**Chapter 4: CENTRAL NERVOUS SYSTEM**
**Updated: April 2025**

**The following prescribing guidelines are relevant to the Central Nervous System chapter and can be found here**

- Antipsychotics – Clozapine (GP information)
- Antipsychotics – Prescribing and Management for mental health conditions
- Chloral hydrate position statement
- Dementia – management in primary care
- Dementia – managing behavioural problems
- Depression and the use of antidepressants
- Domperidone – off license use
- Insomnia - Melatonin – for the treatment of sleep disorders in children
- Insomnia – Daridorexant Prescribing Guideline
- Liothyronine for the management of treatment resistant depression
- Metoclopramide use in gastro-paresis
- Midazolam – management of convulsive seizures in the community
- Pain – Deprescribing and safer prescribing of strong opioids in non-malignant pain
- Pain – Nefopam (position statement)
- Pain – neuropathic pain in primary care
- Pain – non-malignant chronic pain in primary care
- Pain – opioids - choice of strong opioids for cancer pain
- Sativex – for severe spasticity in multiple sclerosis
- Smoking cessation – Nicotine replacement therapy formulary

Relevant Resources

- Anticholinergic drugs/ burden – Modified anticholinergic risk scales; drugs on the ACB scale
- SPS- How can nausea and vomiting be treated during pregnancy?
- DHcFT -Medicines and suicide medication review tool
- Reducing the risk of overdose- Patient information leaflet
- Stopping over medication of people with learning disabilities
- Live well with pain
- Ten Footsteps programme
- JUCD Adult Headache Primary Care Pathway
- JUCD Hospitals Approach to Prescribing and Supply of Analgesia on Discharge Following Surgery
- JUCD Managing Pain After Your Surgery – Patient Information Leaflet
- Opioid Resource Pack and Appendices

**Drugs and driving**
It is an offence to drive with certain medicines above specified limits in the blood. See MHRA drug safety update, February 2015 for details.

## 4.1.1 Hypnotics

**Zopiclone** tabs 3.75mg, 7.5mg GREEN

1. Hypnotics should be prescribed at the lowest dose that controls symptoms for the shortest period of time. NICE TA77 recommends hypnotics to be prescribed **for up to two weeks only**, after non-drug measures have failed and the patient's insomnia is severe, disabling or causing the patient extreme distress. This is due to concerns over hypnotic dependence.
2. Zolpidem is an option in patients with swallowing difficulties since the tablets can be crushed and mixed with water for administration. MHRA May 2014 reminder of the risk of impaired driving ability the next day.
3. Adaflex tablets and generic melatonin 2mg MR tablets are the preferred melatonin preparations in Derbyshire - **GREY** after consultant/specialist initiation: for use in children with neurodevelopment

disorders and CAMHS patients. See Insomnia - Melatonin for the treatment of sleep disorders in children.

4. Daridorexant is classified as GREY as per NICE TA922 for treating insomnia in adults with insomnia symptoms lasting for 3 nights or more per week for at least 3 months whose daytime functioning is considerably affected. Only use if cognitive behavioural therapy for insomnia (CBTi) has been tried but not worked, or if CBTi is unsuitable or unavailable. Review treatment after 3 months and regularly thereafter, do not add to repeats and treatment duration should be restricted to 12 months. For more information see Insomnia – Daridorexant Prescribing Guideline
5. Sodium oxybate is classified as **RED** for treatment of narcolepsy with cataplexy. ICB commissioned for adult patients as per the RMOC criteria through the specialist sleep centres; and NHSE commissioned in line with commissioning policy for symptom control in children.

### 4.1.2 Anxiolytics

**Diazepam** tabs 2mg, 5mg
**Chlordiazepoxide** caps 5mg, 10mg (*For alcohol withdrawal only usually under specialised services or GPs with a specialist interest)*

1. Benzodiazepines are indicated for the short-term relief (two to four weeks only) of anxiety that is severe, disabling or subjecting the individual to unacceptable distress (occurring alone or in association with insomnia or short-term psychosomatic, organic or psychotic illness); not for short-term 'mild' anxiety.
2. Hypnotics should be used to treat insomnia only when severe, disabling or subjecting the individual to extreme distress. Only for short-term prescribing (e.g. 2 weeks) in strict accordance with their licensed indications.
3. There may be patients who have been prescribed benzodiazepines or hypnotics for longer durations than recommended. For guidance on deprescribing these see NICE CKS: Benzodiazepine and z-drug withdrawal | Management Guideline and the Deprescribing section of the website.
4. MHRA March 2020- Benzodiazepines and opioids: reminder of risk of potentially fatal respiratory depression. Only prescribe together if there is no alternative and closely monitor patients for signs of respiratory depression.
5. NICE CG 113- Do not offer a benzodiazepine for the treatment of generalized anxiety disorder (GAD) except as a short-term measure during crises; Benzodiazepines are associated with a less good outcome in the long term and should not be prescribed for the treatment of individuals with panic disorder.
6. Hypnotics to be prescribed at the lowest effective dose for the shortest duration that can treat the patient's symptoms.
7. Hypnotics should be avoided in the elderly who are at greater risk of becoming ataxic and confused, leading to falls and injury.
8. Lorazepam can be used acutely on a 'when required' basis for challenging behaviour associated with delirium usually on the advice of a specialist. This is off-label use and should be reviewed regularly and discontinued as soon as appropriate.

## 4.2 Drugs used in psychoses and related disorders

It is recognised that a significant number of people with intellectual disabilities are prescribed psychotropic medication that, at best, is not helping them. For more information see Psychotropic drug prescribing for people with intellectual disability, mental health problems and/or behaviours that challenge: practice guidelines.

### 4.2.1 Antipsychotic drugs

See JAPC guideline on antipsychotic prescribing and management for mental health conditions.
Most formulary oral antipsychotics have been classified as **GREEN** specialist initiation, with a few exceptions listed as per local guideline.

First generation antipsychotics
**Chlorpromazine** tabs 25mg, 50mg, 100mg, 25mg/5ml oral solution SF,100mg/5ml oral solution
**Flupentixol** tabs 0.5mg, 1mg, 3mg,
**Haloperidol** tabs 1.5mg, 5mg, 10mg, oral solution SF 5mg/5ml, 10mg/5ml
**Sulpiride** tabs 200mg 400mg, oral solution SF 200mg/5ml

**Trifluoperazine** tabs 1mg, 5mg, oral solution SF 5mg/5ml
**Zuclopenthixol** tabs 2mg, 10mg, 25mg

Second generation antipsychotics
**Amisulpride** tabs 50mg, 100mg, 200mg, oral solution SF 100mg/ml
**Aripiprazole** tabs 1mg, 2.5mg, 5mg, 10mg, 15mg, 30mg, 1mg/ml solution
**Olanzapine** tabs 2.5mg, 5mg, 7.5mg, 10mg, 15mg, 20mg
**Quetiapine** tabs 25mg, 100mg, 150mg, 200mg, 300mg
**Risperidone** tabs 500microgram, 1mg, 2mg, 3mg, 4mg, oral solution SF 1mg/ml
**Sulpiride** tabs 200mg, 400mg

