to do this.

This section represents a very brief overview of non-pharmacological management of chronic pain and, if the GP requires more detailed assessment and treatment, then a **referral to specialist services, such as the pain clinic, the physiotherapy service, a pain management programme (for group-based management of mood and activity) or the Health Psychology Service (for management of mood, adjustment and coping issues) is strongly recommended.**

3. Pharmacological management of chronic non-malignant pain

Based on advice from the Faculty of Pain Medicine (FPM), JAPC does not support the World Health Organisation (WHO) 3-step "Ladder" approach previously adopted for non-cancer pain management.

FPM state the analgesic ladder is unhelpful for persistent pain. Unlike acute pain and cancer pain at the end of life, persistent pain not-associated with cancer has an unpredictable course and may persist for many years; substantial reduction in pain intensity is rarely an achievable goal through the use of medication alone. Additionally, persistent pain may be generated by a number of different pathophysiologic mechanisms as well as psychosocial factors that may require different approaches to treatment.

Stepped approach

When making medication choices to support patients with persistent pain, the FPM recommend using a stepped approach, but this should not be determined by reported pain intensity (which is the underlying principle of the analgesic ladder).

Regardless of pain intensity, it is rational to start with non-opioid drugs, where these have some demonstrated efficacy for the condition being treated. Trials of both weak and strong opioid therapy may be considered for some patients with well-defined diagnoses in whom symptoms persist despite first line interventions.

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.

MHRA September 2020 Long-term (>3months) use of opioids in non-cancer pain, even at therapeutic doses, carries an increased risk of dependence and addiction. Before prescribing opioids, discuss with the patient the risks and features of tolerance, dependence, and addiction, and agree together a treatment strategy and plan for end of treatment.

Pharmacological management for non-malignant chronic pain
(With the exceptions of osteoarthritis and low back pain)

1st line:

- **Paracetamol**
  500mg-1g four times daily maximum 4g daily
  (consider dose reduction in patients at risk of hepatotoxicity and those <50kg)

and/ or

- **NSAIDs**
  - Ibuprofen initially 300-400mg 3-4 times daily, increase if necessary to max 2.4g daily, maintenance dose of 0.6-1.2g daily
  - Naproxen-500mg-1g daily in 1-2 divided doses. Use plain tablet not e/c

and/ or

- **TCAs**
  - Amitriptyline 10 to 25 mg once daily maximum 75 mg at night

and/ or

- **Anticonvulsants**
  - Gabapentin initial dose of 300mg, then 300mg bd on day two, 300mg tds on day 3. Based on response and tolerability dose can be further increased in 300mg/day increments every 2-3 days up to a maximum of 3,600mg/day

2nd line:

- **Weak opioids:**
  - Codeine phosphate 30mg-60mg up to four times a day (max.240mg/day)

3rd line:

- **Strong opioid**

*Referral to a pain clinic should be carefully considered before starting patients on strong opioids (such as morphine) because **patients may be reluctant to stop these drugs once they are commenced on them**. (Further details on the safe prescribing of strong opioids can be found in appendix 1).*

4. Criteria for referral to pain clinic

Referral to a pain clinic should be carefully considered before starting patients on strong opioids (such as morphine) because **patients may be reluctant to stop these drugs once they are commenced on them**.

Refer:

a) Neuropathic pain:
   i. No significant improvement after a maximum of 3 months of treatment
   ii. The patient is responding but suffering unacceptable side-effects
   iii. The patient does not want drug therapy
   iv. Need further advice or diagnosis on the particular clinical symptom set
b) Patient intolerance of standard analgesics and still in constant pain
c) Patient with relevant drug allergies
d) Worsening of correctable cause.

Criteria for referral to Health Psychology Service (area formerly covered by North Derbyshire and Hardwick CCGs)

General Practice can refer directly to the Health Psychology service for patients with any kind of chronic pain presentation where they are interested in exploring and would benefit from an individualised psychological approach to support them to:

- manage and influence their pain symptoms
- cope with pain medication and make decisions about treatment
- adjust to changes in everyday life due to their pain and/or treatment
- recover from low mood, anxiety and stress associated with their pain and/or treatment

Inclusion criteria are adults (18+), where enduring or severe mental health issues are stable enough for a patient to be well enough to access and benefit from health psychology approach (with adequate Recovery Team assessment and support) and where any substance misuse has been recognised and been appropriately treated and managed. Patient referrals can be made via e-mail to health.psychology@nhs.net.

Criteria for referral to Pain Management Programme (area formerly covered by North Derbyshire and Hardwick CCGs) – see appendix 5

For adults (18+) who are experiencing difficulties with pain and who would be interested in engaging with an educational group approach, the programme combines explaining the physiological and psychological mechanisms involved in the pain experience. Exploring strategies to help improve both physical function and mood, adopting a gentle approach to making enjoyable and rewarding lifestyle changes that can significantly impact on medication use and quality of life. Many previous participants have said that attending the programme has given them the support and encouragement, guidance and confidence needed to take control of their pain and do something about it. The programme is run jointly by Health Psychology and Physiotherapy. The programme runs in Chesterfield and Clay Cross. Patients can be referred directly to the Pain Management Programme, Physiotherapy Service, Walton Hospital.

