SHARED CARE GUIDELINE FOR THE MANAGEMENT OF PATIENTS ON NALTREXONE FOR ALCOHOL DEPENDENCE

INDICATION

Naltrexone is used as **part** of a comprehensive programme of treatment against alcoholism to reduce the risk of relapse, as support treatment in abstinence and to reduce the craving for alcohol.

NICE CG 115 states:

- After a successful withdrawal for people with moderate and severe alcohol dependence, consider offering acamprosate or oral naltrexone in combination with an individual psychological intervention (cognitive behavioural therapies, behavioural therapies or social network and environment-based therapies) focused specifically on alcohol misuse.
- For harmful drinkers and people with mild alcohol dependence who have not responded to psychological interventions alone, or who have specifically requested a pharmacological intervention, consider offering acamprosate or oral naltrexone in combination with an individual psychological intervention (cognitive behavioural therapies, behavioural therapies or social network and environment-based therapies) or behavioural couple's therapy.
- After a successful withdrawal for people with moderate and severe alcohol dependence, consider offering disulfiram in combination with a psychological intervention to service users who have a goal of abstinence but for whom acamprosate and oral naltrexone are not suitable, **or** prefer disulfiram and understand the relative risks of taking the drug.
- If using oral naltrexone, start treatment after assisted withdrawal
- Service users taking oral naltrexone should stay under supervision, at least monthly, for 6 months, and at reduced but regular intervals if the drug is continued after 6 months. Do not use blood tests routinely, but consider them for older people, for people with obesity, for monitoring recovery of liver function and as a motivational aid for service users to show improvement. If the service user feels unwell advise them to stop the oral naltrexone immediately.

AREAS OF RESPONSIBILITY FOR SHARED CARE

This shared care agreement outlines suggested ways in which the responsibilities for managing the prescribing of naltrexone can be shared between the specialist setting and the patient's GP. GPs are invited to participate. If the GP is not confident to undertake these roles, then he or she is 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. If a specialist asks the GP to prescribe this drug, the GP should reply to this request as soon as practicable.

Sharing of care assumes communication. The intention to share care is usually explained to the patient by the doctor initiating treatment. It is important that patients are consulted about treatment and are in agreement with it.

REFERRAL AND INITIATION

- In accordance with national guidance the therapy should be initiated and supervised by a prescriber experienced in the treatment of alcohol-addicted patients.
- Patients should have been opiate free for 7 to 10 days prior to treatment being started. A negative drug screen confirms this on the day of first treatment.
- When the person is established on a stable dose pattern without side effects and has shown a clear commitment to continue with treatment for an agreed period then the case will be discussed with the person's GP with a view to continued prescribing in primary care.
- Ongoing support to the patient will be clarified before referral to the patient's GP. This may through the specialist team or a non-statutory support service. Patients who do not continue under the care of the specialist service may be referred back for reassessment of treatment outside of any waiting list.
- Treatment duration of at least 3 months is recommended whereas a prolongation might be necessary. Efficacy is proven by controlled studies over a period up to 12 months.

Specialist Responsibilities	
1.	To assess the patient for suitability for prescribing naltrexone, including undertaking a drug screen and baseline LFTs prior to initiating therapy.
2.	To ensure the patient is given a naltrexone warning card and told to keep it on their person.
3.	To advise patients that during treatment, painful conditions should be treated with non-opioid analgesia only and that an attempt to overcome the opioid block caused by naltrexone could result in acute opioid intoxication/death.
4.	To write to the GP requesting shared care ensuring specialist service treatment contract is signed by all relevant parties (Specialist service, GP and Patient).
5.	To advise when it might be appropriate for treatment to be stopped.
6.	To provide leaflets and consent forms on request.
7.	To arrange appropriate ongoing psychosocial support as required.
8.	Specialist service to arrange and monitor (if appropriate) appointments for review.

General Practitioner Responsibilities	
1	Initially to refer the patient for specialist advice.
2	Where appropriate to continue to prescribe naltrexone as part of a shared care arrangement when treatment has been initiated and stabilised by a specialist service and shared care has been agreed.
3	To provide support to enhance compliance
4	To continue prescribing naltrexone and to re-refer the patient or seek specialist advice as necessary.
5	To perform LFTs every 4 months or more frequently if required.
6	To regularly monitor the patients' health and wellbeing and for adverse drug reactions. It is recommended that the patient be seen monthly for the first 3 months and then 3 monthly thereafter.
7	To refer back to the specialist service for any aspect of the patient's care which is of concern to the GP.

