Somerset Healthcare Community Shared Care Protocol for the use of Alfentanil for moderate to severe pain in palliative care patients with severe renal impairment, or intolerance to other opioids

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 (SPC) available for each drug at http://www.medicines.org.uk/emc/

As outlined in NHS England Guidance 2018 (07573), 'Responsibility for Prescribing Between Primary, Secondary and Tertiary Care.' When a consultant considers a patients' condition is stable or predictable he/she may seek the agreement of the patients and their GP to "share" the patients' care. This document provides information on drug treatment for the shared commitment between the consultant 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.

Introduction

Alfentanil is a strong opioid analgesic that can be used as an alternative to subcutaneous morphine, diamorphine or oxycodone for moderate to severe pain. Alfentanil has a rapid onset of action, a relatively short half-life and is metabolised to inactive metabolites by mechanisms that are not dependent on renal function. The combination of inactive metabolites, lack of accumulation and a short duration of action make alfentanil of potential use in patients with severe renal impairment. Many other opioids, or their active metabolites, accumulate in renal impairment and increase the risk of toxicity. Opioid toxicity can manifest as hallucinations, confusion, myoclonic jerks, sedation, agitation and respiratory depression. Many of these effects can be highly distressing to patients, relatives or staff as well as potentially accelerating or precipitating deterioration. The pharmacology of alfentanil may allow better analgesia with fewer side effects in patients with renal impairment. Although evidence to support the use of alfentanil in renal failure is limited to retrospective reports, there is substantial, successful experience of using alfentanil for palliative care and in dialysis units within the UK.

For further information please click on the links below or visit;
British National Formulary
http://www.medicines.org.uk/emc/

Licensed Indications:

Although alfentanil is licensed as an analgesic supplement for use before or during anaesthesia, its use in palliative care is an off licence indication, as is the case with many medications commonly used in palliative care. Alfentanil is indicated as an alternative to other strong opioids in patients with severe renal impairment or intolerance to other opioids.

Dose (posology & method of administration): see individual SPCs at http://www.medicines.org.uk/emc/

The use of subcutaneous alfentanil is off-license, but it has been used successfully for both dressing changes and continuous analgesia in palliative care. Alfentanil should be diluted with Water for Injections prior to administration.

- The appropriate dose will vary between patients (e.g. with age, size, renal and hepatic function) and according to previous opioid exposure.
- In the opioid naive, a low starting dose should be chosen according to the likely needs of the individual. A typical starting dose over 24 hours might be 0.5-1mg alfentanil. It is rare to start Alfentanil without prior PRN use of other strong opioids to assess effect.
- In patients already on an opioid an appropriate conversion should be conducted according to the relative potency of the current opioid. Palliative Care advice should be sought for this conversion (see 'Further support for contact details)

Relative potency;

- Alfentanil 1mg subcutaneously is approximately equivalent to 10mg diamorphine subcutaneously
- Alfentanil 1mg subcutaneously is approximately equivalent to 30 mg morphine orally
- Alfentanil is approximately one quarter the potency of fentanyl

- Adjustment of dose should be made in conjunction with the palliative care team, according to daily opioid requirements. An increased free fraction of alfentanil in patients with renal failure has been reported, this combined with a potential increased permeability of the blood brain barrier in renal failure, may lead to increased sensitivity to any given dose. Cautious conversion and titration is therefore recommended.
- Additional pain relief: The short half-life which is of potential benefit in reducing the risk of toxicity means that PRN subcutaneous alfentanil may last only **one to two hours**. This may be effective for some patients, but for the majority a longer acting opioid such as oxycodone is more appropriate. This represents a risk of accumulating metabolites and toxicity but with careful adjustment of dose and maximum frequency, in most cases an acceptable balance is met to maintain analgesia. Morphine or diamorphine are not recommended.
- Mixture with other drugs in syringe drivers should be checked with the palliative care team due to the risk of incompatibility. Cyclizine is noted to be at risk of incompatibility with alfentanil. However, levomepromazine, metoclopramide, midazolam and hyoscine butylbromide (Buscopan) are compatible.

Contra-indications: see individual SPCs for detail at http://www.medicines.org.uk/emc/

- Known intolerance to alfentanil

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

Special warnings and precautions for use: see individual SPCs for detail at http://www.medicines.org.uk/emc/

- When prescribing and administering, great care should be taken due to potential confusion from similarity in doses and drug names (i.e. fentanyl, alfentanil and 5mg/ml and 500mcg/ml).

- The administration of alfentanil can cause a fall in blood pressure, which may be exaggerated in hypovolaemic patients or in the presence of concomitant sedative medication.

Drug interactions: see individual SPCs for detail at http://www.medicines.org.uk/emc/

- Alfentanil is metabolised mainly via the human cytochrome P450 3A4 enzyme. CYP3A4 inhibitors (e.g. fluconazole, ketoconazole, itraconazole, ritonavir, erythromycin, diltiazem and cimetidine) can cause elevated alfentanil levels. CYP3A4 inducers (e.g. rifampicin) can markedly increase clearance of alfentanil.
- Cardiac medications may exacerbate effects on heart rate or blood pressure
- Concomitant use (or use within the previous 2 weeks) of MAOIs should be avoided if possible

Adverse effects:
Adverse effects are broadly similar to other opioids.
Commonly these include: Nausea and vomiting, constipation, dry mouth, urinary retention
Other reactions include: Hypersensitivity, myoclonus, confusion, hallucinations and respiratory depression

The SPC for alfentanil also lists low blood pressure, muscle rigidity, slow heart rate and rapid heart rate as potential adverse drug reactions. These were primarily indicated for intravenous administration and although they may occur, it is likely that this will be to a much lesser extent when given subcutaneously and at lower doses than might be used in anaesthesia.

