NHS South Yorkshire Integrated Care Board

Guidance on the use of strong opioids in Barnsley

Background[1,2,3,4,5,6]

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

NHS England advise that pharmacological management of chronic non-cancer pain is associated with minimal benefits, and potential harm, when compared to effective biopsychosocial interventions. The evidence base for the use of opioids, and particularly strong opioids, in chronic pain is insufficient to justify their use for this indication, although it is acknowledged that because of dependency people can find it difficult to withdraw from these medicines. Taking an opioid for longer than 3 months increases the risk of dependence and addiction Patients who are supported to reduce or stop opioids that have been prescribed for chronic pain describe improved wellbeing, better quality of life, improved mobility and less pain.

NICE do NOT recommend initiation of opioids for managing chronic primary pain.

Patients prescribed opioids for chronic pain should be reviewed and as part of shared decision making, consideration given to the withdrawal of opioids. (SY ICB tapering guidance is available to assist with opioid withdrawal).

In March 2025 the MHRA issued an alert to prescribers withdrawing the indication for use of prolonged-release opioids in post-operative pain due to the increased risk of persistent post-operative opioid use and opioid-induced ventilatory impairment. The alert includes information for healthcare professionals and patients. It is not recommended that transdermal patches are applied for the treatment of post-operative pain.

This guidance relates to step 3 of the analgesic ladder and considers the following opioids:

- *Morphine*
- *Oxycodone*
- *Fentanyl*
- *Buprenorphine*
- *Methadone*

These drugs are available in a variety of formulations such as modified release preparations, transdermal patches, buccal tablets and granules for suspension.

Parenteral administration is not considered in this guidance.

The WHO[7] analgesic ladder advises prompt oral administration of drugs in a stepwise approach for **cancer pain** relief in adults[1]

Step 1 - Non-opioids (paracetamol, ibuprofen)

Step 2 - Weak opioids (codeine)

Step 3 - Strong opioids (morphine)

Analgesia should be given regularly rather than ‘on demand’ in order to maintain freedom from pain. Administering the right drug in the right dose at the right time is inexpensive and 80-90% effective.

Long-term use of opioids in **chronic primary pain** (longer than 3 months) carries an increased risk of dependence and addiction, even at therapeutic doses; before starting treatment with opioids, agree with the patient a treatment strategy and plan for end of treatment[2]

Morphine is the first line strong opioid of choice

- Morphine is the recommended opioid in the European Association of Palliative Care guidelines.
- Titration of morphine doses to individual patient needs is relatively straightforward.
- Morphine is the most cost-effective option when compared to alternative strong opioids. The formulary choice is Zomorph® (except for the 5mg dose which is only available as MST®)
- There is no compelling evidence to support the use of a non-morphine opioid for first line analgesia in cancer.[8]
- Any decision to use an alternative opioid is determined by adverse effects experienced with morphine or if the patient has renal impairment.
- Reports on the use of morphine in cancer pain state that adverse effects were common but not associated with a high discontinuation rate (4%)[4] suggesting that adverse effects can be managed in most patients.

Non-morphine opioids

- Non-morphine opioids, such as fentanyl, buprenorphine and oxycodone are significantly more expensive than oral morphine.
- There is no consistent evidence to suggest that non-morphine opioids are any more effective or show improved tolerability when compared with oral morphine[6]
- There is not enough evidence to recommend a particular sequencing of opioids[6]

Transdermal opioid preparations should only be used for patients with stable pain who cannot tolerate oral opioids due to severe side effects or if the oral route is unacceptable or if the patient has renal impairment.

Please print the MHRA Patient Information Leaflet for the safe administration and disposal of opioid patches and give to the patient/carer.

A patch may cause serious harm if it accidentally touches or sticks to somebody else's skin or if a child puts it in their mouth.

It is very important for patients to:

- **Follow the instructions for use** – Read the instructions closely every time you use a patch (see instructions on the patch, on the box, and in the leaflet that accompanies your medicine). Never divide or cut the patch. Wash hands after application.
- **Ensure the patch is stuck on securely** – Choose the application site carefully and make sure that the patch is stuck, especially around the edges, by pressing it for 30 seconds.
- **Avoid heating patches** – Make sure the patch doesn't heat up (for example, with a hot-water bottle or a long hot bath); heat can cause a dangerous amount of medicine to come out of the patch.
- **Remove and fold old patches** – Always remove and dispose of old patches before adding a new one. Fold the patch in half as soon it is removed so that the sticky side sticks firmly to itself and put back in the original sachet.
- **Dispose of safely** – Keep patches out of sight and out of reach of children. Dispose of old patches as instructed by your pharmacist.