Access to Derby Royal Hospital Pain Management Clinic psychology services

There is no direct referral route but access can be arranged “in-house”. Aims include for patients to:

- manage and influence their pain symptoms via values-based objectives
- adjust and adapt to changes required in everyday life to manage their pain optimally
- recover from low mood, anxiety and stress associated with their pain

For patients who would benefit from a psycho-educational group, they can be referred in-house for a half day Self-Management Session. Patients may then opt into a full Pain Management Programme, co-run between psychology, physiotherapy and Nurse Specialists. Invited into the psychological elements of Pain Clinic are adults (18+) who are ready to make changes; where enduring or severe mental health issues are stable enough to access and benefit from health psychology (with adequate Recovery Team assessment, risk monitoring and support) and where any substance misuse has been recognised and been appropriately treated and managed.

5. Pharmacological management of osteoarthritis

There is actually a lack of evidence for the effectiveness of most pharmacological therapeutic interventions for the long term management of OA. In addition, recent evidence has identified that many oral NSAIDs, particularly diclofenac, cause additional CV events. As OA is a long term condition and considering the effect of placebo in managing pain, oral NSAIDs should be used with caution, only once the other, safer, options have been tried first.

JAPC has discussed the recommendations in the NICE guideline for the management of OA and broadly agrees with its recommendations. A key message is that the best way to reduce harms of oral NSAIDs is to avoid their use altogether by using alternative pain management strategies.

JAPC have classified all topical rubefacients as Do Not Prescribe (DNP) due to limited evidence (note this does not include topical NSAIDs or capsaicin cream). Patients requesting rubefacients should be encouraged to self-treat and purchase over the counter if necessary.

This is the recommended approach from JAPC:

Pharmacological management of osteoarthritis

First line:

- ***Paracetamol*** 1g 3-4 times daily
  (Consider dose reduction in patients at risk of hepatotoxicity and those <50kg)
- Add ***codeine*** 15-30mg if necessary for flare-ups.

Second line:
Topical NSAID (e.g. ibuprofen gel, ketoprofen gel).

Two weeks trial to assess effectiveness
Use if necessary ***paracetamol +/-codeine with topical NSAID***

Third line:
Consider an ***oral NSAID*** -ibuprofen up to1200mg daily is first-line; *naproxen* up to 1000mg daily second-line (NB avoid enteric-coated tablets).

Add lansoprazole 15mg or omeprazole 20mg daily if high risk for serious GI adverse events as per JAPC guideline.

Topical capsaicin 0.025% is GREY -can be considered as an adjunct after NSAIDs (topical or oral) with or without paracetamol in OA.

6. Prescribing information

Paracetamol

- Paracetamol should be prescribed first line as the starting point of any acute or chronic analgesic regime with the exception of low back pain.
- Paracetamol offers the advantages of relative safety, low cost, high bioavailability, quick onset of action and the choice of several formulations. Paracetamol used in conjunction with a weak opioid significantly increases efficacy over use of the opioid alone.
- Paracetamol has a very low incidence of side-effects making it a very safe drug at therapeutic doses; however some patients may be at increased risk of experiencing toxicity at therapeutic doses, particularly those with a body-weight under 50kg and those with risk factors for hepatotoxicity. Clinical judgement should be used to adjust the dose of oral paracetamol in these patients. Examples of risk factors for hepatotoxicity include malnourishment and long-term treatment with liver enzyme-inducing drugs such as carbamazepine. Example of dosing for these patients adopted from DTHFT: (final dose to be determined on individual basis)

>50kg	500mg-1g every 4-6 hours, Maximum 4g daily
40 - ≤50kg	500mg-1g every 4-6 hours, Maximum 3g daily
30 - 39kg	Dose reduction required

NSAIDs

- The balance of benefits and risks needs to be carefully assessed; think about cardiovascular diseases (especially if taking aspirin), gastrointestinal sensitivity (contraindicated in active peptic ulcer), renal issues and hepatic disease
- Use a safer drug (ibuprofen, then naproxen) in the lowest effective dose for the shortest period
- The MHRA June 2015 have reviewed the safety of high-dose ibuprofen and have concluded that there is an increased cardiovascular risk associated with high dose ibuprofen (≥2400mg/day), which is similar to that seen with COX-2 inhibitors and diclofenac.
- All patients on NSAID at high risk of having serious GI adverse events should routinely be co-prescribed gastro-protection (lansoprazole 15mg or omeprazole 20mg)
  High risk factors are: (See local PPI guidance for more details)

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

  Or have two or more risk factors:

  - ≥65 years of age
  - Oral corticosteroid use
  - Dyspepsia or GORD symptoms
  - SSRIs
  - Severe co-morbidity (malignancy, HF (NYHA III-IV), significant liver or renal disease (e.g. CKD 4&5 and cirrhosis)