Cost:

Drug	Strength	Ampoule size	Cost per ampoule	Dose example	Cost per 28 days
Alfentanil	500mcg/ml	2ml	£0.70	500mcg per 24 hours	£9.80
	500mcg/ml	10ml	£3.20	5mg per 24 hours	£89.60
	5mg/ml (Concentrate)	1ml	£2.50	2mg per 24 hours 5mg per 24 hours 10mg per 24 hours	£70 £70 £140
Rapifen®	500mcg/ml	2ml	£0.64	500mcg per 24 hours	£8.96
	500mcg/ml	10ml	£2.90	5mg per 24 hours	£81.76
	5mg/ml (Concentrate)	1ml	£2.32	2mg per 24 hours 5mg per 24 hours 10mg per 24 hours	£64.96 £64.96 £129.92

Shared Care Responsibilities

Palliative Care Specialist responsibilities:
Under the care of a palliative care specialist, the patient named above has been initiated on alfentanil.
The palliative care specialist considers the patients' condition to be stable on a dose effective for pain control, and wishes the patients' GP agree to ongoing prescribing under this shared care agreement.

Top copy of this agreement to be sent to the patient's GP, the remainder to be given to the patient.

1. Calculate an appropriate dose and initiate treatment with alfentanil
2. Ensure patient/carer understands what the drug is, and why it has been prescribed
3. Ensure patient/carer understands how and when it should be given, and any potential side-effects
4. Organise follow up, either by phone or face to face if indicated within the first 24 hours.
5. If alfentanil is commenced during an out of hours period, ensure there is liaison between hospice and relevant teams.
6. 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.
7. Advise primary care prescribers on request, on appropriate action in the event of relapse of pain control or other concern.
8. Provide guidance and support for any nursing staff that may be required to administer alfentanil.
9. Prescribe one week supply of alfentanil on discharge from Hospice IPU and/or ensure local supplies are available
10. Inform the patient/carer of the arrangement for further prescriptions and support.

Current stabilized dose for alfentanil: ……mcg to be given over 24 hours, via syringe driver

Alfentanil is not usually used as prn medication, due to its short half-life, therefore oxycodone is usually recommended as prn.

The prn medication is …… at a dose of ……mg to be given as needed 2-4 hourly.

Palliative Care Specialist name (print)…… Signature……

Location: …….. Telephone No: (……)……

Additional comments ……...

General Practitioner responsibilities:

1. Accept shared clinical responsibility for the patient provided the above criteria have been met.
2. Reinforce educational points provided by the palliative care team (points 2 & 3 above).
3. Prescribe alfentanil in accordance with specialist advice and patients' changing needs.
4. Inform palliative care specialist of any changes in the patients' medical condition, especially adverse effects, and/or changes to prescribed medication.
5. Undertake monitoring where agreed with Palliative Care Service.
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
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 0845 070 8910.
- Dorothy House 24 hour support is available 01225 722999 0345 0130 555
- Weston Hospice 01934 423912
- Medicines Information department, Musgrove Park Hospital: 01823 342253
- Medicines Information department, Yeovil District Hospital: 01935 384327
- Prescribing & Medicines Management Team, NHS Somerset: 01935 384123
- Medicines Management Team, Somerset Partnership: 01823 368265
- Somerset Pharmacies holding stock of palliative medicines http://formulary.somersetccg.nhs.uk/?page_id=970

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Drawn up by:		
Updated by:		
Updated by:		
Approved by:		
	Drug & Therapeutics Committee, Yeovil and District NHS FT	
	Medicines in clinical practice Committee, Somerset Partnership NHS FT	
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References

Summary of Product Characteristics (SmPC) Rapifen, Janssen-Cilag Ltd, July 2018 available at www.medicines.org.uk

British National Formulary, accessed online via BNF.nice.org.uk

Palliative Care Formulary (sixth edtn) 2017 available at www.palliativedrugs.com

Stockley's Drug Interactions available at www.medicinescomplete.com

King S, Forbes K, Hanks G, Ferro CJ, Chambers EJ. A systematic review of the use of opioid medication for those with moderate to severe cancer pain and renal impairment: an EPCRC opioid guidelines project. *Palliat Med* 2011, in press.

Shared Care Responsibilities – Information for Patients

Sharing of care assumes communication between the specialist, GP and patient. The intention to share care should be explained to, and accepted by, the patient. This provides an opportunity to discuss drug therapy.

The clinician who prescribes the medication has the clinical responsibility for the drug and the consequences of its use.

Palliative Care Specialist responsibilities

Under the care of a palliative care specialist, the patient named above has been initiated on alfentanil. The palliative care specialist considers the patients' condition to be stable on a dose effective for pain control, and wishes the patients' GP agree to ongoing prescribing under this shared care agreement.

1. Calculate an appropriate dose and initiate treatment with alfentanil
2. Ensure patient/carer understands what the drug is, and why it has been prescribed
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7. Advise primary care prescribers on appropriate action in the event of relapse of pain control or other concern.
8. Provide guidance and support for any nursing staff that may be required to administer alfentanil.
9. Prescribe one supply of alfentanil on discharge from Hospice IPU and/or ensure local supplies are available
10. Inform the patient/carer of the arrangement for further prescriptions and support.

General Practitioner responsibilities

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2. Reinforce educational points provided by the palliative care team (points 2 & 3 above).
3. Prescribing alfentanil in accordance with specialist advice and patients' changing needs.
4. Inform palliative care specialist of any changes in the patients' medical condition, especially adverse effects, and/or changes to prescribed medication.
5. Undertake monitoring where agreed with Palliative Care Service.
6. Discuss with PCS on appropriate action in the event of relapse of pain control 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.

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