Introduction:
In November 2014 NICE (National Institute of Clinical Excellence) published the Technology Appraisal Guidance (TAG) (325): Nalmefene for reducing alcohol consumption in people with alcohol dependence. This document sets out the Nalmefene pathway for Cambridgeshire and the clinical responsibilities for GPs, and the treatment service, following the publication of the national TAG.

Indication for use:
Nalmefene (also known as Selincro®) is recommended as a possible treatment for people with alcohol dependence who:

Meets the criteria with mild alcohol dependence classified as follows: Men drinking 7.5 units a day or more but less than 15 units; Women drinking 5 units a day or more but less than 12 units: no history or evidence of physical withdrawal symptoms which would require a detoxification.

Agree to a programme of psychosocial support focussed on treatment adherence and reducing consumption.

Continue to have a high drinking risk level 2 weeks after initial assessment.

Do not need to stop drinking straight away or stop drinking completely.

Prescribing Nalmefene in Cambridgeshire - Clinical Responsibilities
In Cambridgeshire the role of prescribing Nalmefene is to be undertaken by GPs but only on the recommendation of Inclusion Alcohol Service, who will provide a full assessment of a patient’s suitability and on-going support. The patient must comply with the programme of prescribing and support offered. The clinical responsibilities are set out below:

The GP has the following clinical responsibilities:

- Referral to Inclusion where a GP identifies one of their patients may benefit from being prescribed Nalmefene.
- Undertaking a general physical assessment to determine suitability for prescribing including undertaking relevant blood tests.
- Consideration of any contraindications before referral to Inclusion (see Appendix 1 supporting information)
- Prescribing Nalmefene in line with NICE guidelines (TAG 325)
- Stopping prescribing on the advice of the Inclusion
- For any other health issue, that may arise in the course of prescribing Nalmefene
- Communicating openly with Inclusion to assist patients treatment

*If a clinical governance issue arises the Practice will undertake its normal clinical governance processes in line with their GP General Medical Services (GMS) contract

*If a clinical governance issue arises related to these areas the GP will notify the Commissioner at Cambridgeshire County Council at the following address: daat@cambridgeshire.gov.uk and to Inclusion to the following individuals:

Barry.Ord@sssft.nhs.uk – Alcohol Nurse Lead
Mark.Buitendach@sssft.nhs.uk – Clinical Manager Inclusion Cambridgeshire
Inclusion has the following clinical responsibilities:

- Triage and patients and offer an initial assessment referred for Nalmefene prescribing within 14-21 days of receiving a GP referral
- Arrange a follow-up appointment 2 weeks after initial assessment and psychosocial support has been provided which shall include provision of advice/tools for the patient to manage their drinking
- Request the GP prescribes Nalmefene if determined clinically suitable 2 weeks after initial assessment and following delivery of 2 weeks of psychosocial support
- Checking the patient is complying with the GPs Nalmefene prescription
- Providing other treatment options if appropriate following completion of Nalmefene prescribing or should it be discontinued for any other reason
- *Notification to the Commissioner Cambridgeshire County Council if any clinical governance issues arise to the following address: daat@cambridgeshire.gov.uk and to the prescribing GP.

Any clinical governance issues arising from these responsibilities will be assessed by the Inclusion Alcohol Recovery Nurse and escalated through the Inclusion Clinical Governance Framework in line with the SSSFT Policy if necessary. In any cases where an adverse incident occurs this must be reported to Inclusion services. The Service will raise an incident report in accordance with South Staffordshire and Shropshire’s NHS Foundation Trusts Substance Misuse Serious Incident Reporting Policy. The Trust will liaise immediately with the GP (s) and notify the Commissioner Cambridgeshire County Council if any clinical governance issues arise to the following address: daat@cambridgeshire.gov.uk

Where issues arise that cannot be resolved through the clinical governance systems of either the GP, or Inclusion, the two systems will work together and if necessary with the Commissioner to resolve any issues.