If a patch transfers to another person, remove it and ring 999 immediately.

Transdermal (TD) Fentanyl (Fencino® /Opiodur®): please prescribe by *brand name*[5,6,7,8,9,10]

Note: Fencino® is contraindicated in patients allergic to peanut or soya.

- Fentanyl is a potent opioid - a 25microgram/hr patch is equivalent to up to 60-90mg/day Oral Morphine
- There is little evidence of improved tolerability other than a small reduction in the incidence of constipation, and many patients cannot avoid morphine completely (using oral morphine for breakthrough pain).
- Fentanyl is contraindicated for use in all opioid-naïve patients, including those with malignant pain
- The Commission on Human Medicines (CHM) has recommended that fentanyl transdermal patches are contraindicated in opioid-naive patients with chronic primary pain in the UK[7].
- Fentanyl should NOT be used as a first line strong opioid. It is more likely to cause respiratory depression than oral opioids. Rapid titration of fentanyl increases the risk of opioid induced hyperalgesia (OIH)
- Fentanyl patches are significantly more expensive than oral morphine.
- There are many issues to consider relating to the safe and effective use of fentanyl patches:
  - TD fentanyl is inappropriate for unstable pain (its action is not quick enough to manage unstable pain).
  - Proceed cautiously when titrating the dose.
  - It can take 36-48 hours to reach steady state, during which time other analgesia is needed.
  - Fentanyl is eliminated slowly, and significant blood levels persist for at least 24 hours.
  - Fatalities and life-threatening adverse effects have been reported with incorrect use of TD fentanyl (as with all modified release opioids).
  - Patients should be advised to hold the patches on for at least 30 seconds to ensure they stick.
  - The absorption of fentanyl through the skin is affected by temperature (including raised body temperature). Patients should be advised to avoid excessive heat sources

Any patients prescribed > 50 mcg/hr should be reviewed, and referred to the appropriate specialist services as the risks outweigh the benefits

Fentanyl preparations for breakthrough pain *(nasal spray Instanyl ® and Pecfent®, buccal Effentora ®, sublingual Abstral ® and fentanyl lozenges – Actiq®) have only shown efficacy in placebo-controlled trials. In the absence of direct comparator trials their use cannot be recommended in preference to less costly alternatives such as oral morphine, unless prescribed by a specialist. These preparations are included in the NHS England guidance 'Drugs not to be routinely prescribed in primary care' [10] except for use in palliative care.*

Transdermal (TD) Buprenorphine: please prescribe by brand name[18,19,20].

Avoid cutting of a patch as this may adversely affect the release mechanism of the medicine and release more than intended.

Transtec® 4 day patches: efficacy has only been shown in placebo-controlled randomised studies.
No good evidence exists for using BuTrans® 7 day patches in cancer pain.
Buprenorphine is probably slightly less potent than Fentanyl: A 5mcg/hr patch is equivalent to approximately oral morphine 12mg in 24 hours.
Buprenorphine may cause less Opioid Induced Hyperalgesia (OIH) than other opioids.
Transdermal buprenorphine preparations are not recommended over less costly options.
7 day patches are lower dose patches equivalent to 5mcg/hr, 10mcg/hr etc as opposed to 3 day patches with doses of 35mcg/hr upwards.
Titrate patch doses NO MORE FREQUENTLY THAN WEEKLY, When patients are needing rapid titration of a strong opioid then a patch preparation is not the right choice.

If rapid titration is required, this should be done with oral or sub-cutaneous injections (palliative care) and switch to a patch when pain control is stable.

Sevodyne® - First line choice 7 day patch

- When starting therapy evaluate analgesic effect after 72 hours. Thereafter the 7-day dosing interval should be maintained.
- Other opioids should not be administered within 24 hours of patch removal
- Sevodyne® is not licensed for malignant pain

Bupeaze® - First line choice 4 day patch

- When starting therapy evaluate analgesic effect after at least 96 hours
- (In practice patients are advised to replace the patch twice weekly, on the same days each week.(E.g. Monday morning and Thursday evening.
- It can take up to 30 hours for the plasma buprenorphine concentration to decrease by 50% after the patch is removed
- In view of the long duration of action, patients who have severe side effects should be monitored for up to 30 hours after removing patch

Hapoctasin® - First line choice 3 day patch

- When starting therapy evaluate analgesic effect after at least 72 hours
- Other opioids should not be administered within 24 hours after removal of hapoctasin® patches.

