Naltrexone

Information sheet for Primary Care Prescribers

Licensed Indications

Oral naltrexone is recommended as a treatment option in patients who have completed opioid detoxification and are highly motivated to remain abstinent from using opioids[1,2] (NICE TA115 and DOH Orange Guidance). It should only be prescribed as part of a programme of supportive care[1,2].

Oral naltrexone is also recommended as a treatment option for people who have detoxified from using alcohol. Please see the Nottinghamshire Primary Care Alcohol Dependence Guideline for more information on this indication (link).

Therapeutic Summary

Naltrexone hydrochloride is a non-elective opioid antagonist capable of blocking the effects of heroin and opioids (including morphine-like medicines). It does not block the effects of other illicit substances (e.g., cocaine, amphetamines).

Medicines Initiation

Naltrexone should only be administered under adequate supervision to people who have been fully counselled on the potential adverse effects of treatment. These include:

- The importance of being opioid free prior to starting treatment, and the risk of acute withdrawal, if the patient is not opioid free.
- The risk of overdose from attempting to overcome the antagonist effect of naltrexone during treatment.
- The importance of not using opioid medicines during treatment (this includes over-the-counter cough, cold and anti-diarrhoeal medicines).
- The loss of tolerance to opioids that occurs after a period of abstinence and the risk of overdose if the person lapses to opioid use.

Naltrexone treatment must begin only when the opioid has been discontinued for a sufficiently long period (about 5 to 10 days). A urine test is necessary to confirm abstinence from opioids before initiation of treatment.

Naltrexone will be initiated by the specialist service. When care is transferred to the GP a letter will be sent with contact details of the specialists that initiated the medicine. The patient will have been given a card indicating to others that they are prescribed naltrexone.

Products available

Naltrexone hydrochloride 50mg, 28 film-coated tablets - £77.84 (Drug Tariff, July 2022)[3].

Dosages and Route of Administration[3,4]

Once it is confirmed a patient is opioid free, 25mg (half a tablet) is given on day one. The patient is observed for 1 hour, and if there is no opioid withdrawal then 50mg is initiated daily. Doses can be taken 50mg daily, or three days a week to improve compliance (100mg Monday and Wednesday, 150mg Friday). The maximum dose is 350mg per week.

Where there is significant other/third party involvement, with the patient's consent, it may be useful to enlist their support in the administration of naltrexone.

Duration of Treatment
Patients prescribed naltrexone should be reviewed regularly (at least monthly) by the specialist service during treatment. Duration of treatment is usually 3 months[5]. Ongoing treatment should be based on clinical judgement and shared decision with the patient. It is unusual for treatment to be continued for more than 12 months.

Naltrexone should be stopped if the patient lapses into opioid use.

Monitoring Requirements and Responsibilities
The specialist will arrange for the necessary blood tests, inform primary care of the results and any follow up that is required. Baseline monitoring should be carried out as close to initiating naltrexone as possible. The specialist will apply clinical judgement, on an individual patient basis, to decide whether previous blood tests can be used as a baseline measure.

General Monitoring Requirements *Naltrexone should NOT be initiated without checking baseline liver and renal function.*		
	Before treatment	**During treatment**
Renal Function	√	Check if concerns re: renal function
Liver Function Tests	√	Repeat 4 weeks after start of treatment, annually and when clinically indicated

Side effects[4,5]
For a comprehensive list of side effects, refer to the SPC.

Gradual introduction with abstinence prior to initiation will help prevent side effects, and support with nausea management will be beneficial (there are no known interactions with standard anti-emetics). Side effects should have settled by the time treatment has been transferred to primary care.

