Naltrexone in heroin dependence

This information should be read in conjunction with the product information literature from the distributor.

The treatment for opioid dependence with the strongest evidence base is long term methadone or buprenorphine.

Concerns around using naltrexone for opioid dependence include overdose risk once the effects of the naltrexone have ceased.

Naltrexone is not available on the PBS for opioid dependence; it is only available for alcohol dependence management.

In Australia naltrexone is available mostly as an oral 50mg tablet. Parenteral preparations are not available. A few services provide naltrexone implants which last several months. However these have not been well researched and good evidence supporting their use is scant.

1. Mode of action

Naltrexone is a pure opioid antagonist which blocks the action of opioids on the opioid receptor. Hence naltrexone:

- blocks the analgesic effect of opioids
- precipitates opioid withdrawal in opioid dependent patients
- reduces the incidence of relapse in alcohol dependent patients
- may prevent relapse in opioid dependent patients who have withdrawn from opioids. (There are reservations about the strength of this claim, including on the part of the Australian distributors of naltrexone).
- naltrexone is also a pupillary constrictor by an unknown mechanism.

2. Assessment

Before starting naltrexone for opioid dependent patients take:

- a detailed history of the heroin dependence
- a detailed history of other drug use/abuse/dependence
- examine the patient particularly for clinical signs of recent injections, infections, liver damage. Note any signs of intoxication or withdrawal
- appropriate investigations, including liver function tests:
  - If the ALT is raised monitor LFTs monthly for three months
  - If the ALT is 5x normal naltrexone should be implemented very cautiously (see below)
- Ensure that patients are fully withdrawn from heroin. Patients need to be opioid free for seven days if they have been on heroin and methadone free for fourteen days. If there is any doubt do a naloxone challenge test to ensure the patient is fully withdrawn. Seek further advice from the Drug and Alcohol Clinical Advisory Service (DACAS) on (08) 7087 1742.

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3. Clinical use of naltrexone

Preventing alcohol relapse - strong indication – PBS supported

This is the main indication for naltrexone. See the Naltrexone for alcohol dependence (PDF 282KB) factsheet.

Preventing relapse into heroin dependence – possibly indicated in some situations.

Naltrexone should not be started until the patient has been thoroughly withdrawn. (See assessment above).

The dose for heroin relapse prevention is the same as for alcohol relapse prevention, i.e. 25 mg for the first two days and 50 mg thereafter. Published data on naltrexone in preventing opioid relapse is disappointing. Its relative failure appears to be due to poor medication compliance. The contrast between the poor results with naltrexone and the positive studies for methadone is impressive.

Use in opioid withdrawal – not recommended.

Naltrexone has been used to precipitate a short-lived but severe opioid withdrawal, which is treated either with heavy sedation or under anaesthesia. These are called 'Rapid Opioid Detoxification' with various extra descriptors, some of which have even been patented. These techniques are not recommended for the ordinary prescriber. They are expensive and there is an increased risk of death compared with standard withdrawal procedures. They have yet to be subjected to appropriate scientific evaluation, and this technique is not recommended by the drug company.

4. Concern in the use of naltrexone

Naltrexone precipitates opioid withdrawal

Naltrexone will precipitate withdrawal in opioid dependent people. This effect is maximal if people are currently using heroin and the likelihood of precipitating withdrawal usually lasts about a week.

Naltrexone precipitates pain if opioids are being taken for pain

Risk of death

- From attempts to overcome naltrexone blockade - the blocking effect of naltrexone is not easily surmountable by high doses of heroin or other opioids, but attempts to do so could end in respiratory depression and death, especially if heroin is administered close to the time the effect of naltrexone ceases. This usually occurs between 48 and 72 hours after the last dose of naltrexone.

  Under these conditions the same dose of heroin, which the previous day had no effect, may be fatal next time. This is a major concern in prescribing naltrexone in unstable heroin users. Patients should be warned about this effect.
- From increased opioid sensitivity (reduced tolerance to opioids) - former opioid dependent patients, who have been on naltrexone and stopped taking it, will be more sensitive to opioids than when they were dependent. Hence doses which were earlier innocuous may be fatal this time.
- From intermittent heroin and naltrexone use - Intermittent heroin and naltrexone use leads to rapidly fluctuating degrees of opioid tolerance and sensitivity. Hence the effect of a dose of heroin is quite unpredictable and may be fatal.

Analgesia in patients using naltrexone

Non-steroidal anti-inflammatory drugs and paracetamol will still work normally in patients on naltrexone. If patients require further analgesia while on naltrexone consider:

- Regional analgesia
- Sedation with benzodiazepines, but note sedation does not reduce pain
- General anaesthesia. Again this may not reduce pain
- If high doses of opioids are used to try and obtain some degree of pain control, respiratory depression may be precipitated and be prolonged. This should only be attempted in an intensive monitoring situation by experienced practitioners
- Ketamine anaesthesia may be considered by practitioners experienced in the technique.

Naltrexone and liver disease

Naltrexone in higher doses than usually prescribed can cause a reversible rise in transaminases. Check LFTs before starting the patient on naltrexone, especially if the patient has viral or alcoholic hepatitis. Use with caution if ALTs are raised. Monitor LFTs monthly. If unchanged cease after three months. Naltrexone is relatively contra indicated if the ALTs are more than 5x normal.

Side effects of naltrexone

The main side effect is nausea. This occurs in about 10% of patients and can be severe enough for patients to want to stop naltrexone. This can be minimised by starting the patients on 25 mg (1/2 tablet) a day for two days before continuing on the full dose of 50 mg per day. Some patients describe a degree of dysphoria which may require treatment. For a full list of side effects consult MIMS or the product insert.

Cost of naltrexone

This is a major consideration in prescribing naltrexone. Retail prices may vary from $200- 250 per month.

5. Managing heroin withdrawal precipitated by naltrexone

They are probably best observed in an emergency department unless the condition is mild. See fact sheet: Heroin withdrawal precipitated by naltrexone (PDF 280KB).

Disclaimer

This information is a general guide for the use of naltrexone in the management of heroin dependence. Consultation with a specialist drug and alcohol service such as the Drug and Alcohol Clinical Advisory Service (DACAS) is recommended for patients using multiple drugs or with serious medical or psychiatric conditions. Telephone DACAS on (08) 7087 1742**.** The drug doses given are a guide only and should be adjusted to suit individuals.

For more information

Drug and Alcohol Clinical Advisory Service (DACAS)
Specialist support and advice for health professionals
Telephone: (08) 7087 1742
24 hours 7 days/week including public holidays
HealthDACASEnquiries@sa.gov.au

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