1. Haloperidol: MHRA Dec 2021 states risks when used in elderly patients for the acute treatment of delirium
   - only consider haloperidol for delirium when non-pharmacological interventions are ineffective, and no contraindications are present (including Parkinson's disease and dementia with Lewy bodies)
   - before initiating treatment, a baseline ECG and correction of any electrolyte disturbances is recommended; cardiac and electrolyte monitoring should be repeated during treatment
   - prescribe the lowest possible dose for the shortest possible time, ensuring that any dose up-titration is gradual and reviewed frequently
   - monitor for and investigate early any extrapyramidal adverse effects, such as acute dystonia, parkinsonism, tardive dyskinesia, akathisia, hypersalivation, and dysphagia
2. Orodispersible tablets are significantly more expensive compared to plain tablets.
3. Prescribing of antipsychotic medication to children and adolescents is occasionally required. Such prescribing will be initiated and maintained in secondary care, along with any medication-specific physical health monitoring.
4. Amisulpride 400mg strength significantly more expensive- use combination of lower strength instead.
5. Low dose amisulpride (max. 50mg/day) is **GREEN** specialist recommendation for treatment of chronic depression (NICE NG222)
6. Aripiprazole oral for treating moderate to severe manic episodes in adolescents with bipolar I disorder (NICE TA292), and aripiprazole injection and depot injection are classified as **RED**. MHRA Dec 2023 Aripiprazole (Abilify and generic brands): risk of pathological gambling - be alert to the risk of addictive gambling and other impulse control disorders. Advise patients and their caregivers to be alert to the development of new or increased urges to gamble and other impulse control symptoms, such as excessive eating or spending, or an abnormally high sex drive. Consider dose reduction or stopping the medication if a patient develops these symptoms.
7. Quetiapine MR is more expensive than standard formulation and classified as **GREY** (preferred brands Brancico XL or Sondate XL). Prescribe under exceptional circumstances only for:
   - patients who have discontinued their treatment with quetiapine and currently have to re-titrate over the period of a week and;
   - patients who require once daily administration but are unable to tolerate titration to the therapeutic dose with once daily plain tablets.
   - Consumption of a high-fat meal increases bioavailability of quetiapine in the modified-release formulations. Food has a minimal effect on quetiapine absorption in the immediate release formulations. The modified-release tablets are administered once daily without food, at least one hour before a meal.

   Specialists should document the exceptionality when communicating with the primary care prescriber.
8. Clozapine (Zaponex brand used by DHCFT) is a **RED** drug but an information sheet for GPs is provided for filling in the patient primary care notes. MHRA Oct 2017 Clozapine: potentially fatal risk of intestinal obstruction, faecal impaction, and paralytic ileus. It is vital that constipation is recognised and actively treated. Advise patients to report constipation immediately. Smoking tobacco reduces plasma levels of clozapine by up to 50%, smokers may require higher doses, care should also be taken for patients who are planning on stopping smoking.

### 4.2.2 Antipsychotic depot injections
These are classified **RED**

### 4.2.3. Antimanic drugs
*Follow consultant advice*

**Carbamazepine** ***GREEN** after consultant/specialist recommendation*
**Sodium Valproate** (see NICE CG185 on bipolar disorder) ***GREEN** after consultant/specialist recommendation*
Lithium is **AMBER** - see shared care guideline
**Lithium carbonate m/r tabs (Priadel, Camcolit, Liskonum)**
**Lithium citrate liquid 5.4mmol/5ml (Priadel, Li-Liquid)**(5.4mmol equivalent to 200mg lithium carbonate)

1. Lithium
   - Prescribe lithium by brand name.
   - Sampling should be 12 hours post dose. To facilitate this dose should routinely be taken at night.
   - All patients on lithium should have the "purple book" or 'app'. The purple book can be obtained from Primary Care Support England (PCSE) through the following link http://pcse.england.nhs.uk/ using your practice log in details.
   - Consultant/specialist responsibility: Provide patient with lithium information, alert card and record book, ensuring details are recorded. Advise on the availability of a smartphone 'App' if the patient prefers.
   - Lithium tablets and liquids are not interchangeable. Liquid formulations contain lithium citrate and doses are not equivalent to lithium carbonate; bioavailability is significantly different. If a switch in formulation is considered, discuss with the specialist team. Extra care must be taken when prescribing lithium in liquid form, as some offer different strengths under the same brand names, and some brands are used for the liquid and tablet forms. Lack of clarity may lead to the patient receiving a sub-therapeutic or toxic dose.
2. Sodium Valproate
   - NPSA November 2023; MHRA January 2024 Valproate (Belvo, Convulex, Depakote, Dyzantil, Epilim, Epilim Chrono or Chronosphere, Episenta, Epival, and Syonell▼): new safety and educational materials to support regulatory measures in men and women under 55 years of age.
     - valproate must not be started in new patients (male or female) younger than 55 years, unless two specialists independently consider and document that there is no other effective or tolerated treatment, or there are compelling reasons that the reproductive risks do not apply. For the majority of patients, other effective treatment options are available.
     - at their next annual specialist review, women of childbearing potential and girls receiving valproate should be reviewed using the revised valproate Annual Risk Acknowledgement Form. A second specialist signature will be needed if the patient is to continue on valproate, however subsequent annual reviews will only require one specialist.
     - general practice and pharmacy teams should continue to prescribe and dispense valproate and if required offer patients a referral to a specialist to discuss their treatment options. Valproate should be dispensed in the manufacturer's original full pack
     - A retrospective observational study has reported a possible association between valproate use by men and a small increased risk of a range of neurodevelopmental disorders in their children (aged 0 to 11 years) when compared to men prescribed lamotrigine or levetiracetam. As a precautionary measure, the MHRA (September 2024) recommends that male patients and their partner use effective contraception during valproate treatment and for at least three months after stopping valproate.
   - MHRA February 2016- children exposed to valproate in utero are at high risk of developmental disorders and congenital malformations. A guidance/ toolkit (MHRA 2018) to help understanding of the risks of valproate and pregnancy has been launched to ensure female patients are better informed about the risks of taking valproate medicines during pregnancy. See also MHRA Dec22, MHRA 2021, MHRA 2020, MHRA January 2015.
   - EMA March 2018 recommends a ban on the use of valproate-containing medicines for migraine or bipolar disorder during pregnancy, and a ban on treating epilepsy during pregnancy unless there is no other effective treatment available. Valproate-containing medicines must not be used in any woman or girl able to have children unless the conditions of a new pregnancy prevention programme are met. These include:
     - an assessment of each patient's potential for becoming pregnant
     - pregnancy tests before starting and during treatment as needed
     - counselling about the risks of valproate treatment and the need for effective contraception throughout treatment
     - a review of ongoing treatment by a specialist at least annually
     - introduction of a new risk acknowledgement form that patients and prescribers will go through at each such annual review to confirm that appropriate advice has been given and understood.

## 4.3 Antidepressants

See JAPC guideline Depression and the use of Antidepressants. Do not routinely offer antidepressant medication as first line treatment in less severe depression, unless that is the person's preference.