The patient has responsibilities as part of their treatment these are set out in the patient leaflet (see Appendix 2)
Stage 1 GP Referral
- Patient requests/GP considers Nalmefene prescribing. Patient meets criteria as indicated by:
  - evidence of mild alcohol dependence classified as:
    - Men drinking 7.5 units a day or more but less than 15 units: Women drinking 5 units a day or more but less than 12 units: no history or evidence of physical withdrawal symptoms which would require a detoxification.
- Considerations include: Concomitantly prescribed medication (particularly inhibitors of the UGT2B7 enzyme and UGT inducers) and opioid agonists, Potential contraindications to treatment (renal or hepatic impairment), Factors that make treatment unsuitable, i.e. immediate abstinence desired
- If Nalmefene is potentially suitable, the GP makes a referral to Inclusion Alcohol Services for assessment and supported treatment before any prescribing takes place. GP offers brief advice and gives a drink diary to the patient where possible

Stage 2 - Inclusion Initial Assessment within 14 to 21 days of GP referral
- Inclusion to offer assessment appt within 21 days of referral, alcohol screening tools to be completed, level of drinking to be established
- If the patient does meet the criteria – provide brief intervention and drink diary, provide a 2 week follow-up app
- Where patient does not meet requirements by
  - drinking more than 15 units daily - offer further Tier 3 treatment pathway
  - drinking less than 5 units daily - offer brief interventions/extended brief interventions

Stage 3 – Inclusion 2nd assessment after 2 weeks of psychosocial support
- Inclusion follow up appointment within 14 days of initial assessment to establish if the patient continues to meet the criteria for prescribing, further individual or group brief interventions to be offered, drink diary continued. A request made to GP to initiate Nalmefene prescribing for a initial 2 week period
- Inclusion to offer follow up appointment within 2 weeks of prescribing, further brief intervention work, drink diary and recovery focused groups provided. Review of progress to consider on-going prescribing – GP to be updated on progress
- In some cases psychosocial support will be sufficient and Nalmefene will not be required, the specialist service will advise the GP if this is the case

Stage 4 - Inclusion review patient monthly for three months
- Inclusion to review the patients progress monthly for a period of 3 months
- If at any point of the treatment the patient misses their appointment/ drinking increase’s and/or other risks are disclosed Inclusion must inform the GP to stop prescribing
- If at any time the GP feels that Nalmefene is no longer clinically appropriate, prescribing will stop. GP’s are required to advise Inclusion of decisions to stop Nalmefene prescribing
- Further brief intervention work, drink diary and individual or group brief interventions to continue. Inclusion to routinely report information on the patient’s progress in reducing alcohol consumption, overall functioning, treatment adherence, and any potential side effects back to the patient’s GP

Stage 5 - Inclusion review monthly for a further 3 months
- Inclusion may ask the patients GP to continue to prescribe for up to a further three months if deemed appropriate if there are on-going benefits from continued prescribing. Ongoing individual/group brief intervention work will continue to be offered and the patient will continue to complete a drink diary.
- Inclusion will update the patient GP on progress on a monthly basis.
Stage 5 - Inclusion review monthly for a further 3 months
- Inclusion may ask the patients GP to continue to prescribe for up to a further three months if deemed appropriate if there are on-going benefits from continued prescribing. Ongoing individual/group brief intervention work will continue to be offered and the patient will continue to complete a drink diary.
- Inclusion will update the patient GP on progress on a monthly basis.

Stage 6 - Inclusion six monthly reviews
- After 6 months Inclusion will review the patients progress and treatment options and will consider:
  - discharge from Inclusion back to the GP where progress has been maintained or problem resolved
  - further ongoing prescribing with monthly reviews and monitoring by Inclusion to continue for a further period of up to 6 months (the current recommended maximum length of prescribing is 6-12 months)
Nalmefene is to be taken as-needed: on each day the patient perceives a risk of drinking alcohol; one tablet should be taken, preferably 1-2 hours prior to the anticipated time of drinking. If the patient has started drinking alcohol without taking nalmefene, the patient should take one tablet as soon as possible.

The maximum dose of nalmefene is one tablet per day. Nalmefene can be taken with or without food.

