

# 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.

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| **Document Title** | **Guidelines for the use of subcutaneous parecoxib in palliative patients with cancer pain** |
| **Document Date** | March 2024 |
| **Document Purpose and Intended Audience** | This guideline provides information about the use of subcutaneous parecoxib in palliative care patients for cancer pain |
| **Authors** | Dr Nadia Khan |
| **References** | At end of document |
| **Consultation Process** | Discussed and ratified at SPAGG |
| **Monitoring** | Review by SPAGG |
| **Review Date** | March 2027  |
| **Approval Signatures:** |  |
| SPAGG chair | Dr Jon Tomas |
| SPAGG deputy chair |  |
| SPAGG secretary | Dr Alice Martin  |
| **Date Approved by SPAGG: 6th March 2024**  |  |
| **Date submitted to Area Prescribing Committee:** |

**Version History**

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| **Version** | **Date** | **Summary of Change/Process** |
| 1.0 | 3/3/21 |  |
| 2.0 | March 2024 | Reviewed and update by M Aslett |

### 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 CNS1.

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 care1.

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 routes2. A small but growing body of evidence examining its use in the palliative care setting suggests parecoxib to be efficacious and generally well tolerated3,4,5,6. 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 via the subcutaneous route either as once or twice daily injections or as a continuous infusion using a syringe driver (CSCI).
* Dose options are 40mg subcut ONCE or TWICE daily or 40-80mg/24hr subcut CSCI
* The maximum licensed dose is 80mg/24 hours2.
* In moderate liver impairment, several renal failure1 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.

**Prescribing Points**

* Parecoxib is available as two formulations:-
	+ 40mg powder for solution for injection vials (pack of 10)
	+ 40mg powder and solvent for solution for injection vials (pack of 5)
* At the time of writing the guidelines, parecoxib is approximately £5 per 40mg vial
* In primary care it may take 24-48 hours to obtain supplies given that this is an item not routinely stocked by community pharmacists. Please allow time to obtain supplies to avoid disruptions in symptom management for patients established on parecoxib.

**Clinical Points**

* Duration of action of parecoxib is reported as 6-12 hours from a single dose 9
* Onset of analgesic effect has been reported from 23-39 minutes 9
* Interactions with Parecoxib will be as listed for NSAIDs.
* One notable interaction for palliative care is that if fluconazole is being used concomitantly then the dose of parecoxib needs to be reduced.

**Volumes, Diluent and Compatibility**

* **Sodium chloride is the only diluent to be used with parecoxib injection** – if water for injection is used the resulting solution is not isotonic and therefore can cause more site reactions1.
* Parecoxib should be diluted to a volume of 22ml, to reduce the risk of site reactions1 .
* CSCI Parecoxib has been combined with dexamethasone 500 micrograms in cases of site reactions3 where the increase in diluent volume or change in site has not helped.
* There is very limited evidence for compatibility of subcutaneous parecoxib with other medications, apart from ranitidine and esomeprazole 7, and ideally should not be combined with any other medications in the CSCI route.

**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 usage apply to parecoxib.

## Contraindications include2:

## 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

* Cautions include2:
	+ 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
* Gastroprotection
	+ where parecoxib has been used in existing palliative care settings, most patients have been prescribed gastroprotection, although this may not be necessary1. Parecoxib is compatible with ranitidine and esomeprazole7.
* 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 placebo8

**Monitoring of the guidelines**

The use of this guideline will be monitored via regional data collection/audit by SPAGG. Audit data should capture:

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| Setting of Use |
| Patient Info: |
| Age |
| Sex |
| Diagnosis |
| Indication for NSAID |
| Switched from Oral or Topical NSAID? |
| Liver impairment? |
| eGFR if known |
| Dose used and frequency OD/BD/CSCI |
| Duration of use of Parecoxib |
| MME (mean morphine equivalent):- |
| * Before Parecoxib
 |
| * Day 1 of Parecoxib
 |
| * Day 3 of Parecoxib
 |
| * Day 7 of Parecoxib
 |
| Mean pain score:- |
| * Before Parecoxib
 |
| * Day 1 of Parecoxib
 |
| * Day 3 of Parecoxib
 |
| * Day 7 of Parecoxib
 |
| PRN analgesia frequency:- |
| * Before Parecoxib
 |
| * Day 1 of Parecoxib
 |
| * Day 3 of Parecoxib
 |
| * Day 7 of Parecoxib
 |
| Was gastroprotection co-prescribed |
| Adverse effects reported:- |
| Site irritation |
| GI effects e.g. nausea, heartburn |
| GI bleed |
| Reduced renal function |
| Other |

**References**

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