### 4.3.1 Tricyclic and related antidepressant drugs

**Amitriptyline** tabs 10mg, 25mg, 50mg**,** 25mg/5ml oral solution SF, 50mg/5ml oral solution SF
**Lofepramine** tabs 70mg
**Trazodone** caps 50mg, 100mg, tabs 150mg, 50mg/5ml oral solution

1. Amitriptyline use in neuropathic pain see local guideline.
2. Pregabalin
   - The role of pregabalin (prescribed generically) for generalised anxiety disorder (GAD) is restricted as per NICECG113. Pregabalin is **GREEN** after specialist initiation for GAD, where SSRIs or venlafaxine are ineffective, poorly tolerated or considered clinically inappropriate.
   - Pregabalin and gabapentin are classified as Schedule 3 controlled drugs. See MHRA April 2019.
   - MHRA February 2021: Pregabalin has been associated with infrequent reports of severe respiratory depression, including some cases without the presence of concomitant opioid medicines. Patients with compromised respiratory function, respiratory or neurological disease, renal impairment; those using concomitant CNS depressants; and people older than 65 years might be at higher risk of experiencing these events and adjustments in dose or dosing regimen may be necessary.
   - MHRA April 2022: Pregabalin (Lyrica): pregabalin may slightly increase the risk of major congenital malformations if used in pregnancy. Patients should continue to use effective contraception during treatment and avoid use in pregnancy unless clearly necessary.
3. Nortriptyline is **GREY** for use as second line to amitriptyline for neuropathic pain and also as an adjunct in treatment resistant depression. Amitriptyline is the cost-effective choice compared to nortriptyline
4. Dosulepin is **Do Not Prescribe (DNP)** not recommended/commissioned for new patients. It is particularly dangerous in over dosage and not recommended for depression. Existing patients on treatment should not have their medication stopped abruptly. Careful review is required which may require specialist input.
5. Doxepin is **GREY** after consultant/specialist initiation for use in dermatology patients after a trial of conventional antihistamines.

### 4.3.2 Monoamine-oxidase inhibitors

**Moclobemide** tabs 150mg, 300mg

1. Moclobemide (**GREEN**) is claimed to cause less potentiation of the pressor effect of tyramine than the traditional (irreversible) MAOIs, but patients should avoid consuming large amounts of tyramine-rich food (such as mature cheese, yeast extracts and fermented soya bean products).
2. Phenelzine is **GREEN** specialist initiation for unipolar depression

### 4.3.3 Selective serotonin re-uptake inhibitors

**Citalopram** tabs 10mg, 20mg, 40mg, 40mg/ml oral drops
**Fluoxetine** caps 20mg
**Sertraline** tabs 50mg, 100mg
**Vortioxetine** tab 5mg, 10mg, 20mg *see antidepressant guideline- step3*

1. The SSRI of choice is dependent on the patient presenting, for example sertraline is the preferred SSRI in breast-feeding women. See JAPC Depression and the use of antidepressants guideline.
2. There is an association between the use of SSRIs and upper GI bleeds. The use of SSRIs with concomitant NSAIDs increases the risk of upper GI bleeding further.
   If an SSRI is required in a patient at high risk of an upper GI bleed, then the use of a gastro-protective agent could be considered. See local PPI guidance for further detail.
3. MHRA January 2021: SSRI/SNRI antidepressants- small increased risk of postpartum haemorrhage. SSRIs and SNRIs (venlafaxine) are known to increase the bleeding risk; observational data suggest that the use of some antidepressants in the last month before delivery may increase the risk of postpartum haemorrhage. Continue to consider the benefits and risks for use of antidepressants during pregnancy, and the risks of untreated depression in pregnancy.

4. Risk of hyponatraemia – any antidepressant may be associated with this. Recommendation is for baseline serum sodium and repeat within first month. Risk is greater in older adults or those taking concurrent natriuretic medicines e.g. diuretics or with low body weight or in warm weather. See JAPC Depression and the use of antidepressants guideline.
5. Sertraline:
    - If low doses of sertraline are required, the most cost-effective option is to consider halving the 50mg tablets. Alternatively, if higher doses are required, use a combination of 50mg & 100mg tablets if possible.
6. Citalopram
    - Maximum dose is 40mg daily in adults; 20mg in elderly (>65 years of age) and those with reduced hepatic function
    - Contraindicated in patients with known QT interval prolongation or congenital long QT syndrome; or use with other medicines known to prolong QT interval
    - Use is cautioned in patients at higher risk of developing Torsade de Pointes, including those with congestive heart failure, recent myocardial infarction, bradyarrhythmias, or a predisposition to hypokalaemia or hypomagnesaemia due to illness or drug therapy.
    - The dose for citalopram oral drops should be stated in drops, not in millilitres to avoid confusion for patients and for ease of administration.
        - The drops contain a different salt to the tablets. The dose of the tablets corresponds to the doses of drops as follows:

| Tablets/dose equivalent | Drops |
|---|---|
| 10mg | 8mg (4 drops) |
| 20mg | 16mg (8 drops) |
| 30mg | 24mg (12 drops) |
| 40mg | 32mg (16 drops) |

    - Use in children is **GREY** after consultant/specialist initiation - 2nd line as per NICE NG134
7. Fluoxetine is **GREEN** after consultant/specialist initiation when used in children and adolescents in primary care at the licensed dose. This group of patients will be initiated with treatment by the Children Adolescent Mental Health Services (CAMHS) and prescribing handed over to primary care under patient specific management plans. Sertraline use in children is **GREY** after consultant/specialist initiation - 2nd line as per NICE
8. Fluoxetine 20mg dispersible tablets (**GREEN**) is a cost-effective option for patients with swallowing difficulties.
9. Vortioxetine has been re-classified to **GREEN** for treating major depressive episodes as per NICE TA367. It is step3 in local antidepressant guideline- only when there has been no or limited response to at least 2 previous antidepressants.

### 4.3.4 Other antidepressants drugs

**Mirtazapine** tabs 15mg, 30mg, 45mg
**Venlafaxine** tabs 37.5mg, 75mg, tabs 37.5mg m/r, 75mg m/r, 150mg m/r

1. Mirtazapine oral solution is **GREY**. Use mirtazapine orodispersible tablet instead.
2. The most cost-effective strength of venlafaxine should be prescribed.
3. Venlafaxine should be avoided in those with pre-existing heart disease and in anyone who has uncontrolled or untreated hypertension. Consider ECG for patients at risk of heart disease. Review blood pressure after initiation, dose increase, and annually- if raised, only continue venlafaxine if BP under control and alternative antidepressant not suitable.
4. Duloxetine has limited place in therapy for depression (alternative to venlafaxine for patients with previous history of antidepressant benefit). See full traffic light classification for further details.

## 4.4 CNS stimulants and drugs used for attention deficit hyperactivity disorder

**Modafinil** tabs 100mg, 200mg

1. Modafinil is **GREEN** after specialist initiation to treat narcolepsy and narcolepsy secondary to Parkinson's disease. For other indications it is **Do Not Prescribe (DNP)**.
2. MHRA November 2020:- Modafinil: increased risk of congenital malformations if used during pregnancy

- Modafinil should not be used during pregnancy and women of childbearing potential must use effective contraception during treatment and for 2 months after stopping modafinil.
- Modafinil may reduce the effectiveness of steroidal contraceptives, including oral contraceptives, through the induction of CYP3A4/5. Alternative or concomitant methods of contraception are required.