SIDE EFFECTS	ACTION
Very common (≥1/10)	
Nervousness, Anxiety, Insomnia	These are usually transient and self-limiting, should not require cessation of the drug.
Abdominal Pain, Cramps, Nausea, Vomiting	
Arthralgia, myalgia	
Headaches, restlessness	
Common (≥1/100; <1/10)	
Decreased Appetite	These are usually transient and self-limiting, should not require cessation of the drug.
Irritability, Mood swings	
Chest Pain, Tachycardia, heart palpitation	
Dizziness	
Diarrhoea, Constipation	
Rash	
Thirst, increased energy, chills, hyperhidrosis	
Delayed Ejaculation, erectile dysfunction, libido disorders	

Contraindications[4,5]

- Hypersensitivity to naltrexone or any excipients
- Severe renal impairment
- Severe or acute hepatic impairment
- Acute hepatitis or liver failure
- Opioid addicted patients with a current abuse of opioids since an acute withdrawal syndrome may ensue.
- Positive screening result for opioids or after failure of the naloxone provocation test
- Use in conjunction with an opioid – containing medication
- In combination with methadone or buprenorphine
- Breastfeeding
- Rare hereditary galactose intolerance, total lactase deficiency or glucose-galactose malabsorption

Precautions[4,5]

- Naltrexone should be used only when an opioid has been discontinued for a sufficiently long period (about 5-10 days). The patient should be aware of the risk of overdose from any attempts to overcome the blockade effect of the medication. If the patient has been using opioids prior to the administration of naltrexone then severe and prolonged withdrawal symptoms can follow.
- Patients taking naltrexone will have no benefit from opioids prescribed for acute pain. If a patient on naltrexone is scheduled for elective surgery that is likely to be acutely painful, oral naltrexone may be discontinued 48-72 hours before the procedure[2].
- During treatment pain conditions should be treated with non-opioid analgesia only.
- Mild to moderate liver impairment.
- Mild to moderate renal impairment.

Clinically Relevant Medicine Interactions and Their Management[4,5]

- Concomitant administration with any opioid-containing medication should be avoided (including opioid containing cough medication and opioid containing medication for diarrhoea)
- There are no known interactions with alcohol
- Naltrexone may significantly increase acamprosate plasma levels
- Caution is advised with barbiturates, benzodiazepines, anxiolytics, hypnotics, sedative antidepressants and sedative antihistamines.

Pregnancy and breastfeeding[4,5]

- There is no clinical data on naltrexone use in pregnancy. Data from animal studies have shown reproductive toxicity. Naltrexone should therefore only be given to pregnant women when, in the judgement of the specialist, the potential benefits outweigh the possible risks.
- There is no clinical data on naltrexone use in breastfeeding. Breastfeeding is not recommended during naltrexone treatment.

Patient information

- Patient information leaflets for naltrexone, other medications and mental health conditions can be found at:

www.choiceandmedication.org/nottinghamshirehealthcare

References and Version Control

1) NICE TA115: Naltrexone for the management of opioid dependence (2007), https://www.nice.org.uk/guidance/ta115/resources/naltrexone-for-the-management-of-opioid-dependence-pdf-82598074558405
2) Department of Health and Social Care (2017), *Drug misuse and dependence: UK guidelines on clinical management*, https://www.gov.uk/government/publications/drug-misuse-and-dependence-uk-guidelines-on-clinical-management
3) The Electronic Drug Tariff https://www.drugtariff.nhsbsa.nhs.uk/#/00798052-DC/DC00798043/Home [Accessed on 28/07/2022].
4) Joint Formulary Committee. *British National Formulary* (online) London:BMJ Group and Pharmaceutical Press. https://www.medicinescomplete.com/mc/bnf/current/ [Accessed on 23/05/2022].
5) Adepend 50mg tablets – AOP Orphan Ltd. Summary of Product Characteristics (last updated 16/01/20). http://www.medicines.org.uk [Accessed on 23/05/2022].

Version Control - **Naltrexone Information Sheet**			
Version	Author(s)	Date	Changes
1.0	Nick Sherwood	June 2019	
2.0	Hannah Godden, Specialist Mental Health Interface Pharmacist, NHS Nottingham and Nottinghamshire ICB	July 2022	-Added standard APC header and version control -Counselling points added under medicines initiation -LFT monitoring requirements updated -Updated contraindications, precautions, side effects and medicine interactions sections as per SPC -New section on pregnancy and breast feeding

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