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Medicines Optimisation *Key Messages – Bulletin 40*

Initiation and Management of Opioids in Palliative Care

KEY MESSAGE: Achieve control of pain by administering the right drug at the right dose at the right time

Starting strong opioids

- Patients with advanced and progressive disease may require treatment with strong opioids.
- **First line choice of strong opioid is oral morphine**;
  - For opioid naïve patients a starting dose of 2.5mg-5mg of immediate release oral morphine at 4 hourly intervals plus 'when required' doses is recommended[1].
  - Lower doses may be required in elderly or patients, those with renal impairment or opioid sensitivity.
  - For patients already taking opioids, the dose of morphine will depend on the strength and dose of the opioid currently being taken – see 'Conversion of common opioids' below.
- Regular and 'when required' doses may be **increased by up to 30%** if pain control is inadequate and there is no evidence of toxicity.
- Regular and 'when required' doses should be titrated until effective 4 hourly analgesia is achieved.
- The total daily amount of oral release morphine should then be converted to a sustained release morphine preparation given **12 hourly**. For example a total daily dose of 60mg of oral immediate release morphine should be converted to 30mg of oral sustained released morphine, twice dally.
- The preferred choice of cost effective sustained release oral morphine preparation is **Zomorph® Modified Release Capsules.**
- Break though analgesia should be provided for when required doses in the form of immediate release oral morphine at approximately one-tenth to one-sixth of the total daily dose of sustained release morphine.

Cost effective brand prescribing of strong opioids is encouraged, however, to avoid delay in obtaining urgent analgesia, it may be prudent to prescribe generically

Alternative strong opioids

- Alternative opioids may be considered if a patient develops intolerable side effects without achieving adequate pain relief[1].
- The nature of the pain (i.e. onset and duration), the pharmacokinetic and pharmacodynamics of the opioid plus the patients response and tolerability to previous opioid should be taken in to consideration when switching to a second line opioid.

Oxycodone

- **Oral Oxycodone** may be used as an alternative to morphine. **Oral oxycodone is approximately twice as potent as oral morphine.**
- Oxycodone and it's metabolites may accumulate in renal impairment and should be **avoided if eGFR <10mL/min/1.73m^2**
- **Oxypro® MR tablets** are the preferred cost effective choice of sustained release oral oxycodone (July 2022)[3]
- Break though analgesia should be provided at approximately one sixth of the total daily oxycodone dose.

Alternative strong opioids

Fentanyl

- Transdermal fentanyl may be used as an alternative to oral morphine where sedation or constipation are problematic. However, it will not relieve pain that is unresponsive to morphine.
- Cost effective choices of fentanyl patch include **Matrifen®** [3]
- **DO NOT** use fentanyl patches in opioid naïve patients. Transdermal fentanyl is approximately **150 times more potent** than oral morphine. See BNF or http://book.pallcare.info/index.php?tid=125 for guidance on conversion from oral morphine.
- **DO NOT** use immediate release fentanyl for break though pain[2]. Buccal preparations (Effentora®, Breakyl®), lozenges (Actiq®), nasal sprays (Instanyl®, PecFent®) are **TAG Double Red**[4]. Immediate release oral morphine should be used first line for break through pain. Sublingual fentanyl tablets (Abstral®) may be used as a third-line treatment option for breakthrough pain in cancer but prescribing responsibility should remain with consultant or palliative care specialist (**TAG RED**)[4].

Anti-emetics and Laxatives

- Patients started on strong opioids should have access to **anti-emetics** for the first 5 -7 days and also be prescribed a **regular laxative** to prevent constipation[1].
- Nausea is likely to occur when starting strong opioids and at dose increase, however, it is likely to be transient. Haloperidol or metoclopramide should be used as first line anti-emetics for opioid induced nausea[5]. If nausea persists ensure anti-emetic treatment is optimised before switching to an alternative opioid.
- First line choice of **laxatives** for opioid induced constipation are a **stimulant** (bisacodyl or senna) and / or **macrogrol** (Laxido® or Cosmocol®).
- **Laxatives should be prescribed regularly, not PRN**. Patients should be advised of the importance of adherence to laxative treatment and that treatment for constipation may take time to work.
- If constipation persists despite 2 weeks regular use of a stimulant and an osmotic laxative in **combination** consider a trial of Naloxegol (**TAG Double Green**[4]) – see local treatment pathway for Management of Opioid Induced Constipation[6].

Conversion of common opioids and factors to consider

- There will be variation in response to different opioids between individual patients therefore, **equivalence values are only approximate**.
- Manufacturers' conversion rates are cautious and may overestimate relative potency of their drug.
- Incomplete cross tolerance (tolerance to currently administered opioid that does not extend completely to other opioids) means that a **dose reduction of 25-50% of the new opioid may be required**.
- **Caution** should be used in the **elderly** and in patients with **renal or significant hepatic impairment**.
- Patients should be carefully monitored after any change in opioid and dose titrated accordingly.

	Relative potency to oral morphine	Equivalent 24 hr dose to 30mg PO Morphine
Codeine PO	**0.1**	**300mg**
Tramadol PO	**0.1**	**300mg**
Alfentanil SC	**30**	**1mg**
Buprenorphine TD	**100**	**300micrograms (12.5micrograms per hour)**
Diamorphine SC	**3**	**10mg**
Fentanyl SC	**150**	**200micrograms**
Fentanyl TD	**150**	**200micrograms (8.33micrograms per hour)**
Morphine PO	**1**	**30mg**
Morphine SC	**2**	**15mg**
Oxycodone PO	**2**	**15mg**
Oxycodone SC	**3**	**10mg**

- **Based on manufacturer's datasheet recommendations[1]. An opioid dose conversion calculator is also available through Palliative Care Guidelines Plus http://book.pallcare.info/index.php?op=plugin&src=opiconv**

References

1. Palliative Care Guidelines Plus http://book.pallcare.info/index.php
2. Palliative care for adults: strong opioids for pain relief https://www.nice.org.uk/guidance/cg140
3. Low risk, Cost-effective Prescribing QIPP Support Scheme 1st July 2022 to 30th September 2022, Norfolk & Waveney Clinical Commissioning Group, v1.0
4. Norfolk and Waveney Therapeutics Advisory Group (TAG) http://nww.knowledgeanglia.nhs.uk/tag/tag_recommend_report.pdf
5. BNF August 2016 https://www.medicinescomplete.com/mc/bnf/current/PHP107735-prescribing-in-palliative-care.htm?q=palliative&t=search&ss=text&tot=57&p=1#_hit
6. Management of Opioid-Induced Constipation http://nww.knowledgeanglia.nhs.uk/tag/opioid_constipation_pathway.pdf

Title	KEY MESSAGES Bulletin 40 Initiation and Management of Opioids in Palliative Care
Description of policy	*To inform healthcare professionals*
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Evidence base / Legislation	Level of Evidence: *A. based on national research-based evidence and is considered best evidence* ***B. mix of national and local consensus*** *C. based on local good practice and consensus in the absence of national research based information.*
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