Shared Care Protocol
Alfentanil for moderate to severe pain in palliative care patients with severe renal impairment or intolerance to other opioids

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This shared care protocol (SCP) sets out details for the sharing of care ***for palliative care patients with moderate to severe pain, and severe renal impairment, who are prescribed alfentanil****.*

It should be read in conjunction with the latest Summary of Products Characteristics (SmPC) available at http://www.medicines.org.uk/emc/

As outlined in NHS England Guidance 2018 (07573), 'Responsibility for Prescribing Between Primary & Secondary/Tertiary Care': When a specialist considers a patient's condition to be stable or predictable, they may seek the agreement of the GP concerned (and the patient) to share their care.

This document provides information on drug treatment for the shared commitment between the specialist and GP concerned. GPs are invited to participate. If the GP is not confident to undertake these roles, then they are under no obligation to do so. In such an event, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist. The doctor who prescribes the medication has the clinical responsibility for the drug and the consequences of its use.

N.B. If the GP decides not to participate in shared care for a particular patient, they must inform the relevant specialist in writing, within 2 weeks of receipt of a request to share care.*

**Given the patient population for this shared care protocol – it is anticipated that GP's would discuss with the specialist as soon as possible if they have any concerns regarding shared care*

Introduction

- Alfentanil is a strong opioid analgesic that can be used as an alternative to subcutaneous morphine, diamorphine, or oxycodone for moderate to severe opioid-responsive pain.
- Alfentanil has a rapid onset of action and a relatively short half-life.

- Alfentanil is metabolised in the liver to inactive metabolites that are excreted in the urine.
- Alfentanil does not accumulate in renal failure and is therefore of potential use in patients with severe renal impairment.
- Many other opioids and their active metabolites accumulate in patients with impaired renal function and increase the risk of toxicity. Opioid toxicity can manifest as hallucinations, confusion, myoclonic jerks, sedation, and respiratory depression. Many of these effects can be highly distressing to patients, relatives, or staff as well as potentially accelerating or precipitating deterioration.
- While evidence to support the use of alfentanil in patients with renal impairment is limited to retrospective reports, there is substantial, successful experience and wide use in palliative care and dialysis units within the UK.

For further information please click on the links below or visit:

- Summary of Product Characteristics (SmPC) available at:
  www.medicines.org.uk/emc/search?q=alfentanil
- Alfentanil | Drugs | BNF | NICE
- Palliative Care Formulary | MedicinesComplete
- Stockley's Drug Interactions | MedicinesComplete
- Scottish Palliative Care Guidelines - Alfentanil
- Wessex Palliative Care Handbook

Indications and dose:

Alfentanil is licensed as an analgesic supplement for use before or during anaesthesia. Its use in palliative care is off-label, as is the case with many medications.

Alfentanil is indicated for moderate to severe opioid-responsive pain in patients:

- unable to tolerate other strong opioids
- with severe renal impairment or stage 4-5 chronic kidney disease (eGFR <30ml/min)

Alfentanil may also be used for episodic/incident pain (for example, with movement/ dressing changes) or where volumes of infusion of morphine and oxycodone cause problems.

The appropriate dose will vary between patients, for example - with age, body weight, renal and liver function, underlying pathological condition, use of other medication or alcohol, and previous opioid use. In the elderly and debilitated patients, a dose reduction is recommended.

- In opioid-naïve patients, a low starting dose should be chosen according to the likely needs of the individual - a typical starting dose of alfentanil might be 0.5-1mg via syringe driver over 24hrs.
- For patients already on an opioid, an appropriate conversion should be conducted, based on their previous opioid requirements.

Opioid conversion:

Approximate conversions are shown below, and the dose may be adjusted according to pain or other factors. Alfentanil is approximately one quarter the potency of fentanyl.

Table 1: Approximate equivalent doses of opioids

oral morphine	subcutaneous morphine	subcutaneous diamorphine	subcutaneous alfentanil
30mg	15mg	10mg	1mg

- Be aware of the wide variability in the conversion of alfentanil, as the potency ratio of diamorphine:alfentanil can vary from 1:10 to 1:6. It is recommended to use the more conservative ratio when rotating from one to the other.
- Alfentanil is an unfamiliar opioid and must be used with specialist advice and support. Opioid conversion and adjustment of dose should be made in conjunction with the palliative care team.

