DERBYSHIRE JOINT AREA PRESCRIBING COMMITTEE (JAPC)

Deprescribing & Safer prescribing of strong opioids in non-malignant pain

There is little evidence for the efficacy of long-term opioid use in persistent non-malignant pain. NICE no longer recommends initiating opioids for chronic primary pain, or long-term use in low back pain & sciatica or headaches, and its use in neuropathic pain should only be after careful assessment and consideration for referral.

JAPC recognises that for existing patients, withdrawing opioids remains challenging, and may not be feasible/ appropriate, especially for stable patients, partly due to current limitations in capacity and service provision for alternative non-pharmacological treatment options.

This guideline provides relevant information for the safe prescribing of strong opioid treatment, for those patients who continue to report benefit at a safe dose and few harms; as well as advice on tapering for those patients reporting little benefit or significant harm. See also JAPC opioid resource page.

Key message:

- Opioids have a range of effects including endocrine, immunological, cognitive and emotive. Long-term opioid use is associated with numerous adverse reactions most commonly nausea, vomiting, constipation, pruritus, dizziness, dry mouth and sedation. The continuing management plan needs to incorporate a process of regular review for the risk and occurrence of adverse events.

- 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, insomnia, sweating, myalgia, widespread or increased pain, irritability and agitation, and nausea and vomiting.

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

- 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.

- MHRA warns of risk of severe respiratory depression, especially in concomitant opioid medicines with gabapentin, pregabalin, or benzodiazepines. See relevant drug safety warnings.

1. General 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
- See MHRA Safety leaflet on opioid medicines- Opioid medicines and the risk of addiction

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.

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 medications that significantly increase the risk of serious harm such as benzodiazepines and other sedatives (including sedating antihistamines), gabapentinoids and beta-blockers (see potential under recognised risk of harm from the use of propranolol).
- 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

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.

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.*

Renal impairment

Patients with renal impairment treated with opioid analgesics (e.g. morphine) should have their dose reduced or opioids should be avoided. 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/1.73m^2. Seek renal physician advice for options in severe renal impairment.

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)

Concomitant medication

MHRA warns of **risk of severe respiratory depression**, especially in concomitant opioid medicines with gabapentin, pregabalin, or benzodiazepines.

- Gabapentin (Neurontin): risk of severe respiratory depression. When prescribing gabapentin in patients who require concomitant treatment with opioid medicines, patients should be carefully observed for signs of CNS depression, such as somnolence, sedation, and respiratory depression, and the dose of either gabapentin or the opioid should be reduced appropriately.
- Pregabalin (Lyrica): reports of severe respiratory depression. Use of pregabalin with opioid medicines or other CNS depressant medicines has been previously associated with reports of respiratory failure, coma, and deaths. Studies show use of high doses of pregabalin (over 300mg

a day) alongside opioid medicines to be particularly associated with an increased risk of opioid-related death. Consider whether adjustments in dose or dosing regimen are necessary for patients at higher risk of respiratory depression.

- Benzodiazepines and opioids: reminder of risk of potentially fatal respiratory depression. Benzodiazepines (and benzodiazepine-like drugs) and opioids can both cause respiratory depression. When used together, additive effects on the central nervous system increase the risks of sedation, respiratory depression, coma, and death. Only prescribe benzodiazepines (or benzodiazepine-like drugs) and opioids together if there is no alternative.
- Morphine is contra-indicated with the concurrent use of monoamine oxidase inhibitors or within two weeks of discontinuation of their use.

Adverse effects

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

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 **Addiction** **Overdosage**	Monitor from baseline, reduce dose and review Seek addiction advice (see appendix 4) Prescribe small amounts (e.g. weekly supply), ensure only one prescriber and likewise pharmacist, assess patient for depression
Other	
Fluid retention and oedema **Occupational and driving impairment** **Diversion potential**	Document, reduce dose, restrict sodium, consider a diuretic Establish baseline and review with reference to reliable co-informants

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.

2. Starting opioids- opioid trial

NICE no longer recommends initiating opioids for chronic primary pain, or long term use in low back pain & sciatica or headaches, and its use in neuropathic pain should only be after careful assessment and consideration for referral.

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.
- 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)

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

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.
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).

a) 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.

b) 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.

c) 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.

d) 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.

e) 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, **further** 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.

3. Information on other strong opioids including switching

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

Oral Oxycodone

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 (£26.83)
	50mg every 12 hours (£15.24)	25mg 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 October 2021 and are for 30 days treatment.

- 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.

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)
- 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.
  Advice for healthcare professionals:
  Always fully inform patients and their caregivers about directions for safe use for fentanyl patches, including the importance of:
  - not exceeding the prescribed dose
  - following the correct frequency of patch application, avoiding touching the adhesive side of patches, and washing hands after application

- not cutting patches and avoiding exposure of patches to heat including via hot water (bath, shower)
- ensuring old patches are removed before applying a new one
- following instructions for safe storage and properly disposing of used patches or those which are not needed

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.

- Cutting fentanyl patches is for exceptional circumstances and on advice of a palliative care consultant only, following individualised treatment plan. e.g. for a starting dose where dose required is smaller than available whole patch. 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.”
- 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
- 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 (Matrifen £15.04)
60mg daily	‘25’ patch (Matrifen £21.52)
120mg daily	‘50’ patch (Matrifen £40.24) max. titrated dose without specialist input
180mg daily	‘75’ patch
240mg daily	‘100’ patch

Source BNF 74 Costs are from MIMS October 2021 and based on one of the local formulary choice brands, Matrifen 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 source. 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 and Sevodyne are 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

Other 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.