The following drugs are classified as **AMBER** -see ADHD shared care guidelines

**Methylphenidate**
**Lisdexamfetamine**
**Dexamfetamine**
**Atomoxetine**
**Guanfacine**

1. MHRA Sept 2022 Methylphenidate long-acting (modified-release) preparations: caution if switching patients between different long-acting formulations of methylphenidate.
   - **Prescribe by brand name**
   - caution if long-acting formulations of methylphenidate are to be used interchangeably due to the differences between formulations in dosing frequency, administration with food, amount and timing of the modified-release component, and overall clinical effect. Follow specific dosage recommendations for each formulation. See SPS for further information.

   If considering a switch to another long-acting preparation:
   - consult with the patient (and their parent or caregiver if relevant) to discuss the reasons for this and the possible changes they may experience in symptom management and side effects (and what to do if these occur)
   - consider patient preferences such as their individual needs, dose frequency, possible side effects, or other issues related to the patient's condition
   - reiterate the instructions for use for the newly prescribed formulation, especially whether it should be taken with or without food

## 4.5 Drugs used in the treatment of obesity

**Orlistat** caps 120mg

1. NICE clinical guideline 246 (guidance on the prevention of overweight and obesity in adults and children) must be **strictly** adhered to.
2. All GLP-1s licensed for weight loss (liraglutide, semaglutide and tirzepatide) are classified as **RED**. Not suitable for primary care prescribing.

## 4.6 Drugs used in nausea and vertigo

**Metoclopramide** tabs 10mg
**Domperidone** tabs 10mg
**Cyclizine** tab 50mg
**Prochlorperazine** tabs 5mg, injection 12.5mg/ml
**Cinnarizine** tabs 15mg
**Betahistine** tabs 8mg, 16mg

1. Metoclopramide – MHRA Dec 2014 risk of neurological adverse effect:
   - In adults, metoclopramide remains indicated for prevention of postoperative/ radiotherapy-induced/ delayed chemotherapy-induced nausea and vomiting (N&V) and symptomatic treatment of N&V including that associated with acute migraine (where it may also be used to improve absorption of oral analgesics). The maximum dose in 24 hours is 30mg (or 0.5mg per kg for patients up to 60kg bodyweight). The usual dose is 10mg three times a day and should only be prescribed for short-term use (up to 5 days)
   - in children aged 1–18 years, metoclopramide should only be used as a 2nd line option for short-term use (up to 5 days) for prevention of delayed chemotherapy-induced N&V, and for treatment of established postoperative N&V.
   - Use of metoclopramide is contraindicated in children younger than 1 year
   - Off label use of metoclopramide is recognised as standard practice in palliative medicine. JAPC recognises that long term use of metoclopramide may be appropriate in some palliative care patients when given orally/parentally

For off-label use in gastroparesis and other gastric outlet physiological impairment, metoclopramide is classified as **GREY** after consultant/specialist initiation – see the JAPC local position statement.

2. Domperidone – MHRA advice (2014) risks of cardiac side effects MHRA advice (2019)
   - Domperidone may be associated with a small increased risk of serious ventricular arrhythmia or sudden cardiac death. These risks may be higher in patients older than 60 years and in patients who receive daily oral doses of more than 30 mg.
   - Domperidone is restricted to use in the relief of nausea and vomiting; it should be used at the lowest effective dose for the shortest possible time. For adults the maximum dose in 24 hours is 30mg. The duration of treatment should not usually exceed one week
   - Domperidone is preferred in patients where the risk of dystonic reactions is high i.e., young women, children, the elderly, and those with Parkinson's disease.
   - Domperidone is no longer licensed for children under 12 years of age due to lack of efficacy. Where it is used outside of its authorised indications in children for gastrokinetic effects in conditions other than nausea and vomiting, specialist input is required.

   For off-label use in gastroparesis and other gastric outlet physiological impairment, in babies and children, and in nursing mothers to promote lactation, domperidone is classified as **GREY** after consultant/specialist initiation – see the JAPC local position statement
3. Prochlorperazine is useful in the treatment of vertigo but should be avoided in the elderly if possible because of extrapyramidal effects.
4. Haloperidol is recommended for the control of chemically induced (e.g. opioids) nausea and induced vomiting in palliative care, these are unlicensed indications. See Haloperidol | Drugs | BNF | NICE for dosage information.
5. NICE NG201 Antenatal care gives advice on treatment of nausea and vomiting in pregnancy
   - Reassure women that mild to moderate nausea and vomiting are common in pregnancy and likely to resolve before 16-20 weeks.
   - For pregnant women with mild-to-moderate nausea and vomiting who prefer a non-pharmacological option, suggest that they try ginger, avoid stimuli, have small bland meals.
   - When considering pharmacological treatments for nausea and vomiting in pregnancy, discuss the advantages and disadvantages of different antiemetics with the woman. Consider her preferences and her experience with treatments in previous pregnancies. For pregnant women with nausea and vomiting who choose a pharmacological treatment, offer an antiemetic. See NICE table 1 on the advantages and disadvantages of different pharmacological treatments for nausea and vomiting in pregnancy.
6. For further information on nausea & vomiting in pregnancy see SPS - Nausea and Vomiting: treatment during pregnancy.

## 4.7 Analgesics

### 4.7.1 Non- opioid analgesics

For treatments of minor, short-term medical conditions such as mild toothache, headaches, period pain, mild fever and back pain, patients are encouraged to self-care with over-the-counter painkillers and lifestyle changes. See JUCD for more information.

**Paracetamol** tabs 500mg, suspension 120mg/5ml, 250mg/5ml

Compound analgesic preparations
**Co-Codamol** tabs 30/500

1. Paracetamol is the simple analgesic of choice. Co-codamol 8/500 (tablet more cost effective), 15/500 and co-dydramol 10/500 are listed by the BNF as less suitable for prescribing and are both now removed in the local traffic light formulary.
2. There is a lack of efficacy from trial data over paracetamol but may be considered for patients unresponsive to full licensed doses of paracetamol alone before using more potent and costly analgesia.
3. Avoid effervescent products (unless genuine swallowing difficulties) as they have high sodium content and are associated with significantly increased odds of adverse cardiovascular events compared with standard formulations of those same drugs. These preparations should be prescribed with caution only if the perceived benefits outweigh these risks and should be avoided if possible. (This does not apply to aspirin 75mg dispersible which contains very low levels of sodium). Paracetamol effervescent and co-codamol effervescent tablets are **GREY**.
4. Paracetamol 500mg effervescent tablets are more cost effective than soluble tablets.