St Margaret's Hospice 24-hour support available on Tel: 01823 333822

Hepatic impairment:

The half-life and the free fraction of alfentanil increase in hepatic impairment (e.g. liver cirrhosis) - cautious titration is advised and an empirical dose reduction of 30-50% may be necessary.

Renal Impairment:

A cautious conversion and titration is recommended in renal failure, as the free fraction of alfentanil and the permeability of the blood-brain barrier can lead to increased sensitivity to any given dose.

Additional pain relief:

- The short half-life and duration of action of alfentanil reduces risk of toxicity, however, PRN subcutaneous alfentanil may last only 1-1.5 hours, so is not ideal for PRN use.
- There is clinical experience and limited objective data to support the use of oxycodone as an alternative to alfentanil for initial analgesia and breakthrough pain, in severe renal impairment and failure.
- Oxycodone is metabolised in the liver and has a longer half-life, compared with alfentanil. Accumulation of oxycodone in renal impairment is limited, however, the half-life may vary, and plasma concentration may increase up to 50%. A reduced starting dose, for example, of 50% of normal dose and increased dose interval, is therefore recommended, with slower titration and careful monitoring of response and for toxic effects.
- The ease of obtaining, administrating, and titrating the opioid are important considerations in a community setting. To continue with the existing, more familiar opioid e.g. morphine, may be appropriate when symptoms are relieved, without unacceptable undesirable effects, especially when the prognosis is hours - days.
- In general, however, it is preferable to use a strong opioid that has less clinically relevant active metabolites than morphine in severe renal impairment e.g. oxycodone.
- See **Guidance on opioid prescribing & anticipatory prescribing in renal failure in palliative care** for further information.

Contra-indications:

For full details see SmPCs at http://www.medicines.org.uk/emc/

- Known intolerance to alfentanil

Although there are factors that require caution, in the palliative care population there are no other absolute contra-indications.

Special warnings and precautions:

For full details see SmPCs at http://www.medicines.org.uk/emc/

- Do not confuse it with Fentanyl.
- There are 2 different strengths of alfentanil, so caution is required in prescribing and administering, due to potential confusion from the similarity in drug names and doses.
- The administration of alfentanil can cause a fall in blood pressure, which may be exaggerated in hypovolaemic patients or the presence of concomitant sedative medication.

Drug interactions:

- Alfentanil is metabolised via cytochrome P450 3A4/5 enzymes. Caution is required with concurrent use of drugs that inhibit or induce these enzymes and dose adjustment may be required.

Table 2: Common interactions between alfentanil and other drugs involving CYP450

Plasma concentrations of Alfentanil	
Increased by:	**Decreased by:**
• Azoles e.g. fluconazole, ketoconazole, itraconazole • Cimetidine • Diltiazem • Macrolide antibiotics e.g. clarithromycin, erythromycin • Protease inhibitors e.g. indinavir, nelfinavir, ritonavir	• Efavirenz • Rifampicin • Carbamazepine

- Cardiac medications may exacerbate effects on heart rate or blood pressure.
- Concomitant use (or use within the previous 2 weeks) of Monoamine Oxidase Inhibitors (MAOIs) should be avoided if possible.

Drug compatibility:

- Alfentanil is compatible with and may be mixed with most other commonly used drugs in palliative care, for example – levomepromazine, metoclopramide, midazolam, and hyoscine butylbromide (Buscopan®).
- Concentration-dependent incompatibility may occur with cyclizine.
- Alfentanil in a syringe driver should be diluted with Water for Injections, prior to administration.
- Ask the specialist palliative care team or pharmacist for advice, due to the risk of incompatibility.

Adverse effects:

For full details see SmPCs at http://www.medicines.org.uk/emc/

Adverse effects of alfentanil are, in general, similar to morphine and other strong opioids.

Table 3: Adverse effects and reactions to alfentanil

Common	***More common on initiation***	**Nausea and vomiting, drowsiness**
		Constipation, dry mouth
Less common		Hypersensitivity, myoclonus, delirium, hallucinations, skin changes, urinary retention, postural hypotension, and respiratory depression

The SmPC for alfentanil also lists low and high blood pressure, muscle rigidity, and slow and rapid heart rate as potential Adverse Drug Reactions (ADRs), primarily associated with intravenous administration. ADRs are likely to occur to a much lesser extent when alfentanil is given subcutaneously and at lower doses than might be used in anaesthesia.

