Guidance on the use of strong opioids in Barnsley

NHS Barnsley Clinical Commissioning Group

Pain should be managed in a stepwise approach

The WHO 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]

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 modified release preparations, transdermal patches, buccal tablets and granules for suspension. Parenteral administration is not considered in this guidance.

Morphine is the first line strong opioid of choice

- Morphine is the recommended opioid in the European Association of Palliative Care guidelines.[3]
- 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.[4]
- 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.[4]
- There is not enough evidence to recommend a particular sequencing of opioids.[4]

Transdermal (TD) Fentanyl (Fencino® / Matrifen®) : please prescribe by *brand name*

- Fentanyl is a potent opioid - a 25microgram/hr patch is equivalent to up to 90mg/day Oral Morphine[5,6]
- There is little evidence of improved tolerability other than a small reduction in the incidence of constipation[4], 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[6,7]
- 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 1st 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)[5]
- 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 a minute 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.[6-8]

Any patients prescribed > 50mcg/hr should be reviewed, and referred to the appropriate specialist services as the risks outweigh the benefits[9]

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.*

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Transdermal (TD) Buprenorphine: please prescribe by *brand name*

Transtec® 4 day patches: efficacy has only been shown in placebo-controlled randomised studies.[4]
No good evidence exists for using BuTrans® 7 day patches in cancer pain.[4]
Buprenorphine is probably slightly less potent than Fentanyl: A 5mcg/hr patch is equivalent to approximately oral morphine 12mg in 24 hours.[5]
Buprenorphine may cause less Opioid Induced Hyperalgesia (OIH) than other opioids.[5]
Transdermal buprenorphine preparations are not recommended over less costly options.

Sevodyne® - First line choice 7 day patch

- When starting therapy evaluate analgesic effect after 72 hours
- Adjust dose at 3 day intervals if required
- 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 24 hours
- Adjust dose at 96 hour intervals if required (in practice patients are advised to replace the patch twice weekly, on the same days each week)
- 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

Transdermal Opioid Preparations

Preparation	Strengths available(mcg/hr)	Cost per 30 days[11,12]	Comments
Fentanyl Patches (prescribed generically) / 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® (Fentanyl)	12 25 50 75 100	£ 16.92 £ 24.20 £ 45.24 £ 63.08 £77.76	Apply each patch for 72 hours
Matrifen®(Fentanyl)	12 25 50 75 100	£15.04 £21.52 £40.24 £56.12 £69.14	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.
Bupeaze® Patches (Buprenorphine)	35 52.5 70	£ 23.68 £ 34.98 £ 44.98	Apply each patch for up to 96 hours. For practical purposes change patch TWICE a week at regular intervals

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

Please refer patients to this Patient Information Leaflet for the safe administration and disposal of opioid patches

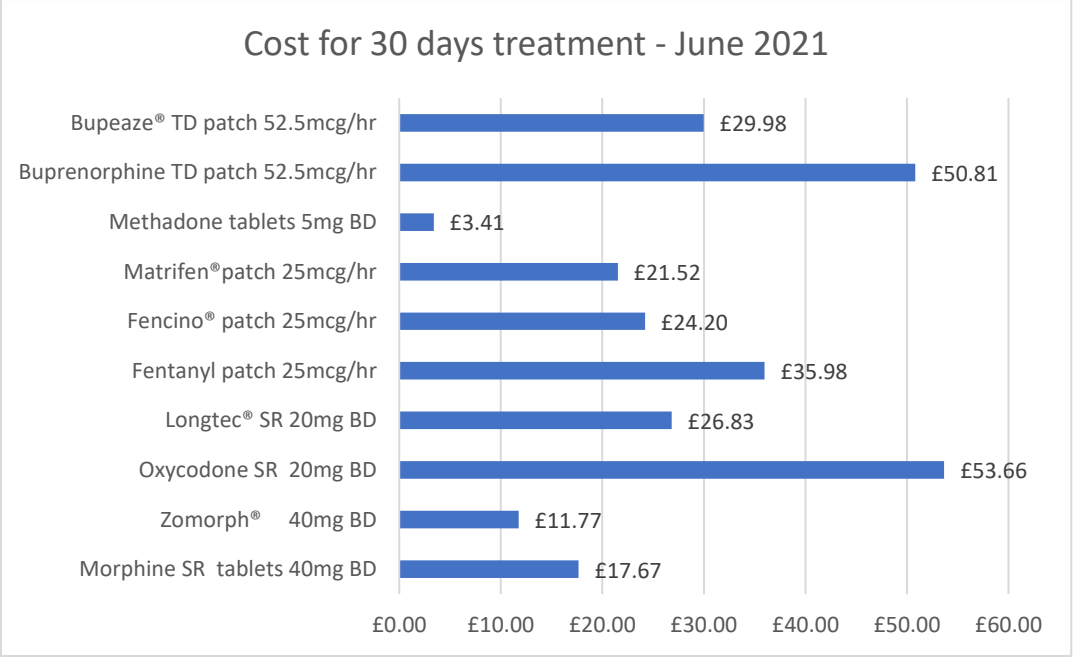
Oxycodone Modified Release (Longtec®) and Oxycodone Immediate Release (Shortec®)

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]
In July 2010 an MTRAC review concluded that Oxycodone MR was suitable for prescribing in primary care as a second-line option in patients unable to take morphine.[14]
As with morphine, oxycodone is available as modified release **and** standard release tablets/capsules. Particular care should be taken when selecting the preparation of oxycodone to prescribe. Oxycodone should also be prescribed by brand name – the preferred brand in Barnsley is Longtec®/ Shortec.®

Methadone

- Methadone is increasingly being used to control pain in palliative care patients.
- 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.

The chart below provides a cost comparison [11,12] of the opioids discussed in this briefing:



Patients with a history of addiction to opioids or other drugs need referral to services with expertise in pain and addiction management [9]

This guideline was endorsed by the Area Prescribing Committee on 13th October 2021. It is due for review in October 2024.

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