**Duration of Treatment:**

The NICE guidance does not include clear information about when treatment should be stopped. Clinical data for the use of Nalmefene under randomised controlled conditions are available for a period of 6 to 12 months. Caution is advised if Nalmefene is prescribed for more than 1 year. During treatment, the GP and specialist service should continue to assess the patient’s progress in reducing alcohol consumption, overall functioning, treatment adherence, and any potential side effects.

**Contraindications of Nalmefene treatment:**

- Hypersensitivity to the active substance or to any of the excipients listed (refer to SPC).
- Patients taking opioid analgesics
- Patients with current or recent opioid addiction
- Patients with acute symptoms of opioid withdrawal
- Patients for whom recent use of opioids is suspected
- Patients with severe hepatic impairment (Child-Pugh classification)
- Patients with severe renal impairment (eGFR <30 ml/min per 1.73 m2)
- Patients with a recent history of acute alcohol withdrawal syndrome (including hallucinations, seizures, and delirium tremens).
- Patients with rare hereditary problems of galactose intolerance, Lapp lactase deficiency, or glucose-galactose malabsorption (medicine contains lactose)

**Cautions / special situations:**

- Nalmefene is not for patients for whom the treatment goal is immediate abstinence. Reduction of alcohol consumption is an intermediate goal on the way to abstinence.
- Nalmefene is not recommended for use in patients who are pregnant or breastfeeding
- Opioid administration
  - In an emergency situation when opioids must be administered to a patient taking Nalmefene, the amount of opioid required to obtain the desired effect may be greater than usual. The patient should be closely monitored for symptoms of respiratory depression as a result of the opioid administration and for other adverse reactions.
  - If opioids are needed in an emergency, the dose must always be titrated individually. If unusually large doses are required, close observation is necessary.
  - Nalmefene should be temporarily discontinued for 1 week prior to the anticipated use of opioids, for example, if opioid analgesics might be used during elective
surgery.

• The prescriber should advise patients that it is important to inform their health care professional of last Nalmefene intake if opioid use becomes necessary.

• Caution should be exercised when using medicinal products containing opioids (for example, cough medicines, opioid analgesics (see section 4.5)).

• Psychiatric disorders

  • Psychiatric effects were reported in clinical studies. If patients develop psychiatric symptoms that are not associated with treatment initiation with Nalmefene, and/or that are not transient, the prescriber should consider alternative causes of the symptoms and assess the need for continuing treatment with Nalmefene.

  • Nalmefene has not been investigated in patients with unstable psychiatric disease. Caution should be exercised if Nalmefene is prescribed to patients with current psychiatric comorbidity such as major depressive disorder.

• Seizure disorders - there is limited experience in patients with a history of seizure disorders, including alcohol withdrawal seizures. Caution is advised if treatment aimed at reduction of alcohol consumption is started in such patients.

• Elderly patients (≥65 years of age) – limited clinical data are available on the use of Nalmefene in patients ≥65 years of age with alcohol dependence.

**Potential side-effects**

Nausea, vomiting, dry mouth, weight loss, decreased appetite, tachycardia, palpitation, dizziness, headache, somnolence, tremor, disturbance in attention, paraesthesia, hypoesthesia, malaise, sleep disorders, confusion, restlessness, decreased libido, muscle spasms, hyperhidrosis. Hallucinations and dissociation also reported.

**Interactions:**

Co-administration with medicinal products that are potent inhibitors of the UGT2B7 enzyme (for example, diclofenac, fluconazole, medroxyprogesterone acetate, meclofenamic acid) may significantly increase the exposure to Nalmefene. This is unlikely to present a problem with occasional use, but if long-term concurrent treatment with a potent UGT2B7 inhibitor is initiated, a potential for an increase in Nalmefene exposure cannot be excluded.

Conversely, concomitant administration with a UGT inducer (for example, dexamethasone, phenobarbital, rifampicin, omeprazole) may potentially lead to subtherapeutic nalmefene plasma concentrations.

If Nalmefene is taken concomitantly with opioid agonists (for example, certain types of cough and cold medicinal products, certain antidiarrhoeal medicinal products, and opioid analgesics), the patient may not benefit from the opioid agonist.

Simultaneous intake of alcohol and Nalmefene does not prevent the intoxicating effects of alcohol.