This list is not exhaustive. The manufacturer's Summary of Product Characteristics (SmPC) and the most current edition of the British National Formulary should be consulted for full information on contra-indications, warnings, side-effects and drug interactions.

Shared Care Responsibilities

Palliative Care Specialist responsibilities:

1. Calculate an appropriate dose and initiate treatment with alfentanil
2. Counsel the patient/carer with regard to the benefits and risks of treatment and provide the patient/carer with any relevant information and advice.
3. Ensure patient/carer understands what the drug is, why it has been prescribed, how and when it will be given, and any potential side-effects.
4. Once the palliative care specialist considers the patient's condition is stable on a dose effective for pain control, a request can be made to the patient's GP to 'share' the patient's care.
5. Organise follow up, either by phone or face to face, if indicated, within the first 24 hours.
6. If alfentanil is commenced during an out of hours period, ensure there is liaison between hospice and relevant teams.
7. Agree monitoring to be undertaken by the Community Palliative Care Nurse Specialist, District Nurse, or GP depending on the complexity of the clinical situation and practicalities.
8. Advise primary care prescribers on request, on appropriate action in the event of relapse of pain control or other concern.
9. Provide guidance and support for any nursing staff that may be required to administer alfentanil.
10. Prescribe one week's supply of alfentanil on discharge from Hospice IPU and/or ensure local supplies are available
11. Inform the patient/carer of the arrangement for further prescriptions and support.

General Practitioner responsibilities:

1. Accept request to take on prescribing of alfentanil once the palliative care specialist considers the patient's condition to be stable on a dose effective for pain control.
2. Reinforce educational points provided by the palliative care team (points 2 & 3 above).
3. Prescribe alfentanil in accordance with specialist advice and patient's changing needs.
4. Inform palliative care specialist of any changes in the patient's medical condition, especially adverse effects and/or changes to prescribed medication.
5. Undertake monitoring where agreed with Palliative Care Service (PCS).
6. Discuss with PCS appropriate action in the event of relapse of pain or other concerns.
7. Refer prescribing back to the specialist should problems arise that cannot be readily corrected.

Patient/carer responsibilities

1. To report any significant signs or symptoms relating to their condition, including side effects, to the GP or member of the Palliative Care team

Further support

- St Margaret's Hospice 24 hour support is available 01823 333822
- Dorothy House 24 hour support is available 01225 722999 / 0345 0130 555
- Weston Hospice 24 hour support is available 01934 423912
- Medicines Information department, Musgrove Park Hospital: 01823 342253
- Medicines Information department, Yeovil District Hospital: 01935 384937
- Prescribing & Medicines Management Team, NHS Somerset: 01935 384123
- Medicines Management Team, Somerset NHS Foundation Trust: 01823 368265
- List of Somerset Community Pharmacies holding stock of palliative medicines (Specialist Medicines Enhanced Service pharmacies) available at: https://formulary.nhssomerset.nhs.uk/?page_id=471

References:

- Alfentanil 500 micrograms/ml solution for injection - Summary of Product Characteristics (SmPC) - (emc) (medicines.org.uk)
- Alfentanil | Drugs | BNF | NICE
- Palliative Care Formulary | MedicinesComplete
- Stockley's Drug Interactions | MedicinesComplete
- Scottish Palliative Care Guidelines - Alfentanil
- Wessex Palliative Care Handbook
- King, S., Forbes, K., Hanks, G.W., Ferro, C.J. and Chambers, E.J., 2011. A systematic review of the use of opioid medication for those with moderate to severe cancer pain and renal impairment: a European Palliative Care Research Collaborative opioid guidelines project. *Palliative medicine*, *25*(5), pp.525-552.
- Sande, T.A., Laird, B.J. and Fallon, M.T., 2017. The use of opioids in cancer patients with renal impairment—a systematic review. *Supportive Care in Cancer*, *25*(2), pp.661-675.
- Cran, A., Dorman, S. and Kirkham, S., 2017. Opioid rotation to alfentanil: comparative evaluation of conversion ratios. *BMJ Supportive & Palliative Care*, *7*(3), pp.265-266.
- Updated Clinical Pharmacokinetics and Pharmacodynamics of Oxycodone | SpringerLink
- Pharmacokinetics of oxycodone/naloxone and its metabolites in patients with end-stage renal disease during and between haemodialysis sessions | Nephrology Dialysis Transplantation | Oxford Academic (oup.com)

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