Tramadol

- Tramadol is neither more effective nor better tolerated than other weak opioid analgesics for moderate to severe pain and its safety profile is problematic. An audit of Adverse Drug Reactions (ADRs) at Chesterfield Royal Hospital highlighted an increase in admissions related to Tramadol ADRs in parallel with increasing use.
- Co-prescribing of high doses of tramadol and amitriptyline should be avoided due to the increased risk of CNS toxicity with this combination.
- Tramadol became a Schedule 3 controlled drug on 10th June 2014.
- Tramadol can induce convulsions and increase the potential for SSRIs, SNRIs, TCAs, anti-psychotics and other seizure threshold lowering medicinal products to cause convulsions.
- Tramadol MR Tablets (classified as **GREY**): this can be very expensive please contact the Medicine Management Team for advice on most cost-effective alternative.
- Tramacet (classified as Do Not Prescribe (DNP)) is a fixed dose combination of Tramadol 37.5mg and a sub therapeutic dose of paracetamol 325mg. Prescribing of this product is not recommended as it offers little advantage in terms of efficacy, adverse effects or convenience over standard analgesics.

References

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3. NICE CG177 Osteoarthritis: care and management. February 2014 https://www.nice.org.uk/guidance/cg177
4. SIGN 136 Management of chronic pain. Updated August 2019 https://www.sign.ac.uk/sign-136-management-of-chronic-pain.html
5. The West Midlands Palliative Care Physicians Guideline for the use of drugs in symptom control. Revised edition January 2012.
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8. Safe prescribing pf opioids for persistent non cancer pain. Australian Prescriber Volume 35: Number 1 February 2012
9. Derry s, Matthews PRL, Wiffen PJ, Moore RA. Salicylate-containing rubefacients for acute and chornic musculoskeletal pain in adults. Cochrane Database of systematic reviews. Nvoember 2014, issue 11. Art. No.: CD007403. DOI:10.1002/14651858.CD007403.pub3 Accessed 27/02/2015.

Useful contacts

UHDB - Chronic pain (outpatient services). Referral pain proforma can be found at https://www.uhdb.nhs.uk/service-chronic-pain
General appointments or queries please telephone 01332 786086
Health Psychology Service, Walton Hospital, Chesterfield. 01246 515520

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Derbyshire Guideline Group

Document updates	Date updated
Additional information on tapering inserted to p.11	July 2020
MHRA drug safety warning on opioid addiction and fentanyl patch added	October 2020
Back pain & sciatica section removed. See separate local guideline	August 2021

Appendix 1: Safe prescribing of strong opioids

There is little evidence for the efficacy of long-term opioid use in persistent non-malignant pain. Opioids may reasonably be included in the repertoire of cautious attempts to find some therapy that works when all the obvious ones have been tried.

Before undertaking a longer-term period of opioid treatment like morphine the patient should be assessed following an initial trial period. This follows an emerging picture that shows an increase in abuse treatment, admissions, and deaths due to prescription opioids. **Once opioids are started they are difficult to stop.** If the medication does not work they should be stopped, do not try increasing the dose. Patients who do not achieve useful pain relief from opioids within 2-4 weeks are unlikely to gain benefit in the long term, and short-term efficacy does not guarantee long-term efficacy.

Current recommendations are that no patients should exceed the equivalent of 120mg per day of oral morphine. If a patient exceeds this dosage then efforts should be made to reduce the opiate to 120mg/day of oral morphine equivalent or less.
JAPC advise that patients receiving opioid doses of >50mg/day morphine equivalent should be reviewed regularly (at least annually). Clinicians may seek specialist advice for doses >90mg/day morphine equivalent.

The FPM has produced useful resources for patients and healthcare professionals to support prescribing of opioid medicines for pain. This web based resource has received contributions from several medical royal colleges. NICE, Royal pharmaceutical society, the British Pain Society, Public Health England, NHS England, the CQC and the NHS Business Services Authority

Choice of drug

- There is little evidence that one opioid is more effective and associated with fewer side effects than others.
- **Oral morphine is the drug of first choice**.
- If the first opioid tried is helpful and causes intolerable side effects, it is reasonable to try an alternative opioid.

Outcomes

The goals of opioid therapy should be agreed between the prescriber, the patient and their carer(s).
This will include:

- Clear objectives and realistic goals
- Period of review
- Possibility of treatment failure and the need for a process to discontinue if objectives are not met
- Asking patients to keep a pain diary (see below for further details)

Opioid trial

A trial of opioid therapy should be considered if the clinician and patient agree a trial could be effective in the management of the patient's pain, (i.e. achieves any reduction in pain).

1. Starting the trial

The patient and clinician should agree some readily accessible outcomes that indicate that opioids may play a role in the patient's management. Examples of outcomes include:

- Reduction in pain intensity
- Some specific functional improvement
- Improvement in sleep.