8	To deal with the general health issues of the patient

Patient's role (or that of carer)	
1	To take naltrexone regularly and not take/use alcohol or opiates.
2	Report any adverse effects to their GP/specialist service whilst taking naltrexone.
3	To ensure they have a clear understanding of their treatment.
4	To carry the naltrexone warning card on their person.
5	To attend any necessary appointments with specialist services.
6	To actively remain in a structured care programme for the duration of their treatment with naltrexone.

SUPPORTING INFORMATION

Monitoring

Baseline liver function tests should be performed before commencing treatment, and then monitored every four months during treatment.

Patients with liver or renal impairment should be supervised carefully during treatment. Liver function tests should be conducted before and during therapy

Dosage and Administration

NICE CG 115 suggests: Start prescribing at a dose of 25 mg per day and aim for a maintenance dose of 50mg per day. Draw the service user's attention to the information card that is issued with oral naltrexone about its impact on opioid-based analgesics. Oral naltrexone should usually be prescribed for up to 6 months, or longer for those benefiting from the drug who want to continue with it. It should be stopped if drinking persists 4–6 weeks after starting the drug.

Contraindications

Contraindications listed:

- Hypersensitivity to naltrexone hydrochloride or to any of the excipients
- Acute hepatitis
- Severe or acute liver impairment
- Severe renal impairment
- Patients taking opioid-analgesics
- Opioid-addicted patients as acute opioid withdrawal symptoms may occur
- Patients with withdrawal symptoms after administering naloxone hydrochloride (positive result of the naloxone provocation test)
- Positive urine test for opioids.

Cautions

Liver function tests needed before and during treatment, test for opioid dependence with naltrexone before treatment. Avoid concomitant use of opioids but increased dose of analgesic may be required for pain, see below (monitor for opioid intoxication).
Patients should be warned that the use of high dose opioids to neutralize the blockade might result in acute opioid intoxication as soon as the naltrexone has ceased.

Side effects

- Incidence > 10% - difficulty sleeping, anxiety, nervousness, abdominal pain/cramps, nausea, vomiting, low energy, joint/muscle pain and headache.
- Incidence < 10% - loss of appetite, diarrhoea, constipation, increased thirst, increased energy, feeling down, irritability, dizziness, rash, delayed ejaculation, decreased potency, chills, chest pain, increased sweating and increased lacrimation.
- Occasionally – liver function abnormalities.

Interactions

Naltrexone blocks the effects of all opioids.
The SPC states:
"Association to be taken into account: barbiturates; benzodiazepines, anxiolytics others than benzodiazepines (i.e. meprobamate), hypnotics, sedative antidepressants (amitriptyline, doxepin, mianserin, trimipramine), sedative antihistaminics H1, neuroleptics, (droperidol).
Data from a safety and tolerability study of the co-administration of naltrexone with acamprosate in non-treatment seeking, alcohol dependent individuals showed that naltrexone administration significantly increased acamprosate plasma level.
There have been reports of cases of lethargy and somnolence following concomitant administration of naltrexone and thioridazine."

Special Recommendations

If the patient requires analgesia for mild pain then a non-opioid analgesic should be used. If the patient requires opiate analgesia consider specialist anaesthetic assessment as the doses required to obtain adequate pain relief are such that the resulting respiratory depression may be deeper and prolonged.
Naltrexone is not recommended for use in children and adolescents below 18 in this indication due to a lack of data on safety and efficacy

Drug cost

At 50mg daily dose, 28 day cost = £22.34
(BNF 68, Sept 2014)

This list is not exhaustive. The manufacturer's summary of product characteristics (SPC) and the most current edition of the British National Formulary should be consulted for full information on contra-indications, warnings, side-effects and drug interactions.

References

1. Adepend ® (AOP Orphan Pharmaceuticals) Summary of Product Characteristics. Updated 16-Dec-2014
2. Naltrexone for the management of opioid dependence. NICE TA 115. Published Jan 2007 http://www.nice.org.uk/guidance/ta115
3. British Association for Psychopharmacology updated guidelines: evidence-based guidelines for the pharmacological management of substance abuse, harmful use, addiction and comorbidity: recommendations from BAP. Journal of Psychopharmacology 0(0) 1-54
4. British National Formulary no 68. Sept 2014-March 2015

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Approved By	**Dorset Medicines Advisory Group**	**May 2015**
Review Date	**May 2018 or before in the light of new evidence and/or recommendations**	