



# Palliative care support of a patient with metastatic breast cancer

Accessing palliative care treatment guidance to manage the symptoms and common side effects of a patient with metastatic breast cancer.

Independent, specialist information, grounded in clinical practice



**Palliative Care Formulary**

Available through

 **Medicines  
Complete**



# Palliative Care support of a patient with metastatic breast cancer

Using essential knowledge at the point of care



Joan Kirkman, a 68-year-old patient with breast cancer, attends the oncology clinic at her local hospital. Unfortunately, her breast cancer has progressed to Stage 4 with bone metastases and she is referred to the palliative care team for further care.

At her appointment, Joan explains that she is currently experiencing severe pain that is not controlled by regular non-opioid analgesics. Her oncology registrar wants to start oral morphine and consults the Morphine monograph for guidance on an appropriate starting dose and advice on titration.

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Subsections	Related Content
Class	
Indications	
Contra-indications:	
Pharmacology	
Cautions	
Drug interactions	
Undesirable effects	
Dose and use	
Supply	

**Oral**

Morphine is available as:

- immediate-release products: tablets, orodispersible tablets, solutions
- m/r products: tablets, capsules, suspensions (not UK).

Most m/r products are administered b.d., some once daily. Because the pharmacokinetic profiles of m/r products differ, <sup>22-23</sup>it is best to keep individual patients on the same brand. M/r tablets should be swallowed whole; crushing or chewing them will lead to a rapid release of an overdose of morphine. For administration of immediate-release and m/r morphine to patients with swallowing difficulties or enteral feeding tubes (see Supply and [Swallowing difficulties and FFT, Table 2](#)).

Patients can be started on either an ordinary (immediate-release) or an m/r formulation (Box A). <sup>30-31</sup>An observational study supports a starting dose of 5mg q4h as generally safe for opioid-naïve patients, and 10mg q4h for those being switched from a regular weak opioid. <sup>32</sup>However, slight variation exists between guidelines, e.g. in the recommended starting dose. <sup>33</sup>It is important to recognize that guidelines are just guidelines; for each patient, when deciding the starting dose, it is necessary to consider the individual circumstances, e.g. severity of the pain, current analgesia, presence of renal impairment, increasing age or frailty. In every case, the patient must be monitored closely and the dose titrated as necessary.

**Box A** Starting a patient on PO morphine

The starting dose of morphine is calculated to give a greater analgesic effect than the medication already in use:

- if the patient was previously receiving a weak opioid regularly (e.g. codeine 240mg/24h or equivalent), give morphine 10mg q4h or m/r 20–30mg q12h, but less if suspected to be a poor codeine metabolizer (see [codeine phosphate](#))
- if changing from an alternative strong opioid (e.g. fentanyl, methadone), a much higher dose of morphine may be needed

## Community review

A week later, Joan visits her GP to request a continuation of her morphine supply. She is constipated despite taking senna at night. To find out what further course of action is recommended, her GP accesses the **Quick Clinical Guide: Opioid-induced constipation**.

The Royal Pharmaceutical Society's Knowledge Business

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Quick Clinical Guide: Opioid-induced constipation

**Palliative Care Formulary**  
Publication last updated on 14-Sep-2021

The Palliative Care Formulary provides unrivalled and independent drug information for health professionals when caring for adult patients facing progressive life-limiting diseases and their care givers. This trusted source goes beyond standard drug reference works, empowering health professionals to select the right drugs and treatment regimens at the point of care to help improve quality of life.

**Quick Clinical Guide: Opioid-induced constipation**  
Updated (minor change) January 2020

Generally, all patients prescribed an opioid should also be prescribed a laxative, with the aim of achieving bowel movement without straining every 1–3 days. A standardized protocol aids management.

Although all laxatives given in sufficient quantities are capable of normalizing bowel function in constipated patients, PCF favours a stimulant laxative based on efficacy, convenience and cost.

Sometimes, rather than automatically changing to the local standard laxative, it may be more appropriate to optimize a patient's existing regimen.

*These guidelines can also be followed in patients who are not on opioids, although smaller doses may well suffice.*

1. Ask about the patient's past and present bowel habit and use of laxatives; record the date of last bowel action.
2. Palpate for faecal masses in the line of the colon; examine the rectum digitally if the bowels have not been open for ≥3 days or if the patient reports rectal discomfort or has diarrhoea suggestive of faecal impaction with overflow.
3. For inpatients, keep a daily record of bowel actions.
4. Encourage fluids generally, and fruit juice and fruit specifically.

Subsections: Palliative Care Formulary, AHFS Drug Information, ASHP Injectable Drug Information, Agilia: Diagnosis and Treatment Guidance

Joan asks her GP about using cannabis products as they have been in the press recently. The GP refreshes their knowledge on the evidence for the use of cannabinoids in palliative care from the **Cannabinoids monograph** and answers Joan's questions.