2. Patient assessment

Example of factors to be considered when assessing the patient for morphine includes:

- History of substance misuse: this includes misuse of illegal drugs (heroin), legal drugs (alcohol), prescription drugs (benzodiazepines), and any purchased medicines.
- Previously poorly tolerated opioid treatment
- Interactions between opioid and other medicines
- Psychiatric risk – previous intentional overdoses
- Depression
- Obstructive sleep apnoea
- Severe GORD or GI hypomotility

- Other existing conditions e.g. many patients with porphyria have sensitivity to several opioids
- Occupation e.g. aviation and driving HGVs
- Elderly: the British Pain Society advised to take account of relevant age-related changes in pharmacokinetics and pharmacodynamics hence starting dose should be cautious with frequent assessment and dose adjustment. The side effects are worse in older people e.g. falls, confusion, and constipation.
- Multidisciplinary treatment plan may be required to comprehensively assess both pain and addiction.
- Concerns about problem drug use should prompt referral to specialised addiction services.
- Renal or hepatic impairment: refer to BNF/SPC (Summary of Product Characteristics) for full prescribing advice
- Pregnancy: specialist referral is required particularly if the patient is planning pregnancy and on opioids
- Patients who cannot assess and or clearly describe pain for themselves: such as patients with dementia, learning difficulties or language and cultural issues.

3. Duration of the opioid trial

Duration of the opioid trial is dependent on the periodicity of the patient's pain. For example:

- For constant pain, the opioid trial may be concluded in 1-2 weeks.
- For intermittent disabling flare ups of pain on a background of more manageable symptoms, the trial should be long enough to observe the effect of opioids on 2 or 3 episodes of increased pain.

4. Choice of opioid route/formulation and dose

The oral route is preferred route of administration. In most setting an initial opioid trial is probably best achieved using immediate release formulation for very short period of time (i.e. 1-2 weeks).

- Prescribe short (1-2 weeks) of immediate release morphine tablets/capsules or liquid.
- Advise patient to explore doses within a specified range e.g. morphine 5-10mg.
- If reduction in pain is not achieved following a single dose of immediate relief morphine 20mg, opioids are unlikely to beneficial in the long term.
- Trial of fixed dose regimens using modified release preparations needs to allow for one or two or two upwards dose adjustments and may therefore take three weeks or more.

Use of immediate release preparations (Sevredol is preferred brand for IR morphine) is justified when:

- The pain is intermittent and short-lived.
- Pain intensity varies significantly: use of regimens including immediate release preparations allows flexibility to reduce the dose on days when pain is or is expected to be less severe.
- Background pain is well controlled with modified release preparations, but the patient has infrequent, short-lived episodes of increased pain.

Modified release (Zomorph is preferred brand for MR morphine) may be more appropriate:

- For patients with persistent pain throughout the day and night.

5. Assessing whether the opioid trial is a success.

- Encourage the patient to keep a diary during the opioid trial. This should include a twice-daily report of pain intensity, comment on sleep, note of activity levels and how any of these are changed following a dose of opioid.
- All doses of opioids should be recorded in the diary with a comment on side effects.
- If the opioid trial is not successful, the drugs should be tapered and stopped within one week. A 30% reduction in pain should be demonstrable to justify long term prescribing.
- If the opioid trial demonstrates some benefit from the opioids, **<u>further</u>** exploration may be helpful. A successful short term trial does not predict long-term efficacy.
- Assess potential merits and contraindications for opioids in patients unresponsive to other 'first-line' treatments
- Consider whether depression is a complication and needs treatment before a trial of opioids. Chronic pain and depression often coexist and depression may be a reason why some patients respond poorly to initial treatments

It is advisable that if prescribing strong opioids for more than 12 months, a second opinion should be sought from a specialist.

Prescribing note 1:
Ensure where a dose increase is intended, that the calculated dose is safe for the patient (e.g. for oral morphine or oxycodone in adults this is not normally more than 50% higher than the previous dose)

Prescribing note 2:
Opioids have a range of effects including endocrine, immunological, cognitive and emotive. Long-term opioid use is associated with numerous adverse reactions (examples are listed in table 1 below). The continuing management plan needs to incorporate a process of regular review for the risk and occurrence of adverse events

Tapering and stopping

It is important to taper or stop the opioid regimen if:

- The medication is not providing useful pain relief. The dose above which harms outweigh the benefits is 120mg oral morphine in 24 hours. Increasing the opioid load above this dose is unlikely to yield further benefits but exposes the patient to increased harms.
- The underlying painful condition resolves
- The patient receives a definitive pain relieving intervention (e.g. joint replacement)
- The patient develops intolerable side effects

The decision to taper/stop an established opioid regimen needs to be discussed carefully with the patient:

- explanation of the rationale for stopping opioids including the potential benefits of opioid reduction (avoidance of long term harms and improvement in ability to engage in self-management strategies)
- agreeing outcomes of opioid tapering
- arrangements for monitoring and support during opioid taper
- documented agreement of tapering schedule

The dose of drug can be tapered by 10% weekly or two weekly, although slower tapering (reduced by 10-25% monthly) may be better tolerated therefore preferred. Limit the number (type) of opioids and maintain the same opioid drug(s) during tapering, as conversion values are inconsistent across population.

Considerations for patients at high risk of opioid harm

- Schedule frequent reviews and at each appointment: ask about and emphasise the benefits of tapering; assess risk of harm
- Facilitate psychosocial support for the patient
- Check for co-prescription of benzodiazepines and other sedatives that significantly increase risk of serious harm.
- Consider rationalising to a single opioid if applicable.
- Consider specialist input if patient is experiencing serious challenges or the main problem is opioid dependency rather than pain

Adverse effects

Most common adverse effects include nausea, vomiting, constipation, pruritus, dizziness, dry mouth and sedation. Opioid-associated adverse effects should be anticipated and appropriate counselling about common side effects and their management should be provided to the patient before the first prescription. Strategies for dealing with opioid induced adverse effects can be seen in table 1.