5. Some patients may be at increased risk of experiencing toxicity at therapeutic doses, particularly those with a body weight under 50kg and those with risk factors for hepatotoxicity (e.g., alcohol dependency, malnourishment, chronic dehydration, severe liver disease, increasing age and/or frailty, long-term treatment with liver enzyme-inducing drugs such as carbamazepine). If risk factors are present or weight <50kg, use clinical judgement to adjust the dose (CKS).

| | |
|---|---|
| >50 kg with risk factors | Consider reducing the total daily dose of paracetamol to max. 3g in 24h e.g. 500mg QDS or 1g TDS |
| <50kg | Consider reducing dose use 15mg/kg (max. 60mg/kg in 24h) every 4-6 hours as a guide. Note UHDBFT advises 500mg QDS max. 2g in 24h |

6. The prescribing of Co-proxamol is not supported and clinicians should move patients to suitable alternatives. Its use has been linked to death by fatal poisoning. Co-proxamol is unlicensed and has been classified locally as **Do Not Prescribe (DNP)**.
7. JAPC has classified nefopam as **Do Not Prescribe (DNP)** due to a lack of data on effectiveness, safety concerns, and it not being cost-effective compared with standard therapy. Patients already on treatment should be able to continue treatment until their next medication review where their NHS clinician might consider it appropriate to switch or stop treatment. For further information see the JAPC's position statement.
8. MHRA January 2018 Co-dydramol: prescribe and dispense by strength to minimise risk of medication error. Previously co-dydramol (dihydrocodeine/paracetamol) was available only in the ratio 1:50 (co-dydramol 10/500 mg). Two products are now available with a higher strength of dihydrocodeine (co-dydramol 20/500 mg and 30/500 mg tablets). It is therefore important that co-dydramol products are prescribed and dispensed by strength to minimise dispensing errors and the risk of accidental opioid overdose.

### 4.7.2 Opioid analgesics

MHRA March 2020 - Benzodiazepines and opioids: reminder of risk of potentially fatal respiratory depression. Only prescribe together if there is no alternative and closely monitor patients for signs of respiratory depression. At the end of treatment, taper dosage slowly to reduce the risk of withdrawal effects. Consider the possibility of hyperalgesia if a patient on long-term opioid therapy presents with increased sensitivity to pain.

MHRA September 2020 - Opioids: long-term (>3months) use in non-cancer pain, even at therapeutic doses, carries an increased risk of dependence and addiction. Before prescribing opioids, discuss with the patient the risks and features of tolerance, dependence, and addiction, and agree together a treatment strategy and plan for end of treatment. See non-malignant chronic pain guideline for further detail.

**Codeine phosphate** 15mg, 30mg, 60mg tabs **GREEN**
**Dihydrocodeine** tabs 30mg **GREEN**

1. NICE (NG193) no longer recommends initiation of opioids for the management of chronic primary pain. See local guideline management of non-malignant chronic pain.
2. Following MHRA July 2013 advice codeine should only be taken to relieve acute moderate pain in children older than 12 years and only if it cannot be relieved by other painkillers such as paracetamol or ibuprofen alone.
3. Tramadol - **GREY**
   - Consider for neuropathic pain only if acute rescue therapy is needed as NICE advices against using long-term unless advised by specialist (see local guideline).
   - It has a high incidence of ADRs and drug interactions. Locally it's linked with hospital admissions.
   - It is a schedule 3 controlled drug. Prescription needs to comply with CD requirements with the dose being stated, total quantity to be supplied given in both word and figures, also limits to validity of prescriptions and length of supply that can be provided. See the Controlled Drugs page here for more information.
   - Tramadol MR is significantly more expensive than standard release formulation. (Preferred brand is Marol).
   - See tramadol educational resources including patient information leaflet

Strong opioids (see choice of strong opioids for cancer pain)

*1st line*

**Morphine Sulphate** Modified release caps (Zomorph) 10mg, 30mg, 60mg, 100mg, 200mg
Immediate release tabs 10mg, 20mg
Oral solution (Oramorph) 10mg/5ml
Injection ampoules 10mg/ml *see end of life pathway*

*2nd line*

**Oxycodone** Modified release tabs (Oxypro/Oxeltra) 5mg, 10mg, 15mg, 20mg, 30mg, 40mg, 60mg, 80mg, 120mg
Immediate release caps (Shortec) 5mg, 10mg, 20mg
Oral solution 5mg/5ml (generic)

**Fentanyl** Patch (Opiodur) 12, 25, 50, 75, 100 micrograms
*Other brands previously recommended include Fencino, Matrifen and Mezolar, which may be used if Opiodur is not suitable or not available.*

1. For non-cancer pain, JAPC advise that patients receiving opioid doses of >50mg/day morphine equivalent should be reviewed regularly (at least annually). Clinicians may seek specialist advice for doses >90mg/day morphine equivalent.
2. NICE (NG193) no longer recommends initiation of opioids for management of chronic primary pain. See local guideline management of non-malignant chronic pain; Deprescribing & Safer prescribing of strong opioids in non-malignant pain.
3. Prescribe laxatives when starting regular morphine and continue while on opioid. Consider anti-emetic if appropriate.
4. Reducing dosing errors with opioid medicines:
   When opioid medicines are prescribed, dispensed or administered, in anything other than acute emergencies, the healthcare practitioner concerned, or their clinical supervisor, should:
   - Confirm any recent opioid dose, formulation, frequency of administration and any other analgesic medicines prescribed for the patient. This may be done for example through discussion with the patient or their representative (although not in the case of treatment for addiction), the prescriber or through medication records.
   - Ensure where a dose increase is intended, that the calculated dose is safe for the patient (e.g., for oral morphine or oxycodone in adult patients, not **normally** more than 50% higher than the previous dose).
   - Ensure they are familiar with the following characteristics of that medicine and formulation: usual starting dose, frequency of administration, standard dosing increments, symptoms of overdose, common side effects.
5. Prescribe m/r morphine by brand name. Zomorph is the cost-effective option. To aid compliance the capsule can be opened and content sprinkled onto food. MXL (once daily MR morphine) is **GREY.**
6. For all liquid formulations, the administration label must state the dose (in mg, mcg, g, etc) as well as the number of mls this pertains to in brackets. For any other formulation conversions, reducing/increasing dose regimes or any other regimes which requires dose calculations, if the person who is issuing the prescription feels this needs a double check, they can ask a pharmacist to do so.
7. Morphine orodispersible tablets (Actimorph) have been classified as **GREY**. For exceptional use where risk assessment indicates.
   - risk of harm to self or through confusion
   - chronic pain and at risk of intentional overdose (e.g. depression, EUPD)
   - pain/palliative care and at risk of unintentional overdose (dementia, Alzheimer's)
   - additional patient factors e.g. poor manual dexterity
8. Morphine 100mcg/ml oral solution and Morphine 500mcg/ml oral solution are **RED** For Neonatal abstinence syndrome (NAS).
9. Diamorphine injection was previously a first line analgesia in palliative care. However, due to long-term and ongoing supply issue with 5 & 10mg strength commonly used in primary care and associated increased cost, morphine injection is now recommended as first line. See local end of life pathway.
10. For a guide to equivalent doses of opioids see the table in Derbyshire End of Life - Symptom Management

Fentanyl

1. MHRA (October 2018) warns of the risk of serious and fatal overdose of fentanyl patches due to dosing errors, accidental exposure (particularly in children), and exposure of the patch to heat.
   Advice for healthcare professionals:
   Always fully inform patients and their caregivers about directions for safe use for fentanyl patches, including the importance of:
   - not exceeding the prescribed dose
   - following the correct frequency of patch application, avoiding touching the adhesive side of patches, and washing hands after application
   - not cutting patches and avoiding exposure of patches to heat including via hot water (bath, shower)
   - ensuring old patches are removed before applying a new one
   - following instructions for safe storage and properly disposing of used patches or those which are not needed

