SPAGG

Coversheet for Specialist Palliative Audit and Guideline Group Agreed Documentation

This sheet is to accompany all documentation agreed by SPAGG. This will assist maintenance of the guidelines as well as demonstrating the governance process undertaken prior to members seeking local approval in their areas of work.

Document Title	**Guidelines for the use of subcutaneous parecoxib in palliative patients with cancer pain**
Document Date	March 2021
Document Purpose and Intended Audience	This guideline provides information about the use of subcutaneous parecoxib in palliative care patients for cancer pain
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References	At end of document
Consultation Process	Discussed and ratified at SPAGG
Monitoring	Review by SPAGG
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Approval Signatures:	
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Date submitted to Area Prescribing Committee:	

Version History

Version	Date	Summary of Change/Process
1.0	3/3/21	

Scope of the Guideline

This guidance has been produced to support the use of subcutaneous parecoxib in palliative care patients for cancer pain. It is aimed at the inpatient setting, although use in the community setting may be considered where responsibility for its use, prescription and monitoring is jointly agreed between specialist palliative and primary care.

General information

This guidance has been developed to establish a degree of consensus in clinical practice that is likely to be beneficial to symptom control management in palliative care, despite the current low quality evidence level.

Background information

Non-steroidal anti-inflammatory drugs (NSAIDs) are essential medications for cancer pain management, featuring on the WHO analgesic ladder for mild or moderate pain, with a well-recognised role for metastatic bone pain. The analgesic effect occurs through multiple modes of actions; one proposed mechanism of action is the prevention or reversal of inflammation-induced hyperalgesia locally and in the CNS[1].

The choice of NSAID in the palliative care setting is influenced by factors such as availability, side effect profile, concomitant health conditions, interactions with other medications and co-morbidities, available routes of administration, local guidelines and cost. There is no evidence to suggest any particular NSAID is more beneficial in cancer pain. Whilst the renal risks of different NSAIDs are similar and are not a factor in determining choice, selective COX-2 inhibitors have a lower propensity for gastrointestinal side-effects and complications, with the PCF7 suggesting that celecoxib is now probably the overall NSAID of choice in palliative care[1].

Parecoxib, a prodrug of valdecoxib, is an injectable selective COX-2 inhibiter, licensed in the UK for the short-term treatment of postoperative pain in adults by the intramuscular or intravenous routes[2]. A small but growing body of evidence examining its use in the palliative care setting suggests parecoxib to be efficacious and generally well tolerated[3,4,5,6]. It may therefore hold a valuable place in the management of cancer pain particularly towards the end of life when oral medication is no longer possible, and the significantly higher GI risk of CSCI ketorolac or diclofenac preclude their use. This is reflected by the inclusion of parecoxib within the Palliative Care Formulary.

Guideline Statements

Indication

- Subcutaneous parecoxib has a potential role in cancer pain management, particularly malignant bone pain, especially in patients who are unable to take medications orally.
- The use of subcutaneous parecoxib in palliative care is off-license for both the route of administration and indication, and this should be discussed with the patient before use.

Dosing

- Parecoxib can be given 40mg SC once or twice daily (twice daily may be clinically preferred due to its limited duration of action), or 40-80mg/24hr via continuous subcutaneous infusion (CSCI). The maximum licensed dose in 80mg/24 hours[2].
- In moderate liver impairment, several renal failure[1] and for the elderly (body-weight up to 50kg) [2], an initial dose of 20mg and maximum dose of 40mg may be appropriate. Manufacturers also recommend a lower initial dose of 20mg if GFR<30.

Volumes, Diluent and Compatibility

- Parecoxib should be diluted to a volume of 22ml, to reduce the risk of site reactions[1] .
- 0.9% saline is the preferred diluent, in order to reduce the risk of site reactions[1].
- There is very limited evidence for compatibility of subcutaneous parecoxib with other medications, apart from ranitidine [7], and currently should not be combined with any other medications in the CSCI route.
- CSCI Parecoxib has been combined with dexamethasone 500 micrograms in cases of site reactions[3].

Duration of usage

- There is no evidence to limit the duration of usage for parecoxib in the palliative setting. Evidence of parecoxib use in a non-palliative setting has been based on short-term usage in the acute setting (less than 7 days).

Monitoring

- Baseline and repeat monitoring of renal function should be considered, especially in those who may have pre-existing renal impairment, are receiving concomitant nephrotoxic medications, or receive prolonged administration of parecoxib where the risk to renal function could feasibly change.