Table 1 **Managing opioid-induced adverse effects** **(includes some additional changes)**

Adverse effect	Suggested strategy
Gastrointestinal	
Nausea and vomiting	Reduce dose, consider alternate formulation (sublingual, transdermal), exclude chronic constipation
Chronic constipation and related sequelae including abdominal pain, reflux, haemorrhoids, colonic hypomotility	Recommend regular bulking agent, extra fluids, non-osmotic laxatives
Reduced salivary flow posing dental problems	Six-monthly dentist reviews, brushing and flossing teeth, extra fluoride treatment, encourage salivary flow after meals, diet
Gastro-oesophageal reflux disease	Specific treatment e.g. proton pump inhibitor such as omeprazole Consider reducing or stopping opioids
Neurological	

Impaired cognition	Periodic assessment, mini-mental state examination
Impaired coordination	Heel-toe gait testing
Sedation	Consider monitoring with Epworth Sleepiness Scale (for excessive daytime somnolence) and with family and other witness accounts (e.g. pharmacist)
Hyperalgesia	Some patients can develop hyperalgesia (increased sensitivity to pain) with long-term use of opioids. This might be qualitatively and anatomically distinct from pain related to disease progression or to breakthrough pain resulting from development of opioid tolerance. These symptoms may resolve with a gradual reduction in opioid dose. (MHRA sept 2020) Consider possibility of drug interaction (e.g. benzodiazepines) and review dosages and need periodic assessment, avoid doses >120 mg (mg morphine equivalent). Management requires a dose reduction or changing to an alternative
Endocrine (Long-term administration of opioids is associated with endocrine abnormalities.)	
(Note there is insufficient evidence to recommend routine monitoring of asymptomatic patients taking opioids in the long-term for hormonal deficiencies) • If endocrine impairment is demonstrated, patients should be referred to an endocrinologist	
Hyperprolactinaemia (and galactorrhea)	Monitor prolactin
Hypogonadism	Monitor testosterone
Osteoporosis	Monitor from baseline, check vitamin D status, seek specialist guidance
Respiratory	
Exacerbation of obstructive sleep apnoea	Consult respiratory physician
Inducing central sleep apnoea	Likely contraindication (e.g. methadone), reduce dose, sleep study (polysomnography), consult respiratory physician
Respiratory depression	Especially in patients with type 2 respiratory failure (CO2 retention) and those on home oxygen therapy. Deterioration requires specialist intervention and probable opioid discontinuation.
Cardiovascular	
Prolonged QTc	Electrocardiogram (particularly with methadone and oxycodone)
Psychiatric	
Mood disorder	Monitor from baseline, reduce dose and review
Addiction	Seek addiction advice (see appendix 4)
Overdosage	Prescribe small amounts (e.g. weekly supply), ensure only one prescriber and likewise pharmacist, assess patient for depression
Other	
Fluid retention and oedema	Document, reduce dose, restrict sodium, consider a diuretic
Occupational and driving impairment	Establish baseline and review with reference to reliable co-informants
Diversion potential	

Table adapted from Australian Prescriber 2012; 35:20-4

- Most patients will develop tolerance to the side effects of Morphine (except constipation). If patients suffer from nausea when first starting morphine a short course of metoclopramide may be appropriate until tolerance develops. Haloperidol is often used as an alternative to Metoclopramide in palliative care
- A laxative should always be prescribed with Morphine. Encourage lots of fluids, fruit and fibre.
- Influences on both the hypothalamic-pituitary-adrenal axis and the hypothalamic-pituitary-gonadal axis have been demonstrated in patients taking oral opioids with consequent hypogonadism and adrenal insufficiency in both sexes.
- Hypogonadism and decreased levels of dehydroepiandrosterone sulfate have been reported in men and women.
- Hypoadrenalism-Symptoms include tiredness and/or dizziness on standing and/or Nausea/vomiting/ weight loss. If present check 9am cortisol.

Endocrine effects are probably dose related and can lead to:

- Amenorrhoea in women
- Reduced libido in both sexes
- Erectile dysfunction in men
- Infertility
- Depression and fatigue

Patients (particularly women of childbearing age) should be told about these effects before starting opioids.

Endocrine function should be monitored regularly if a patient reports symptoms consistent with potential dysfunction, such as decreased libido, sexual dysfunction or fatigue. (NB these symptoms can also occur as part of the presentation of chronic pain)

Recommended tests include:

- blood pressure
- electrolytes (especially if tramadol is used)
- fasting glucose levels
- thyroid function tests
- serum testosterone, sex-binding globulin, LH/FSH and oestradiol levels
- Bone density (in an 'at-risk' group).

If endocrine impairment is demonstrated, patients should be referred to an endocrinologist for advice regarding the benefits of hormonal replacement therapy.
There is insufficient evidence to recommend routine monitoring of asymptomatic patients taking opioids in the long-term for hormonal deficiencies.

Caution

- Patients with renal impairment treated with opioid analgesics (e.g. morphine) should have their dose reduced or opioids should be avoided.