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\*Cannabinoids

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**Currently available exogenous cannabinoids**

*Δ<sup>9</sup>-THC analogues*

*Δ<sup>9</sup>-THC* is a CB<sub>1</sub> and CB<sub>2</sub> partial agonist. Its effects include muscle relaxation, analgesia and anti-emesis, but it can also cause sedation, anxiety and psychosis. **Dronabinol** (not UK) is a synthetic preparation of its (-)-*trans* isomer, the best studied of several isomers present in *Cannabis sativa*; **nabilone** is a synthetic analogue.

*Cannabidiol (CBD)*

**Cannabidiol** is a negative allosteric CB<sub>1</sub> modulator<sup>22</sup> and a FAAH inhibitor (the enzyme that degrades anandamide; see Figure 1).<sup>28</sup> It is also a 5HT<sub>1A</sub> partial agonist (see **Antidepressants**), an adenosine re-uptake inhibitor (see **Psychostimulants**) and a PPAR<sub>γ</sub> agonist (a nuclear receptor with anti-inflammatory effects).<sup>28</sup>

A **cannabidiol** medicinal product (Epidyolex<sup>™</sup>) is authorized for two rare childhood epilepsy syndromes (Lennox-Gestault and Dravet), although the RCTs used to obtain these marketing authorizations have been strongly criticized (see Drug interactions, below). It is important to note that their mechanism and response to treatment differ significantly from other forms of epilepsy. Beyond these specific syndromes, cannabinoids do not have an established role in epilepsy.

Despite claims in the wider media, benefit for anxiety, depression, post-traumatic stress disorder and cancer cell growth has *not* been confirmed in RCTs.<sup>4, 10, 29</sup> Trials examining cannabinoids for *symptom relief* generally use *Δ<sup>9</sup>-THC* or a synthetic analogue, ± **cannabidiol**, and *not cannabidiol alone*. Further, a national registry of cannabinoid use found patient self-reported improvements in pain, insomnia and depressive symptoms were associated with the use of preparations containing higher ratios of *Δ<sup>9</sup>-THC*:CBD.<sup>30</sup>

Products containing **cannabidiol** are legally sold in the UK as food supplements provided there are no health claims (which would then automatically classify them as medicinal products).<sup>31</sup> They are available as oils or as food products containing **cannabidiol**, e.g. chocolate, coffee syrups. Topical products, e.g. oils, sprays and creams, are also available. These products are unregulated, thus there is no standard for quality, safety or the amount of **cannabidiol** that they contain. Such unregulated products may also unknowingly retain traces of *Δ<sup>9</sup>-THC*, subjecting them to Schedule 1 controlled drug legislation, which does not permit prescribing, supply or administration.<sup>32</sup>

Subsections: Indications, Contra-indications, Pharmacology, Cautions, Drug interactions, Undesirable effects, Use of cannabinoids in palliative care, Supply



Joan goes to her community pharmacy to pick up her new prescription. She asks whether she can drive whilst taking morphine, now that her pain is controlled, and she is feeling better. Her pharmacist accesses the information and recommendations in the topic **Drugs and fitness to drive**.

The screenshot shows the Medicines Complete website interface. At the top, there is a search bar containing 'Drugs and fitness to drive'. Below the search bar, the page title is 'Palliative Care Formulary' with a sub-header 'Drugs and fitness to drive'. The page is updated as of July 2021. A sidebar on the left lists 'Subsections' and 'Related Content', with 'Evaluating the effect of drugs on driving performance' selected. The main content area contains a summary of the chapter, stating that it covers centrally acting drugs of relevance to palliative care, such as opioids, anti-epileptics, antidepressants, benzodiazepines, and cannabinoids. It notes that while impaired driving performance is not inevitable, prescribers have a duty to inform patients of the risk of impairment, particularly during initial titration. Key points include:
 

- It is the patient's legal responsibility to drive only if they feel 100% safe to do so.
- Drugs should be taken in accordance with the advice of the PIL or a health professional; specific implications relating to the use of certain drugs and the potential for prosecution are noted.

 The text also mentions that other factors like pain, depression, insomnia, anxiety, frailty, and visual disturbance can impair driving performance, and that treatment of these factors can reverse the impairment. It references DVLA fitness to drive advice in relation to underlying diagnoses like seizures.

## Specialist palliative care clinic review

Two weeks later Joan attends a hospice day centre for a review with a specialist palliative care clinician. The clinician wants to start a bisphosphonate for the prevention of skeletal-related events and consults the **Bisphosphonates monograph** for guidance on dose and use.