   Remind patients (or caregivers) to:
   - Follow the correct frequency of patch application, avoiding touching the adhesive side of patches, and washing hands after application. Remove old patches before applying a new one.
   - Avoiding exposure of patches to heat including via hot water (bath, shower)
   - Follow instructions for safe storage and properly disposing of used patches or those which are not needed. After use, patches should be folded so that the adhesive side of the patch adheres to itself and then placed back into the original sachet.
   - Be aware of the signs and symptoms of fentanyl overdose (e.g., difficulty/ shallow breathing; tiredness; extreme sleepiness/ sedation; feeling faint, dizzy or confused) and seek medical attention immediately (by dialling 999 and requesting an ambulance) if overdose is suspected.
2. Patches should only be considered for patients who are on a stable dose of an opioid and who are unable to swallow/ comply with oral medication. It should not be prescribed for opioid naïve patients due to considerable risk of respiratory depression. (MHRA September 2020)
3. Cutting fentanyl patches is for exceptional circumstances and on advice of a palliative care consultant only, following individualised treatment plan. e.g. for a starting dose where dose required is smaller than available whole patch. For accuracy the matrix patch (e.g. Opiodur, Fencino, Matrifen, Mezolar) should be cut diagonally; the other half should be disposed of, in the correct manner as for a controlled drug. N.B. cutting a fentanyl matrix patch renders the use of the drug as “off licence”.
4. In patients who experience serious adverse events, remove patches immediately and monitor for up to 24 hours after patch removal.
5. Maximum titrated dose for fentanyl patches should not exceed >50microg/hour changed every three days. (12 microg per hour fentanyl patch equates to daily doses of oral morphine of up to 45mg a day) Seek specialist advice if increased doing is required.
6. The CQC states that suitable systems should be in place to ensure the safe and effective use of transdermal fentanyl patches. This should include ongoing education of all staff involved in prescribing, dispensing, administering and disposing of transdermal fentanyl patches.
7. All non-transdermal preparations (i.e., lozenges, tablets, buccal film and sublingual tablets) are classified as **GREY** after palliative care specialist initiation (to allow access in primary care if needed). Prescribe by brand to avoid confusion. These preparations require specialist initiation and titration. **Do Not Prescribe (DNP)** for all non-transdermal preparations initiated outside palliative care.

Buprenorphine

1. Buprenorphine patches are classified as **GREY** - the patches should be prescribed by brand as the frequency to be applied may vary between brands.
2. Buprenorphine patches at lower doses are broadly as effective as codeine or tramadol but much more expensive.
3. The patches are unsuitable in acute or unstable pain due to the need for slow titration of doses; it may take up to 72 hours to achieve a stable blood level after a change in dose.
4. The preferred cost-effective brands for low dose (7 day) patch are Reletrans and Sevodyne.
5. Higher strength patches are also available, but the bioavailability and application varies between brands. Different brands are not interchangeable. Check individual SPC carefully.
6. The preferred cost-effective high strength brand (replace after 96 hours) is Relevtec.

### 4.7.3 Neuropathic pain

See local neuropathic pain guideline

### 4.7.4 Antimigraine drugs

#### 4.7.4.1 Treatment of acute migraine

For treatments of minor short-term conditions such as infrequent migraine patients are encouraged to self-care. Mild infrequent migraines can be adequately treated with over-the-counter analgesics and ~~a number of~~ combination medicines (containing both analgesics and anti-emetics). Below recommendations are based on SIGN 155 Pharmacological management of migraine (Feb 2018, updated March 23).

| | |
|---|---|
| **Aspirin** dispersible tabs 900mg | |
| **Ibuprofen** tabs 400mg | *increase to 600mg if ineffective* |
| **Paracetamol** tabs 1g | *in pregnancy or if unable to take other acute therapies* |
| **Sumatriptan** tabs 50mg, 100mg | *1st line triptan* |

1. Consider metoclopramide 10mg or prochlorperazine 10mg, especially for patients presenting with migraine-associated symptoms of nausea or vomiting. (SIGN155)
2. Patients should be warned about the risk of developing medication-overuse headache when starting acute treatment. see CKS headache- medication overuse.
3. NICE CG150 suggests that riboflavin at a dose of 400mg daily may be effective in reducing migraine frequency and intensity for some patients. This recommendation refers to self-purchase only as there is no licensed riboflavin product available in the UK, nor any cost-effectiveness data to justify its use on NHS prescription.
4. Triptan:
   - Should not be taken by people who have: Uncontrolled or severe hypertension; Cardiovascular disease or are at high risk of cardiovascular disease; Coronary vasospasm (including Prinzmetal's angina).
   - Where triptans are indicated for acute migraine NICE CG150 recommends the use of combination therapy with a triptan and an NSAID, or a triptan and paracetamol, for first-line treatment of acute migraine with or without aura.
   - Consider orodispersible zolmitriptan in patients who cannot manage tablets.
   - Frovatriptan has a substantially longer half-life (26 hours) than all other triptans, but this does not appear to translate into markedly lower relapse rates.
   - If vomiting restricts oral treatment, consider a non-oral formulation (such as sumatriptan nasal spray or subcutaneous sumatriptan. (SIGN155)
   - All triptans except intranasal sumatriptan are unlicensed for use in children under 18. 5HT1 receptor agonists for children (aged 12-17) should be referred and initiated by a specialist. Sumatriptan and zolmitriptan oral formulations are treatment options (see BNF for children).
5. Anti-CGRP agents rimegepant and atogepant are **RED** not suitable for primary care prescribing.

#### 4.7.4.2 Prophylaxis of migraine

| | |
|---|---|
| **Propranolol** 80-240mg daily | 1st line |
| **Amitriptyline** 25-150mg daily | 2nd line |
| **Topiramate** 50-100mg daily | 2nd line ***SEE BELOW WARNING ON PREGNANCY*** |

1. For patients with migraine, maintaining a regular routine is important, including:
   - Encourage regular meals, adequate hydration with water, sleep and exercise
   - Avoid specific triggers if known
   - Consider activities that encourage relaxation such as mindfulness, yoga or meditation.
2. Consider prophylaxis if migraine is disabling and reducing quality of life, e.g., frequent attacks (>1 per week on average) or prolonged severe attacks. Start at low dose and gradually increase according to efficacy and tolerability.
3. If the patient responds well to prophylactic treatment a trial of gradual drug withdrawal should be considered after six months to one year.
4. Good response is a 50% reduction in severity and frequency of attacks; treatment failure is a lack of response to the highest tolerated dose used for 3 months.
5. SIGN 155: candesartan (16 mg daily) can be considered as a prophylactic treatment for patients with episodic or chronic migraine.
6. Topiramate
   - Advise women and girls of childbearing potential that topiramate is associated with a risk of foetal malformations and can impair the effectiveness of hormonal contraceptives. (NICE CG150) Pregnancy testing should be performed before initiating, and a highly effective contraceptive

method advised. For advice on interactions between hormonal contraception and other drugs see FSRH guidance.