GFR (mL/min)	Dose of morphine
20-50	75% normal dose
10-20	Use small doses e.g. 2.5-5mg and extended dosing intervals. Titrate according to response
<10	Use small doses, e.g. 1.25-2.5mg and extended dosing intervals. Titrate according to response

(Source: Renal handbook – morphine)

An immediate release preparation given at longer intervals than normal is more appropriate than using a modified release preparation in these patients. Avoid the use of oxycodone if eGFR <10mL/minute/1.73m2. Seek renal physician advice for options in severe renal impairment.

- Morphine is contra-indicated with the concurrent use of monoamine oxidase inhibitors or within two weeks of discontinuation of their use.

Appendix 2: Switching opioids

Be cautious when switching and monitor regularly. Withdrawal symptoms (such as sweating, abdominal cramps and yawning) occur if an opioid is stopped/reduced abruptly.

The chart below shows opioid dose conversion:
NB: Dose equivalences are approximate only. Manufacturer guidelines states 2:1 ratio of oxycodone: morphine (note other conversion charts use a 1.5: 1 ratio). For illustrative purposes
2:1 ratio is shown below, care should be taken when converting, regular monitoring and review is necessary to avoid both under dosing and excessive dosing.

Strong Opioid	Morphine Sulphate MR (Zomorph® capsules)	Oxycodone MR (Longtec® tablets)
JAPC prescribing advice on product selection	Prescribe cost effective formulation by brand name 'Zomorph'	Treatment option if morphine cannot be tolerated
Starting doses Titrate **slowly** to effect (no more frequently than every 2 weeks)	10mg every 12 hours (£3.47)	5mg every 12 hours (£13.41)
	20mg every 12 hours (£6.94)	10mg every 12 hours (£13.41)
	30mg every 12 hours (£8.30)	15mg every 12 hours (£20.42)
	40mg every 12 hours (£11.77)	20mg every 12 hours (£26.82)
	50mg every 12 hours (£15.24)	25mg (10+15) every 12 hours (£33.83)
Maximum dose for non-cancer pain initiated in primary care	**60mg every 12 hours** (£16.20)	**30mg every 12 hours** (£40.83)
Higher doses by specialist recommendation or advice only		

Costs are from the MIMS January 2018 and are for 30 days treatment.

Oral Oxycodone

- Oxycodone has an efficacy and side-effect profile similar to that of morphine but much more expensive
- Oxycodone is an alternative for patients who develop intolerable adverse effects with oral morphine or who do not respond to morphine
- Oxycodone should only be prescribed if a patient has an intolerance to morphine i.e. develops unacceptable side effects when taking morphine e.g. hallucinations, confusion, cognitive impairment, marked sedation, pruritus and intractable vomiting. Avoid use if eGFR <10mL/minute/1.73m2
- Targinact (Oxycodone / naloxone): is not recommended for use. It is classified as **Do Not Prescribe (DNP)** by JAPC. This product is considerably more expensive than oxycodone prescribed as a single component. Also opioid use may not be the only cause of constipation.

Appendix 3: Other strong opioids

Fentanyl Patches

- These should only be considered for patients who are on a stable dose of an opioid and who are unable to swallow /comply with oral medication. It should not be prescribed for opioid naïve patients due to considerable risk of respiratory depression. (MHRA September 2020)
- Fentanyl patches should not be prescribed for opioid naïve patients. Take care with calculation of dose equivalents. **A 25microgram/hr patch is equivalent to Morphine 60mg per day**. (See chart below)
- There are different types of fentanyl patches available; a reservoir where the drug is held in a solution and a matrix patch where the drug is distributed in a matrix (e.g Fencino, Mezolar and Matrifen). Due to this difference fentanyl patches should be prescribed by brand. Equally effective pain relief is provided by all brands, so the choice of brand rests with the prescriber (local formulary recommendation currently is to prescribe either Matrifen, Mezolar or Fencino brand)
- **Max. titrated dose for fentanyl (Fencino, Mezolar and Matrifen) should not exceed 50microgram/hour changed every three days-** seek specialist advice if increased doing is required.
- Fentanyl patches should be changed every 72 hours
- Fentanyl patches should not be used for acute pain or unstable pain
- If required, **fentanyl matrix patches only**, may be cut in half. For accuracy the matrix patch should be cut diagonally; the other half should be disposed of, in the correct manner as for a controlled drug. N.B. cutting a fentanyl matrix patch renders the use of the drug as "off licence."
- Monitor patients using patches for increased side-effects if fever present (increased absorption possible); avoid exposing application site to external heat for example a hot bath or sauna.
- Respiratory depression: Risk of fatal respiratory depression particularly in patients not previously treated with a strong opioid analgesic. Prescriptions for patches should not exceed 30-days' supply, as DOH guidance, unless there is a justifiable clinical need. The reason for this decision should be recorded in the patient's notes.
- The following 24 hour doses of morphine are considered to be approximately equivalent to the 72-hour fentanyl patches shown below. However when switching due to possible opioid-induced hyperalgesia, reduce the calculated equivalent dose of the new opioid by one-quarter to one-half.