Transdermal Opioid Preparations cost comparison chart[15,16,17]

Preparation	Strengths available (mcg/hr)	Cost per 30 days [11 12]	Comments
Fentanyl Patches (prescribed generically) / Priced as Durogesic DTrans®	12 25 50 75 100	£ 25.18 £ 35.98 £ 67.32 £ 93.98 £115.72	Apply each patch for 72 hours. If prescribed generically, the pharmacy is reimbursed the same cost as for Durogesic DTrans®
Fencino® patches (Fentanyl) Contra-indicated in patients who are allergic to peanuts or soya.	12 25 50 75 100	£ 16.92 £ 24.20 £ 45.24 £ 63.08 £77.76	Apply each patch for 72 hours
Opiodur® patches (Fentanyl))	12 25 50 75 100	£11.28 £16.14 £30.18 £42.10 £51.88	Apply each patch for 72 hours
Sevodyne® Patches (Buprenorphine)	5 10 15 20	£ 5.93 £ 10.64 £ 15.51 £ 19.38	Apply each patch for 7 days.
Hapoctasin® patches **(Buprenorphine)**	35 52.5 70	£9.48 £14.23 £18.96	Apply one patch every 3 days (72 hours)
Bupeaze® Patches (Buprenorphine)	35 52.5 70	£ 20.27 £ 29.97 £ 38.55	Apply each patch for up to 96 hours. For practical purposes change patch TWICE a week at regular intervals

Methadone

- Methadone may be used to control pain in palliative care patients.
- Methadone should be initiated by specialists only.
- Useful alternative to morphine for patients experiencing intolerable side effects with morphine, end stage renal failure or persistent cough in end stage disease unresponsive to other anti- tussives.

Oxycodone Modified Release(OxyPro®) and Oxycodone Immediate Release (Shortec®)

A meta-analysis of three studies comparing oxycodone with morphine have not shown oxycodone to be superior to morphine in terms of efficacy or side effects[13]

Oxycodone may be considered as an option for severe pain in patients who are unable to tolerate morphine where a strong opioid is indicated. Oxycodone may be used as an alternative to morphine when there is renal impairment.

- As with oral morphine, oral oxycodone is available as modified release **and** standard release tablets/capsules. Particular care should be taken when selecting the preparation of oxycodone to prescribe.

To improve patient safety, it is recommended to prescribe solid oral preparations of oxycodone by brand. The preferred brand of oxycodone for use in Primary Care in Barnsley* is:

OxyPro® for **Oxycodone Prolonged Release tablets**
Shortec® is the preferred choice for **short acting oxycodone immediate release capsules.**

- **Oral oxycodone 10-13mg corresponds to approximately 20mg of oral morphine[3]. It is common practice to use a ratio of oral oxycodone 10mg = oral morphine 20mg[1]**

***In-patients at BHNFT prescribed oxycodone prolonged release will be prescribed the brand Longtec®. It has been agreed that both brands will be documented on the D1 discharge letter (e.g. Longtec®/OxyPro®) to indicate that OxyPro® can be substituted for Longtec® following discharge back to primary care.**

Oxycodone child proof blister pack (Oxypro® and other brands) opening instructions

To improve patient safety Oxypro® and some other brands come in child resistant blister packaging.

The tablet cannot be pressed out of the blister pack. If the patient finds it difficult to peel away the cover foil, consider prescribing the second line choice of Longtec® tablets that uses a press out blister pack (liaise with patient and pharmacy).

Prescribe by a brand name to ensure continuity.

For child resistant pack opening instruction video go to this website and click on the video: https://www.oxypro- info.com/patient/#support-materials

1. Pull off a single dose by tearing along the perforated line on the blister
2. An unsealed area is exposed; this area is at the point where the perforated lines intersect with each other.
3. Peel away the cover foil from the from the bottom foil.