- MHRA June 24: Topiramate is now contraindicated in pregnancy and in women of childbearing potential unless the conditions of a Pregnancy Prevention Programme are fulfilled. This follows a review by the MHRA which concluded that the use of topiramate during pregnancy is associated with significant harm to the unborn child. Harms included a higher risk of congenital malformation, low birth weight and a potential increased risk of intellectual disability, autistic spectrum disorder and attention deficit hyperactivity disorder in children of mothers taking topiramate during pregnancy.
- Prescribe tablets as capsules are more expensive

7. EMA March 2018 recommends a ban on the use of valproate-containing medicines for migraine or bipolar disorder during pregnancy, and a ban on treating epilepsy during pregnancy unless there is no other effective treatment available. Valproate-containing medicines must not be used in any woman or girl able to have children unless the conditions of a new pregnancy prevention programme are met. **See section 4.8.1 for more details**.

8. Metoprolol at a dose of 100mg-200mg daily in divided doses is a suitable licensed alternative if propranolol cannot be tolerated; Nortriptyline is 2nd line option (less cost effective) only to be used if amitriptyline is effective but patient unable to tolerate side effects (see JUCD Adult Headache Primary Care Pathway at the bottom of the CNS Chapter page).
9. Verapamil may be considered for prophylactic treatment during a bout of **cluster headache**. If unfamiliar with its use for cluster headache, seek specialist advice before starting verapamil, including advice on electrocardiogram monitoring. (NICE CG150)

### 4.8.1 Control of epilepsy

Antiepileptics are also referred to as antiseizure medications (NICE NG217).
The following are classified as **GREEN** after specialist initiation

| | |
|---|---|
| **Clonazepam** | **Oxcarbazepine** |
| **Carbamazepine** | **Phenobarbital and other barbiturates** |
| **Ethosuximide** | **Phenytoin** |
| **Gabapentin** | **Pregabalin** |
| **Lacosamide** | **Sodium Valproate** |
| **Lamotrigine** | **Topiramate** |
| **Levetiracetam** | **Zonisamide** |

The following are classified as **RED** for those patients referred to and /or under the care of a Derbyshire based specialist/Trust. JAPC advises that request for these drugs from tertiary centres should be in line with the host area prescribing committee's decision (see neighbouring area prescribing formularies).

| | |
|---|---|
| Eslicarbazepine | Perampanel |
| Stiripentol | Rufinamide |
| Vigabatrin* | Tiagabine |
| | Cenobamate (NICE TA753) |

*Vigabatrin is also classified as **AMBER**; shared care with Derby Hospitals NHS Foundation Trust ONLY for treating epilepsy in children.

MHRA 2013 recommends that antiepileptic medications are divided into three risk-based categories.
MHRA 2017 In addition to the 3 risk-based categories, patient-related factors should be considered when deciding whether it is necessary to maintain continuity of supply for a specific product.

| Category | **Category 1:** prescribers are advised that patients receiving treatment for epilepsy are maintained on the same manufacturer | **Category 2:** continuity of manufacturer is based on clinical judgement taking into account factors such as seizure frequency and treatment history | **Category 3:** it is usually unnecessary to ensure a specific manufacturer |
|---|---|---|---|
| Name of medicine | carbamazepine<br>phenytoin<br>phenobarbital<br>primidone | clobazam<br>clonazepam<br>eslicarbazepine<br>lamotrigine<br>oxcarbazepine<br>perampanel<br>rufinamide<br>topiramate<br>valproate<br>zonisamide | ethosuximide<br>gabapentin<br>lacosamide<br>levetiracetam<br>briveracetam<br>pregabalin<br>tiagabine<br>vigabatrin |

1. Antiepileptic drugs in pregnancy- a review of the risks of major congenital malformations and of adverse neurodevelopmental outcomes for antiepileptic drugs by the Commission on Human Medicines has confirmed that lamotrigine (Lamictal) and levetiracetam (Keppra) are the safer of the medicines reviewed during pregnancy. MHRA January 2021
   - Women using antiepileptic drugs who are planning to become pregnant should be offered folic acid 5mg daily before any possibility of pregnancy.
   - Urgently refer women who are planning to become pregnant for specialist advice on their antiepileptic treatment.
   - These are usually initiated by specialist. GPs using antiepileptic drugs for other indications must carefully consider the risk and benefit
2. All new antiseizure medication will be considered **RED** until formal classification at JAPC.
3. Be aware that long-term treatment with some antiseizure medications (such as carbamazepine, phenytoin, primidone and sodium valproate) is associated with decreased bone mineral density and increased risk of osteomalacia. Follow the MHRA safety advice on antiepileptics: adverse effects on bone (MHRA Dec 2014) and consider vitamin D and calcium supplementation for people at risk. (NICE NG217)
4. Be aware that oestrogen-containing hormonal contraceptives and hormone replacement therapy can impair the effectiveness of lamotrigine. (NICE NG217)
5. Valproate
   - NPSA November 2023; MHRA January 2024 Valproate (Belvo, Convulex, Depakote, Dyzantil, Epilim, Epilim Chrono or Chronosphere, Episenta, Epival, and Syonell▼): new safety and educational materials to support regulatory measures in men and women under 55 years of age.
     - valproate must not be started in new patients (male or female) younger than 55 years, unless two specialists independently consider and document that there is no other effective or tolerated treatment, or there are compelling reasons that the reproductive risks do not apply. For the majority of patients, other effective treatment options are available.
     - at their next annual specialist review, women of childbearing potential and girls receiving valproate should be reviewed using the revised valproate Annual Risk Acknowledgement Form. A second specialist signature will be needed if the patient is to continue on valproate, however subsequent annual reviews will only require one specialist.
     - general practice and pharmacy teams should continue to prescribe and dispense valproate and if required offer patients a referral to a specialist to discuss their treatment options. Valproate should be dispensed in the manufacturer's original full pack
   - MHRA February 2016- children exposed to valproate in utero are at high risk of developmental disorders and congenital malformations. A guidance/ toolkit (MHRA 2018) to help understanding of the risks of valproate and pregnancy has been launched to ensure female patients are better informed about the risks of taking valproate medicines during pregnancy. See also MHRA Dec 2022, MHRA 2021, MHRA 2020, MHRA January 2015.
   - EMA March 2018 recommends a ban on the use of valproate-containing medicines for migraine or bipolar disorder during pregnancy, and a ban on treating epilepsy during pregnancy unless there is no other effective treatment available. Valproate-containing medicines must not be used in any woman or girl able to have children unless the conditions of a new pregnancy prevention programme are met. These include:
     - an assessment of each patient's potential for becoming pregnant
     - pregnancy tests before starting and during treatment as needed
     - counselling about the risks of valproate treatment and the need for effective contraception throughout treatment
     - a review of ongoing treatment by a specialist at least annually
     - introduction of a new risk acknowledgement form that patients and prescribers will go through at each such annual review to confirm that appropriate advice has been given and understood.
6. Topiramate
   - MHRA June 24 MHRA have updated advice: Topiramate is now contraindicated in pregnancy and in women of childbearing potential unless the conditions of a Pregnancy Prevention Programme are fulfilled. This follows a review by the MHRA which concluded that the use of topiramate during pregnancy is associated with significant harm to the unborn child. Harms included a higher risk of congenital malformation, low birth weight and a potential increased risk of intellectual disability, autistic spectrum disorder and attention deficit hyperactivity disorder in children of mothers taking topiramate during pregnancy.
   - Prescribe tablets as capsules are more expensive.