**Drug costs (BNF 66)**

Selincro® tablets, f/c, Nalmefene (as hydrochloride dihydrate) 18 mg
The lists of potential side effects and potential drug interactions included within this document are 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:

Summary of Product Characteristics for Selincro® 18mg tablets (Lundbeck Limited, accessed 30/12/2014)

NICE Technology Appraisal 325: Nalmefene for reducing alcohol consumption in people with alcohol dependence (accessed 30/12/2014)
About Nalmefene tablets

Nalmefene will help you to reduce the amount of alcohol you drink if you are not able to do this on your own. It does this by interfering with the processes in your brain which are responsible for your urge to drink.

Type of medicine: Medicine used for alcohol dependence
Used for: To reduce alcohol consumption
Also called: Selincro®
Available as: Tablets only

Before Taking Nalmefene

Your Doctor will refer you to the local Alcohol Service for full assessment prior to prescribing nalmefene. This is to ascertain an accurate level of your drinking and offer on-going support and advice in liaison with your Doctor. As some medicines are not suitable for people with certain conditions, and sometimes a medicine may only be used if extra care is taken. For these reasons, before you start taking nalmefene tablets it is important that the following are taken into consideration:

- If you are pregnant, trying for a baby, or breast-feeding.
- If you have ever had a mental health problem.
- If you have ever had a seizure (fit).
- If you have any problems with the way your liver works, or the way your kidneys work.
- If you have ever had an allergic reaction to a medicine.
- If you are taking any other medicines. In particular if you are taking any strong painkillers. This includes any medicines you are taking which are available to buy without a prescription, such as herbal and complementary medicines.

How to take Nalmefene tablets

- Take nalmefene tablets exactly as your doctor tells you to. Take one tablet a day on each day that you anticipate drinking alcohol. The tablet is best taken 1-2 hours before you drink alcohol, but if you are not able to do this, take it as soon as you can.
- Do not take more than one tablet per day.
- Swallow the tablet whole with a drink of water - do not crush or break the tablet. You can take nalmefene before or
Getting the most from your treatment

- Your progress will be monitored and further ongoing advice offered by the local Alcohol Service who will liaise with your GP.
- Failure to keep appointments while being prescribed Nalmefene may lead to cessation of the treatment
- It may help to tell your family and friends how important it is that you reduce your drinking, so that they can be a support to you.
- Your local Alcohol service will be able to advise you on what further support and self-help groups are available in your area
- If you buy any medicines, check with your doctor, alcohol service or a pharmacist that they are suitable for you to take. This is because strong painkillers (some of which can be bought ‘over the counter’ in a pharmacy) should not be taken with nalmefene tablets.
- If you are due to have an operation or dental treatment, tell the person carrying out the treatment that you are taking nalmefene. You may be advised to stop taking the tablets for a short while because they could affect your treatment.

Can Nalmefene tablets cause problems?

Along with their useful effects, most medicines can cause unwanted side-effects although not everyone experiences them. The table below contains some of the most common ones associated with nalmefene tablets. You will find a full list in the manufacturer’s information leaflet supplied with your medicine. The unwanted effects often improve as your body adjusts to the new medicine, but speak with your doctor or pharmacist if any of the following continue or become troublesome.

<table>
<thead>
<tr>
<th>Very common nalmefene side-effects - these may affect more than 1 in 10 people taking this medicine</th>
<th>What can I do if I experience this?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Feeling sick</td>
<td>Stick to simple meals - avoid rich or spicy foods. Try taking the tablet with a snack, such as a plain biscuit</td>
</tr>
<tr>
<td>Feeling dizzy or sleepy</td>
<td>Do not drive or use tools or machines until you feel better</td>
</tr>
<tr>
<td>Headache</td>
<td>Ask your pharmacist to prescribe a suitable painkiller (but remember to mention that you are taking nalmefene)</td>
</tr>
<tr>
<td>Sleeping problems</td>
<td>If troublesome, speak with your doctor</td>
</tr>
</tbody>
</table>

If you experience any other symptoms which you think may be due to this medicine, speak with your doctor, Alcohol service or pharmacist.