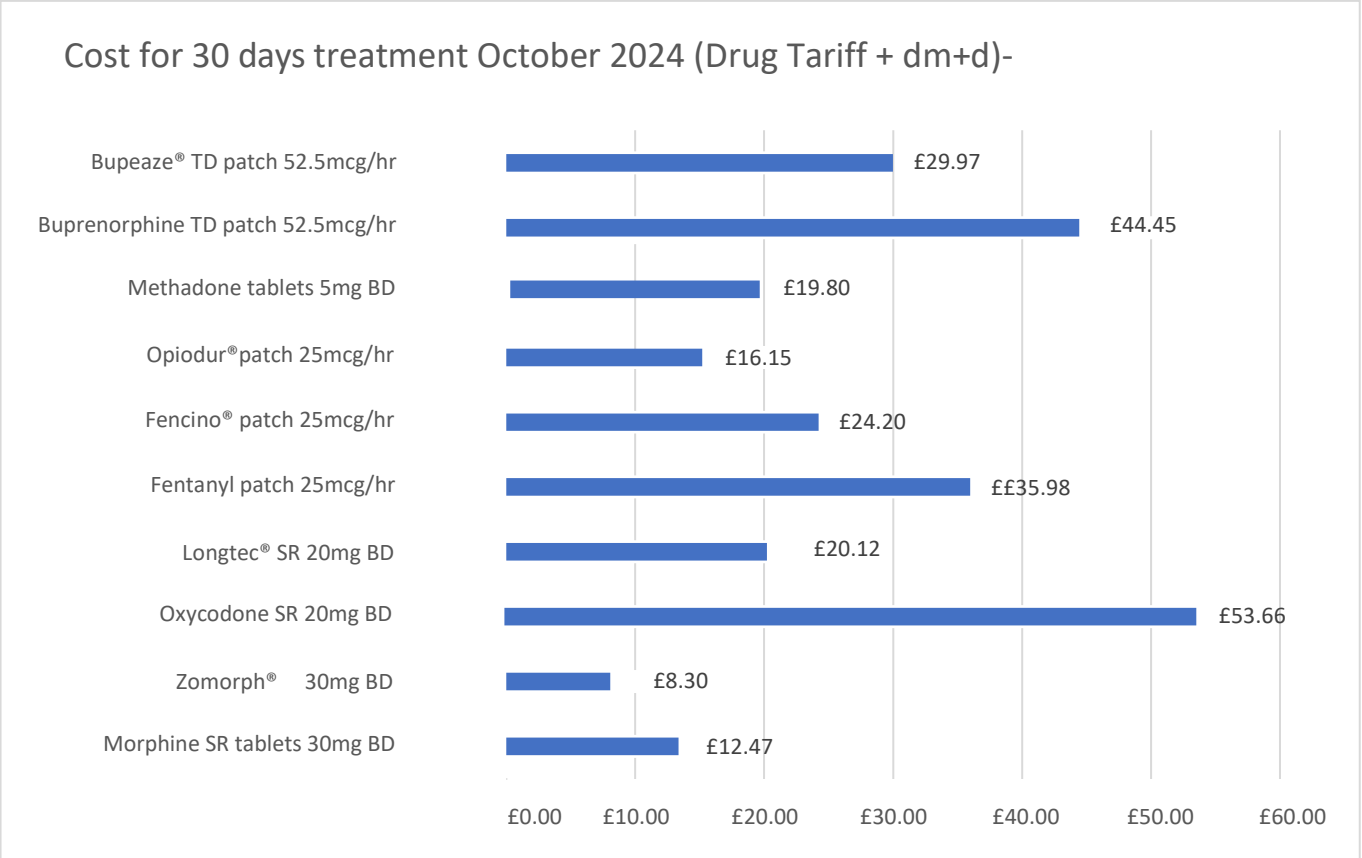
Oxypro® tablets have a diameter of between 6.9-7.3mm and are the same size for all strengths.

Administration

- Oxycodone prolonged release tablets (Oxypro® or Longtec®) must be **swallowed whole, not chewed, divided or crushed** as this may lead to a rapid release and absorption of a potentially fatal dose of oxycodone.
- Oxycodone immediate release capsules**: (**Shortec®**) must be swallowed whole and must not be opened.**
- Oxycodone liquid: **There are significant risks of overdose if a concentrate product is used in error for a normal strength product.**[4]
  - incidents have occurred where oxycodone CONCENTRATE LIQUID 10mg/ml was selected in error when oxycodone 'normal' strength LIQUID 1mg/ml (5mg/5ml) was intended.
  - Oxycodone liquid is available in both strengths to prescribe generically
- Oxycodone Injection:
  - Subcutaneous oxycodone should be considered if:
    - Patients already taking oxycodone orally (regular or PRN) are no longer able to swallow / use the oral route,
    - Subcutaneous strong opioids are required AND morphine cannot be tolerated due to side effects e.g. vomiting, drowsiness, confusion, OR in:
    - Renal impairment where eGFR< 30ml/min/1.73m^2
  - Prescribe oxycodone injection by the 10mg/ml ampoule strength. Avoid excessive quantities by prescribing the 1ml ampoule (10mg/ml).
  - The 50mg/ml injection is rarely used. Only use after discussion with palliative care team. This strength will be required if oxycodone PRN subcutaneous dose is greater than 25mg.

Do Not Prescribe Targinact® (oxycodone and naloxone) - non formulary

The chart below provides a cost comparison of the opioids discussed in this briefing[15,16,17]:



Patients with a history of addiction to opioids or other drugs need referral to services with expertise in pain and addiction management

This guideline was endorsed by the Barnsley Area Prescribing Committee on 12th March 2025. Review due March 2028.

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