7. Phenytoin
    - Usually initiated with a loading dose. The use of loading doses of medicines can be complex and error prone. Incorrect use of loading doses or subsequent maintenance regimens may lead to severe harm or death.
    - Phenytoin tablets although listed as generic medicines have significantly increased in price.
    - Be aware that in people of Han Chinese or Thai family background, phenytoin is associated with an increased risk of serious skin reactions. (NICE NG217)
8. Be aware that carbamazepine and potentially medicines with a similar chemical structure (such as oxcarbazepine and eslicarbazepine acetate) are associated with an increased risk of serious skin reactions in people of Han Chinese, Thai, European or Japanese family background. (NICE NG217)
9. Gabapentin has been associated with a rare risk of severe respiratory depression even without concomitant opioid medicines. See MHRA October 2017. Prescribe gabapentin as capsules - tablets are much more expensive.
10. Pregabalin
    - MHRA February 2021. Pregabalin has been associated with infrequent reports of severe respiratory depression, including some cases without the presence of concomitant opioid medicines. Patients with compromised respiratory function, respiratory or neurological disease, renal impairment; those using concomitant CNS depressants; and people older than 65 years might be at higher risk of experiencing these events and adjustments in dose or dosing regimen may be necessary. See
    - MHRA April 2022) Pregabalin (Lyrica): pregabalin may slightly increase the risk of major congenital malformations if used in pregnancy. Patients should continue to use effective contraception during treatment and avoid use in pregnancy unless clearly necessary (.
11. Brivaracetam is **GREY** after consultant/specialist initiation and stabilisation of three months in patients that have responded to levetiracetam but unable to tolerate the adverse effects

### 4.8.2 Drugs used in status epilepticus

**Midazolam buccal** (**Buccolam)** pre-filled syringe 2.5mg/0.5ml, 5mg/1ml, 7.5mg/1.5ml, 10mg/2ml

*Follow consultant advice* (**GREEN** after consultant/specialist recommendation). See local guideline- Midazolam- management of convulsive seizures in the community.

1. Derbyshire has moved to one preferred buccal midazolam product (Buccolam), for use in both adults (off-licence use) and children (licensed use).
2. Epistatus (10mg/1ml) is classified as **Grey**, when initiated by out-of-area providers.
    - Existing patients on Epistatus should be reviewed by the specialist and switched to the recommended Buccolam preparation at their next review and the patients care plan should be updated accordingly. Do not stop the Epistatus abruptly, without the patient receiving training for the Buccolam preparation. In line with NICE guidance diazepam rectal tubes 2.5, 5, 10mg are no longer recommended first line for seizure control.
    - The relaxation for Epistatus traffic lights is due to JAPC recognising that it may not be practical due to formulary differences to refer to a specialist outside of Derbyshire for a patient already initiated on Epistatus. Under these circumstances it will be at the discretion of the prescribing clinician to switch to Buccolam with the patient and/or carer training and updated care plans, or to continue prescribing Epistatus.

## 4.9 Drugs used in Parkinsonism and related disorders

*Follow consultant advice. See NICE NG71 Parkinson's disease in adults*

1. Ipinnia XL is the preferred cost-effective brand for ropinirole.
2. Pramipexole MR preparation is 2nd line only (Pipexus is a cost-effective brand)
3. Stanek and Sastravi are cost-effective choices of carbidopa/entacapone/levodopa combination

## 4.10 Drugs used in substance dependence

### 4.10.1 Alcohol dependence

The following are classified as **AMBER** see shared care guidelines

**Acamprosate** (For patients seen by/referred to the Derbyshire Recovery partnership)
**Disulfiram** (For patients seen by/referred to the Derbyshire Recovery partnership)
**Naltrexone** (For patients within services commissioned by appropriate body)

1. These drugs should only be prescribed as part of a specialist service
2. For guidance on vitamin supplementation in alcohol misuse see here

### 4.10.2 Nicotine dependence

**Nicotine replacement products** (see nicotine replacement therapy formulary)
**Bupropion** tabs 150mg
**Varenicline** tabs 500mcg, 1mg
**Cytisinicline** tabs 1.5mg

1. To be prescribed in conjunction with specialist smoking cessation support.
2. Varenicline and cytsinicline (Cytisine) are **GREEN and should** be prescribed in general practice following stop smoking service request only.
3. Bupropion (CSM advice)
   - It is contra-indicated in patients with a history of seizures or of eating disorders, a CNS tumour, or who are experiencing acute symptoms of alcohol or benzodiazepine withdrawal. It should not be prescribed to patients with other risk factors for seizures unless the potential benefit of smoking cessation clearly outweighs the risk.
   - Factors that increase the risk of seizures include concomitant administration of drugs that can lower the seizure threshold, alcohol abuse, history of head trauma, diabetes, and use of stimulants and anorectics.
4. MHRA Nov 2020: Bupropion: risk of serotonin syndrome with use with other serotonergic drugs
   - if concomitant prescribing with other serotonergic drugs is clinically warranted: do not exceed the recommended dose; remind patients of the milder symptoms of serotonin syndrome at initiation of treatment and at any change of dose and the importance of seeking medical advice if they occur
   - if serotonin syndrome is suspected, either decrease the dose of bupropion or withdraw therapy depending on the severity of the symptoms

### 4.10.3 Opioid dependence

The following are classified as **AMBER** via Local Enhanced Service (LES) and GP with a special interest (GPSI). See shared care guidelines
**Buprenorphine**
**Methadone**

### 4.11 Drugs for dementia (see local guidance)

These drugs are classified as **GREEN** after consultant/specialist initiation and stabilisation for 3 months

**Donepezil** tabs 5mg, 10mg
**Memantine** tab 10mg, 20mg
**Rivastigmine** caps 1.5mg, 3mg
**Galantamine** XL caps 8mg, 16mg, 24mg

*1st line*

*Alzest is the preferred brand for patch*

Galzemic *XL is the preferred brand for MR caps at 8mg and 16mg strengths. Luventa XL caps are preferred brand for 24mg strength*

1. Donepezil orodispersible is significantly more expensive than the standard tablet formulation.
2. Memantine is **GREEN** for patients with behavioural and psychological symptoms in dementia (BPSD), and as add on to an acetylcholinesterase inhibitor in patients with established Alzheimer's disease. See local dementia guidelines.
3. Rivastigmine 4.5mg and 6mg strength are significantly more expensive- use combination of lower strength instead.
4. **Aspirin and vascular dementia** - NICE NG97 recommendations- Do NOT offer aspirin/ statin to slow the progress of Alzheimer's disease, except as part of a randomised controlled trial. Low-dose aspirin can improve the prognosis of heart disease and stroke, possibly by reducing clot formation within the blood vessels and helping to maintain or improve blood flow to the heart and brain. Many doctors assume that aspirin will also provide some benefit for people with vascular dementia. A Cochrane review, 2012, shows that there is no evidence to suggest that aspirin is useful for people with vascular dementia. It is possible that vascular dementia and stroke are caused by different pathological

processes. Practitioners need to be aware of the risks of aspirin, such as haemorrhages, which can be fatal.