

North Staffordshire and Stoke-on-Trent Area Prescribing Committee

Medicine Review Summary

Drugs in Palliative Care: Midazolam injection, Glycopyrronium bromide injection and Alfentanil (as hydrochloride) injection

Verdict:	
Formulary inclusion:	Midazolam, glycopyrronium bromide and alfentanil are to be included into the North Staffordshire Joint Formulary
Formulary category:	Midazolam (off label use in palliative care): Green 1st line Glycopyrronium (off label use in palliative care): Amber 2 Alfentanil: Amber 2
Restrictions:	Glycopyrronium: Initiation under direction of a specialist in palliative care Alfentanil: Initiation under direction of a specialist in palliative care in renally impaired patients
Reason for including:	The Committee were aware that medications used for palliative patients are used differently than standard medications and are based on established practices with varying degrees of evidence. The Committee were satisfied with evidence for efficacy and safety, cost implications and intended place in therapy.
Link to formulary:	Primary care: http://www.medicinesmanagementstoke.nhs.uk/north_staffs.html Secondary care: Trust Intranet → Clinicians → Support services → Pharmacy → North Staffordshire Joint Formulary
Link to medicine review summary:	Primary care: http://www.medicinesmanagementstoke.nhs.uk/Formulary_Focus.html Secondary care: Trust Intranet → Clinicians → Support services → Pharmacy → North Staffordshire Joint Formulary → Link to Joint formulary Related Documentation → Reviews, Guidelines & Essential Shared Care Guidelines - North Staffordshire Area Prescribing Committee New Medicine Reviews & Verdict Sheets
Link to full review:	Primary care: http://www.medicinesmanagementstoke.nhs.uk/Formulary_Focus.html Secondary care: Trust Intranet → Clinicians → Support services → Pharmacy → North Staffordshire Joint Formulary → Link to Joint formulary Related Documentation → Reviews, Guidelines & Essential Shared Care Guidelines – NSHE Drug Reviews

<p>Review summary:</p> <p>Formulary application: The Stoke-on-Trent and North Staffordshire Medicines Management Committee have requested that midazolam, alfentanil, and glycopyrronium be considered for inclusion in the North Staffordshire Joint Formulary for treatment of symptoms in palliative care. Dr Claire Hookey Palliative Care Consultant, Douglas McMillan Hospice attended the New Medicine Committee meeting on 6th November 2012.</p> <p>Intended local place in therapy: Alfentanil is intended to be used as alternative in patients who are unable to tolerate other strong opioids particularly in renally impaired patients where other options like morphine and diamorphine are not advisable due to accumulation. Glycopyrronium would serve as an alternative to hyoscine butylbromide in the management of respiratory tract secretions. Midazolam will be used in general management of restlessness and agitation in the dying phase especially if anxiety/restlessness predominates.</p> <p>Efficacy:^{1,2}</p> <p>1. West Midlands Palliative Care Physicians. Palliative care, Guidelines for the use of drugs in symptom control. 5th Edition 2012 2. Twycross R, Wilcock A. 2011 Palliative Care Formulary (PCF4) Edition 4th Nottingham: Palliativedrugs.com</p> <p>Midazolam licensed indications:³</p> <ul style="list-style-type: none"> In adults as conscious sedation before and during diagnostic or therapeutic procedures with or without local anaesthesia.

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- As anaesthesia (Premedication before induction of anaesthesia, induction of anaesthesia, as a sedative component in combined anaesthesia)
- As sedation in intensive care units

In Palliative Care:^{1,2}

Midazolam is used in general management of restlessness and agitation in the dying phase especially if anxiety/restlessness predominates. It can be given as SC injection or via syringe driver over 24 hrs. In advanced illness, confusion and terminal restlessness/agitation are common. The main advantage of midazolam in palliative care is that it is water-soluble and compatible with most drugs commonly given by continuous subcutaneous infusion (CSCI) and it does not cause thrombophlebitis. In imminently dying patients, tolerance is not a practical problem. It also serves in patients whom persistent distressing hiccup is contributing to terminal restlessness at a time when sedation is acceptable to aid symptom relief.

Glycopyrronium licensed indication⁴

- To protect against the peripheral muscarinic actions of anticholinesterases such as neostigmine and pyridostigmine, used to reverse residual neuromuscular blockade by non-depolarising muscle relaxants.
- As a pre-operative antimuscarinic agent to reduce salivary, tracheobronchial and pharyngeal secretions and to reduce the acidity of the gastric contents.
- As a pre-operative or intra-operative antimuscarinic to attenuate or prevent intra-operative bradycardia associated with the use of suxamethonium or due to cardiac vagal reflexes.

In Palliative Care:^{1,4}

Glycopyrronium bromide is used as an alternative to hyoscine butylbromide in the management of respiratory secretions. Both glycopyrronium and hyoscine butylbromide are preferred options as they do not cross the blood-brain barrier hence less likely to cause drowsiness, confusion and paradoxical excitation since. The onset of action of glycopyrronium bromide occurs within one minute, with peak activity at around 5 minutes and this makes it a more reliable method of controlling symptom at this critical time.

Alfentanil licensed indication:⁵

Alfentanil is an analgesic supplement for use before and during anaesthesia. It is indicated for short procedures, outpatient surgery and procedures of medium and long duration when given as a bolus followed by supplemental doses or by continuous infusion. At very high doses, alfentanil 500 mcg/ml solution for injection may be used as an anaesthetic induction agent in ventilated patients.

In Palliative Care:¹

Alfentanil is used as suitable parental opioid in advanced renal disease. Many analgesics are excreted by the kidneys and any degree of renal impairment can reduce drug clearance, and therefore the dose of drug required. Alfentanil is the preferred choice as it is extensively metabolised in the liver. Its short duration of action limits its use for breakthrough analgesia.

References:

¹ West Midlands Palliative Care Physicians. Palliative care, Guidelines for the use of drugs in symptom control. 5th Edition 2012

² Twycross R, Wilcock A. 2011 Palliative Care Formulary (PCF4) Edition 4th Nottingham: Palliativedrugs.com

³ Hypnovel® 10mg/2ml solution for injection. Summary of Product Characteristics. Roche Products Limited. Accessed www.medicines.org.uk

⁴ Glycopyrronium bromide 200 micrograms/ml injection. Summary of product Characteristics. Accord Healthcare Limited. Accessed via <http://www.medicines.org.uk>

⁵ Alfentanil 5 mg/ml solution for injection. Summary of Product Characteristics. Hameln pharmaceuticals Ltd. Accessed via www.medicines.org.uk