Oral Morphine salt 24 hour dosing	72 hour Fentanyl patch equivalent
30mg daily (or up to 45mg a day)	'12' patch (£16.92)
60mg daily	'25' patch (£24.20)
120mg daily	'50' patch (£45.24) max. titrated dose without specialist input
180mg daily	'75' patch
240mg daily	'100' patch

Source BNF 74 Sept2017- March2018. Costs are from MIMS January 2018 and are for 30 days treatment.

***Sub-lingual Fentanyl* is for use by a small number of patients only and should be initiated by specialists in pain management. All non-transdermal preparations (lozenges, tablets, buccal film and sublingual tablets) are classified as GREY after palliative care specialist initiation.**

MHRA (October 2018) warns of the risk of serious and fatal overdose of fentanyl patches due to dosing errors, accidental exposure (particularly in children), and exposure of the patch to a heat. Remind patients (or caregivers) to

- Follow the correct frequency of patch application, avoiding touching the adhesive side of patches, and washing hands after application. Remove old patches before applying a new one.
- Avoiding exposure of patches to heat including via hot water (bath, shower)
- Follow instructions for safe storage and properly disposing of used patches or those which are not needed. After use, patches should be folded so that the adhesive side of the patch adheres to itself and then placed back into the original sachet.
- Be aware of the signs and symptoms of fentanyl overdose (e.g. difficulty/ shallow breathing; tiredness; extreme sleepiness/ sedation; feeling faint, dizzy or confused) and seek medical attention immediately (by dialling 999 and requesting an ambulance) if overdose is suspected.

In patients who experience serious adverse events, remove patches immediately and monitor for up to 24 hours after patch removal.

Discontinuing Fentanyl patches

Reasons: opioid toxicity, opioid switch, allergy, non-adherence, patient choice, dose reduction, pain not

controlled.

- After the patch is removed, a reservoir of the drug remains under the skin, and it continues to be released for approximately 17 hours (range 13-22 hours)
- Remove the patch 6 hours before taking the first dose of oral modified release Morphine. For the first 24 hours (i.e. first two doses) give HALF the calculated equivalent dose. After 24 hours increase to the calculated equivalent dose if clinically indicated by pain
  Alternatively, for the first 12-24 hours after removing the patch breakthrough medication only could be prescribed, and then a long acting alternative can be prescribed.

Buprenorphine patches

- Buprenorphine patches- classified as **GREY** and cost several times more than oral morphine in equivalent doses. At lower doses buprenorphine patches are broadly as effective as codeine or tramadol but much more expensive.
- An example of exceptionality includes use in severe renal impairment in patients with CKD 4 or 5 when other treatment options have been considered.
- Be aware there is a wide range of buprenorphine patches, **with different strengths and frequency of replacement**. Check licenced frequency carefully. Prescribe by brand name. (Reletrans is the preferred low dose 7-day patch; Relevtec is the preferred higher strength patch (replaced after 96hours))
- The patches are unsuitable in acute or unstable pain due to the need for slow titration of doses; it may take up to 72 hours to achieve a stable blood level after a change in dose.
- The following 24 hour doses of codeine/tramadol/morphine are considered to be approximately equivalent to the buprenorphine patches shown below. However when switching due to possible opioid-induced hyperalgesia, reduce the calculated equivalent dose of the new opioid by one-quarter to one-half

Buprenorphine patch (microg/h)	Codeine (mg/day)	Tramadol (mg/day)	Oral morphine (mg/day)
'5' patch changed weekly	120mg	100mg	12mg
'10' patch changed weekly	240mg	200mg	24mg
'20' patch changed weekly	-	400mg	48mg
'35' patch (high strength) changed every 3 or 4 days	-	-	84mg

Source Faculty of pain medicine https://www.rcoa.ac.uk/faculty-of-pain-medicine/opioids-aware/structured-approach-to-prescribing/dose-equivalents-and-changing-opioids

Drug Considerations

- Meptazinol (weak opioid): is associated with rebound pain and an unacceptable level of side effects and therefore is not to be prescribed routinely.
- Fixed dose combination products (e.g. Co-codamol 30/500mg) do not allow titration to the most effective analgesic dose to match the individual's requirements and so have a limited role. Low-dose weak opioid and paracetamol preparations (e.g. Co-codamol 8/500mg, Co-dydramol) still lead to opioid adverse effects and there is no evidence to show that they are more effective than paracetamol alone. However combination products may be considered where compliance is an issue.