The screenshot shows the Medicines Complete website interface for the 'Bisphosphonates' monograph. The search bar contains 'Bisphosphonates'. The page title is 'Palliative Care Formulary' with a sub-header 'Bisphosphonates'. The page is updated as of July 2021. A sidebar on the left lists 'Subsections' and 'Related Content', with 'Pharmacology' selected. The main content area contains the title 'Prevention of skeletal-related events (SRE) in patients with advanced malignancies involving bone'. The text states that IV pamidronate disodium, IV zoledronic acid, and PO/IV ibandronic acid are given long-term to patients with bone metastases to decrease the incidence of SRE. Onset of benefit is 2-3 months. SRE can include pathological fracture, radiotherapy to bone, spinal cord compression, surgery to bone and pain. However, the SRE used as outcomes in studies vary (e.g. radiological vs. clinical pathological fracture) and can limit direct comparison of study findings. Thus, more recent trials use symptomatic skeletal events as outcomes, defined as radiation to bone, symptomatic pathological fracture, surgery to bone or symptomatic spinal cord compression. Only studies >6 months in duration have shown a reduction in fractures, hypercalcaemia and the need for radiotherapy. Studies >1 year in duration have also shown a reduced need for orthopaedic surgery. There is no impact on the occurrence of spinal cord compression. Various national guidelines recommend with provisos the routine use of bisphosphonates for the treatment and prevention of SRE in patients with:
 

- symptomatic myeloma, whether or not bone lesions are evident
- breast cancer with bone metastases
- hormone-relapsed prostate cancer with bone metastases





Upon checking her renal function as part of the baseline assessments, the clinician notices that her plasma creatinine is significantly higher than the normal range. The clinician uses the information under the **Renal impairment topic** to assess the degree of impairment and understand how this may impact on the choice of medications that Joan is currently taking.

The screenshot shows the Medines Complete website interface. At the top, there is a search bar containing 'Renal impairment' and a navigation menu with icons for various topics. Below the search bar, the page title is 'Assessing renal function'. On the left, there is a sidebar with 'Subsections' and 'Related Content'. The 'Subsections' list includes: Introduction, Assessing renal function (highlighted), Dose adjustment in renal impairment, Palliative care drugs for long-term use in end-stage renal failure, Simplifying long-term renal drugs, and Last days of life. The main content area contains a text box stating: 'There are limitations to all the formula-based estimations of renal function, with none being suitable for all patients and all situations.' Below this, a paragraph explains that the glomerular filtration rate (GFR) is the best overall measure of renal function, but the most accurate ways of measuring GFR are impractical for routine use. It notes that serum creatinine concentration has traditionally been used as a proxy, but is only a rough guide because a significant proportion of renal function may be lost before creatinine levels rise above the upper limit of normal, particularly in patients with a low body muscle mass or low protein intake. It states that, in practice, formula-based estimations of renal function using serum creatinine are used, typically: 2-4

- estimated GFR (eGFR):
  - Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula
  - Modification of Diet in Renal Disease (MDRD) formula
- estimated creatinine clearance (CrCl):
  - Cockcroft-Gault formula.

## General hospital admission

Unfortunately several months later, Joan significantly deteriorates and is unable to swallow. She is admitted at a weekend to a general hospital ward. The junior doctor asks the on-call pharmacist for advice on administering medications via continuous subcutaneous infusion (CSCI). They discuss administration details, including diluent, infusion volumes and prescribing rescue medication, using the information from the **Continuous subcutaneous infusions topic**.

The screenshot shows the Medines Complete website interface. At the top, there is a search bar containing 'Continuous subcutaneous drug infu' and a navigation menu with icons for various topics. Below the search bar, the page title is 'CSCI in clinical practice'. On the left, there is a sidebar with 'Subsections' and 'Related Content'. The 'Subsections' list includes: CSCI in clinical practice (highlighted), Prescribing CSCI, Diluent, Infusion volume, Infusion duration, Mixing drugs, Site of CSCI, and Infusion devices. The main content area contains a paragraph stating: 'The administration of drugs by continuous subcutaneous infusion (CSCI) is common in palliative care in the UK, particularly in patients for whom swallowing medication has become increasingly difficult or impossible. 1,2' Below this, a paragraph explains that ambulatory battery-powered infusion devices are generally used to administer the CSCI. 2 CSCI is as effective as continuous IV infusion (CIV), 4 and at least as good as intermittent bolus injections. 3 In settings where it is difficult to be certain that intermittent regular injections will be administered on time, CSCI is likely to provide better round-the-clock comfort. Below this, there is a section titled 'Indications for CSCI' which states: 'CSCI is not 'step 4' on the analgesic ladder; it is a useful alternative route of administration in various circumstances, 5 including:

- persistent nausea and vomiting
- dysphagia
- bowel obstruction
- coma
- poor absorption of oral drugs (rare)
- patient preference.