Cautions and contra-indications

- Cautions and relative/absolute contraindications relevant to non-steroidal anti-inflammatory useage apply to parecoxib.
- Contraindications include: active gastro-intestinal bleeding; active gastro-intestinal ulceration; cerebrovascular disease; following coronary artery bypass graft surgery; inflammatory bowel disease; ischaemic heart disease; mild to severe heart failure; peripheral arterial disease[2].
- Cautions include: Allergic disorders; cardiac impairment (NSAIDs may impair renal function); coagulation defects; connective-tissue disorders; dehydration (risk of renal impairment); elderly (risk of serious side-effects and fatalities); history of cardiac failure; history of gastro-intestinal disorders; hypertension; may mask symptoms of infection; oedema; risk factors for cardiovascular events[2].
- Gastroprotection: where parecoxib has been used in existing palliative care settings, most patients have been prescribed gastroprotection, although this may not be necessary. (PCF p. 325). Parecoxib is compatible with ranitidine[7].
- Renal function: the renal risks of different NSAIDs, including parecoxib, are similar; generally NSAIDs are not recommended in severe renal impairment. No significant additional risk to renal function has been identified in studies of parecoxib, to date.
- Cardiovascular events: Both non-selective NSAIDs and COX-2 inhibitors are associated with an increased risk of cardiovascular events in long-term use.
- Parecoxib is also associated with unpredictable but serious skin reactions including angioedema, erythema multiforme and Stevens- Johnson Syndrome. In the event to this, discontinue parecoxib and seek urgent specialist advice.
- In a pooled analysis of 28 placebo-controlled trials of parecoxib and review of post-authorisation safety, for patients receiving up to 7 days of parecoxib administration, the GI ulceration-related events, renal impairment, hypersensitivity reactions, severe cutaneous reactions and cardiovascular embolic/thrombotic events were similar to placebo[8].

Monitoring of the guideline

The use of this guideline will be monitored via regional data collection/audit by SPAGG. Audit data to be captured includes:

- Setting of use (IPU/Hospital/community)
- Age
- Sex
- Diagnosis
- Reason for parecoxib
- Switch from oral/topical NSAID?
- Liver impairment? (if known- Y/N/NA)
- Renal function if known (numerical / NA)
- Length of time on CSCI (days)
- CSCI starting dose
- CSCI end dose
- CSCI length of time
- MME (mean morphine equivalent) background day 1
- MME background day 3
- MME background day 7 / final day (whichever sooner)
- PRN SC analgesia frequency / 24 hours day 1
- PRN SC analgesia frequency / 24 hours day 3
- PRN SC analgesia frequency / 24 hours day 7/final day (whichever sooner)
- Mean pain score day 1
- Mean pain score day 3
- Mean pain score day 7 / final day
- Gastroprotection co-prescribed (Y/N)
- Adverse events
  - Site irritation (mild/moderate/severe)
  - Clinically significant renal impairment
  - GI bleed
  - Other

References

[1] Twycross R and Wilcock A. Palliative Care Formulary (7th edition). Pharmaceutical Press, 2020.

[2] National Institute for Health and Care Excellence. Parecoxib (Internet). NICE 2021. (Cited 12 Jan 2021) Accessed: https://bnf.nice.org.uk/drug/parecoxib.html

[3] Armstrong P, Wilkinson P, McCorry N. Use of parecoxib by continuous subcutaneous infusion for cancer pain in a hospice population. BMJ Support Palliat Care. 2018; 8(1): 25-29.

[4] Kenner D, Bhagat S, Fullerton S. Daily subcutaneous parecoxib injection for cancer pain: an open label pilot study. J Palliat Med, 2015. 18(4): 366-372.

[5] Takerar A et al. Parecoxib as an adjunct therapy for the treatment of refractory non-surgical cancer pain. J Oncol Pharm Practi 2020; 26(6): 1407-1414

[6] Kellett et al. Parecoxib for opioid-induced hyperalgesia. BMJ Support Palliat Care. 2020 Jun 29:bmjspcare-2020-002290. doi: 10.1136/bmjspcare-2020-002290. Online ahead of print.

[7] Palliativedrugs.com. Syringe Driver Survey Database (SDSD) (Internet). Royal Pharmaceutical Society 2021. (Cited 10 Jan 2021). Accessed: https://www.palliativedrugs.com/syringe-driver-database-introduction.html

[8] Schuq S et al. The safety profile of parecoxib for the treatment of postoperative pain: a pooled analysis of 28 randomized, double-blind, placebo-controlled clinical trials and a review of over 10 years of postauthorization data. J Pain Res 2017; 10: 2451-2459.