Appendix 4: Other information

Drugs and driving

From March 2nd 2015 a new driving offence with certain medicines (including opiates) above specified limits in the blood was enforced in England & Wales. See MHRA drug safety update, February 2015 and also Guidance for healthcare professionals on drugs driving 2014

Dependence and addiction

- The prescription of opioids can result in problem drug use. The likelihood of this occurring might be influenced by a number of social, psychological and health related factors.
- Concerns about problem drug use should prompt referral to specialised addiction services.
- Patients with a current or past history of substance misuse or with a comorbid non-substance misuse psychiatric diagnosis may be more likely to develop problems with opioid use. Opioid treatment for these patients should be closely and collaboratively monitored by specialists in pain management and/or addiction medicine.
- Typical signs of addiction are:
    - Expression of craving for the drug, even if it is causing adverse effects on overall health
    - Expression of a need for more, or reporting additional use of other pain-relief medicines
    - Taking medicines for reasons other than pain relief
    - Experiencing withdrawal side effects when opioids are stopped suddenly

Withdrawal reactions

Dependence and addiction to opioids are associated with adverse reactions of withdrawal upon sudden cessation of treatment that make it harder to stop taking these medicines. Withdrawal from an opioid is characterised by shivers, diarrhoea, difficulty sleeping (insomnia), sweating, body aches (myalgia), widespread or increased pain, irritability and agitation, and nausea and vomiting. Other signs and symptoms include restlessness, lacrimation, rhinorrhoea, yawning, mydriasis, palpitations, anxiety, hyperkinesia, tremor, weakness, anorexia, abdominal cramps, and increased blood pressure, respiratory rate, and heart rate.

Supportive medication:

Most common side effects are predictable consequences of opioid use; nausea, vomiting, constipation, pruritus, dizziness, dry mouth and sedation. CNS side effects such as drowsiness and dizziness tend to improve gradually after opioid initiation. Consider prophylaxis of:

Laxatives:

- Constipation may occur in majority of patients on regular opioid medication.
- To avoid unnecessary laxative use, ensure the laxatives are stopped if the opioid analgesics are stopped, unless otherwise clinically indicated.
- Combination medication is usually a good and effective choice e.g. senna + macrogol compound (e.g.Laxido) up to 8 sachets/day may be used in faecal impaction, 1 sachet dissolved in 125ml water). For further details please refer to local formulary chapter for management of constipation in adults

Anti-emetics:

- When required prescribe a single agent based on underlying cause.
- Short term use of first line agents to control nausea and vomiting is usually effective, as the symptoms usually resolve once opioid use is established
- First line agents include:

Metoclopramide (10mg TDS before meals or 30mg/24hr SC and should be prescribed for 5 days only), or Domperidone (10mg 3 times daily; max.30 mg daily for a maximum of 7 days only)

Use regularly and to *maximum dose before changing.*

Appendix 5: North Derbyshire pain management programme referral

NHS
Derbyshire Community Health Services
NHS Foundation Trust

DCHS Pain Management Programme Inclusion/Exclusion Guidelines for Referrers

Version: 1 (01/12/2017)

1. Background/Aims

The Pain Management Programme is a multiple disciplinary group intervention aimed at service users with chronic, ongoing pain. Chronic, persistent pain is defined as pain that has remained for more than 3 months. The groups are run in Chesterfield and Clay Cross. This programme is jointly run by Psychology and Musculoskeletal Physiotherapy clinicians and is for people who are seeking to manage chronic musculoskeletal pain.

The focus of the programme is on improving quality of life, supporting people to live with their condition and placing emphasis on restoration of function rather than treating pain. The aims of the programme are to to increase understanding of how pain works in order to reduce psychological threat and encourage the development of effective coping strategies, to improve physical and psychological well-being, to improve self-management , as well as aiming to improve appropriate use of medication and decrease the demand on General Practice resources. To enable clinicians referring in to the Pain Management Programme have a clear understanding of appropriate referral criteria and process

2. Intended Users:

- GP's
- Nurse Practitioners
- AHP's including Physiotherapists, OT's, Podiatrists and Clinical Psychologists
- Pain Clinic, Orthopaedic and Rheumatology Consultants

3. Definitions/Terms Used:

Persistent pain: pain that has lasted for a period of 3months or more
Malignant source of pain: pain from cancer

4. Full Details of Guidelines

INCLUSION

- Pain that has persisted for more than 3 months.
- Understand it is a group programme of 6 sessions
- Motivated, willing and able to participate.
- No recent significant changes in symptoms.
- Patient has been appropriately medically screened e.g. for cancer and red flags

EXCLUSION

- Under 18's
- Malignant source of pain
- Unstable medical conditions still under active investigations or medical/surgical treatment
- Unstable mental health conditions. (We can treat people who have a stable mental health condition and/or have suicidal ideation but low intent.)
- On-going investigations for aetiology of pain.
- Current drug or alcohol misuse.

Please include all relevant medical history and drug history and send referrals to:

PMP, Physiotherapy Department, Peter McCarthy Suite, Walton Hospital, Whitecotes Lane, Chesterfield, S40 3HW

Group sessions are run on Thursday afternoons in Chesterfield and on Tuesday afternoons at Clay Cross Hospital.

Referral Form:

Chronic Pain Management Programme Referral

Please complete all sections of the form – on the reverse are the inclusion and exclusion criteria.

Patient Name: _____

Date of Birth: _____ NHS no: _____

Address: _____

_____

Daytime Tel No: _____

GP Name: _____ GP Code: _____

GP Practice: Address_____

Diagnosis / duration of problem

Relevant Medical History e.g. including depression/anxiety etc.

Previous treatment for this condition e.g. surgery, physiotherapy, referral to pain clinic etc.

Current drug therapy and dosage – please include print out of meds if appropriate

Relevant investigations / test results – please provide printout/copies if appropriate

Signature:_____ Date of referral:_____

Name of referrer:_____