

Class: Opioid analgesic, mixed opioid agonist-antagonist (*kappa-receptor agonist, partial mu-receptor antagonist*).

Indications: Moderate to severe acute pain, including myocardial infarction, premedication, peri-operative analgesia.

Contra-indications: Chronic use of morphine or other strong mu-receptor agonist, e.g. fentanyl, hydromorphone.

Pharmacology

Nalbuphine is not a controlled drug. It has no place in the management of cancer pain. It is included in PCF because it is being used increasingly by paramedics for pre-hospital analgesia, e.g. for severe chest pain, fractures and burns.^{1,2} This has resulted in problems when given to patients already receiving long-term morphine. In this circumstance nalbuphine acts as an antagonist to morphine and may precipitate an opioid withdrawal syndrome with severe agitation and pain. Doses of morphine or diamorphine greater than expected are then needed to re-establish satisfactory analgesia.³ Such patients should *not* receive nalbuphine; instead they should be given p.r.n. doses of their normal analgesic medication. Patients who are opioid-naïve (i.e. are not physically dependent) and who need additional analgesia after the pre-hospital use of nalbuphine may also need greater than expected doses of morphine/diamorphine.^{4,5}

Nalbuphine is a synthetic opioid which is structurally related to both naloxone and oxymorphone.⁶ Like other mixed agonist-antagonists, nalbuphine manifests a ceiling effect. In the case of nalbuphine this occurs at about 30mg/70kg; up to this level, nalbuphine and morphine are approximately equipotent as analgesics.⁶ The depressant effect on respiratory function has a comparable ceiling.⁷ Nalbuphine is about 1/15 as potent as naloxone as an opioid antagonist.⁸ Nalbuphine reverses pruritus caused by epidural morphine in opioid-naïve subjects without reversing analgesia.⁹

Bio-availability 80% IM, SC; 25%.

Onset of action 2-3min IV, 10-15min SC.

Time to peak plasma concentration 30-40min IM, SC.

Plasma half-life 2.5h.¹⁰

Duration of action 3-6h.

Cautions

Sedation or respiratory depression is increased if nalbuphine is used with other CNS or respiratory depressants. After prolonged use, abrupt discontinuation may precipitate opioid withdrawal symptoms.

Undesirable effects

For full list, see manufacturer's SPC

Very common (>10%): sedation.

Common (<10% >1%): sweating, nausea and/or vomiting, dizziness/vertigo, dry mouth, headache.

Dose and use

Nalbuphine can be administered SC, IM or IV.

Moderate to severe pain

- starting dose 10–20mg for a 70kg adult
- adjust dose according to pain severity, the patient's physical status and other concurrent medication.

Pain relief in suspected myocardial infarction

- give by slow IV injection; some patients may achieve adequate relief on 10mg, others may need 30mg
- a second dose of up to 30mg may be given after 30min if the pain is not relieved.

Supply

Nubain® (Bristol-Myers Squibb 0208 572 7422)

Injection nalbuphine hydrochloride 10mg/1ml amp = £0.70; 20mg/2ml amp = £1.08.

- 1 Stene J *et al.* (1988) Nalbuphine analgesia in the prehospital setting. *Journal of Accident and Emergency Medicine*. **6**: 634-639.
- 2 Chambers J and Guly H (1994) Prehospital intravenous nalbuphine administered by paramedics. *Resuscitation*. **27**: 153-158.
- 3 Smith J and Guly H (2004) Nalbuphine and slow release morphine. *British Medical Journal*. **328**: 1426.
- 4 Robinson N and Burrows N (1999) Excessive morphine requirements after pre-hospital nalbuphine analgesia. *Journal of Accident and Emergency Medicine*. **16**: 392.
- 5 Houlihan K *et al.* (1999) Excessive morphine requirements after pre-hospital nalbuphine analgesia. *Journal of Accident and Emergency Medicine*. **16**: 29-31.
- 6 Errick J and Heel R (1983) Nalbuphine. A preliminary review of its pharmacological properties and therapeutic efficacy. *Drugs*. **26**: 191-211.
- 7 Romagnoli A and Keats A (1980) Ceiling effect for respiratory depression by nalbuphine. *Clinical Pharmacology and Therapeutics*. **27**: 478-485.
- 8 Preston K *et al.* (1989) Antagonist effects of nalbuphine in opioid-dependent human volunteers. *Journal of Pharmacology and Experimental Therapeutics*. **248**: 929-937.
- 9 Cohen SE *et al.* (1992) Nalbuphine is better than naloxone for treatment of side effects after epidural morphine. *Anesthesia and Analgesia*. **75**: 747-752.
- 10 Lo M *et al.* (1987) The pharmacokinetics of intravenous, intramuscular and subcutaneous nalbuphine in healthy subjects. *European Journal of Clinical Pharmacology*. **33**: 297-301.