The pharmacist checks the recommended opioid conversion ratio from an oral dose of morphine to a CSCI of morphine contained in **Appendix 2: Opioid conversion ratios**.

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Appendix 2: Opioid dose conversion

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Subsections: General approach, Determining the dose of the second opioid

Table 3 PCF recommended dose conversion ratios; PO to SC/IV. Before use, see [General approach](#)

Swipe or scroll within the table to navigate

Conversion	Ratio	Calculation	Example	Monograph
Hydromorphone to hydromorphone	2:1 <sup>a</sup>	Divide 24h hydromorphone dose by 2	Hydromorphone 32mg/24h PO → hydromorphone 16mg/24h SC/IV	<a href="#">Hydromorphone</a>
	3:1 <sup>b</sup>	Divide 24h hydromorphone dose by 3	Hydromorphone 32mg/24h PO → hydromorphone 10mg/24h SC/IV	<a href="#">Hydromorphone</a>
Methadone to methadone	2:1 <sup>a</sup>	Divide 24h methadone dose by 2	Methadone 30mg/24h PO → methadone 15mg/24h SC/IV	<a href="#">Methadone</a>
Morphine to alfentanil	30:1	Divide 24h morphine dose by 30	Morphine 60mg/24h PO → alfentanil 2mg/24h	<a href="#">Alfentanil</a>

a. because mean oral bio-availability is 50% (range 35–60%), some centres use a conversion ratio of 2:1 rather than 3:1

b. italicized entry = manufacturer's recommendation

## Community review

A few days later Joan is discharged home. A district nurse arrives to prepare the next CSCI and the GP also visits her before the weekend. The district nurse is unfamiliar with mixing the drugs prescribed for CSCI in the same infusion and checks compatibility using **Appendix 3: Compatibility charts**.

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Appendix 3: Compatibility charts

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Subsections: General key for charts, Compatibility charts for drugs in WFI, Compatibility information for oxycodone 50mg/mL formulation, Compatibility charts for drugs in Sodium chloride 0.9%, Compatibility charts for morphine tartrate

**Chart 5 Compatibility chart for morphine sulfate: three drugs in WFI**

Note. This chart summarizes the compatibility information available for drug combinations in WFI used for CSCI over 24h in palliative care units and the [literature](#). It should be used in conjunction with the [key](#) and the footnotes.

Chart 5 footnote

Concentration-dependent *incompatibility* reported with 2-drug combinations of morphine sulfate + haloperidol.



Joan is anxious and agitated and the GP decides to prescribe 'as needed' medication in anticipation of symptoms over the weekend to ensure rapid symptom relief. The GP consults the information in the **Prescribing in palliative care** topic to guide the most appropriate care for Joan at the end of her life.

The screenshot shows the Medicines Complete website interface. At the top, there is a search bar containing the text "Prescribing in palliative care" and a search icon. To the right of the search bar are several navigation icons: a green cross, a blue circle with a white 'S', a green circle with a white 'P', a yellow circle with a white 'R', and a purple person icon. Below the search bar, the page title "Prescribing in palliative care" is displayed. The main content area is divided into two columns. The left column has a "Subsections" tab selected, showing a list of topics: "General principles", "Prescribing for the elderly", "End-stage heart failure", and "End-stage idiopathic Parkinson's disease". The right column has a "Related Content" tab selected, showing the article "Reviewing medication when a patient is close to death". The article text includes: "When a patient is clearly approaching death:", a list of bullet points: "simplify medication: stop long-term prophylactic medication if not already done so, e.g. statins, antihypertensives, oral hypoglycaemics, warfarin", "when the patient is moribund: stop antidepressants and laxatives", "anticipate and prescribe drugs p.r.n. for common end-of-life problems, e.g. pain, breathlessness, vomiting, agitation, delirium, myoclonus, death rattle (see below)", "prescribe all drugs both PO and SC/IV", and "insulin-dependent diabetes: reduce the dose of insulin as intake decreases", and a reference to "Systemic corticosteroids" for advice about stopping dexamethasone. The article concludes with: "In the last days, some nursing procedures normally regarded as essential may be discontinued. For example, standard care of pressure areas may cause a moribund patient to become distressed. If so, such care should be reduced or stopped."



## Palliative Care Formulary

Palliative Care Formulary (PCF) provides unrivalled and expert drug information for health professionals when caring for adult patients facing progressive life-limiting diseases. Tailored for use in palliative and hospice care settings, this trusted source goes beyond standard references, providing health professionals with in-depth and practical guidance on drugs and treatment regimens to help improve quality of life.

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