4.1 Hynotics and anxiolytics

4.1.1 Hypnotics

Choice	Drug	Dosage
1st choice	**Non-drug treatment**	
2nd choices	Zolpidem tablets 5mg, 10mg Or Zopiclone tablets 3.75mg, 7.5mg Or Temazepam tablets 10mg, 20mg	10mg at bedtime; elderly (or debilitated) 5mg Dose: 7.5mg at bedtime; elderly initially 3.75mg at bedtime increased if necessary Note: In patients with chronic pulmonary insufficiency an initial dose of 3.75mg is recommended Dose: Usually 10-20mg at bedtime

Prescribing Notes

- Non-drug treatments recommended as first-line interventions include sleep hygiene and stimulus control advice. A range of resources are available on the Patient Zone and the Choice and Medication website
- Hypnotics should be used in **short courses only** (review after 1 week) when insomnia is severe, disabling or subjecting the individual to extreme distress
- Hypnotics can affect ability to drive or operate machinery; they also increase the effects of alcohol. Moreover the hangover effects of a night dose may impair driving on the following day
- Existing patients receiving a hypnotic should be reviewed and offered the chance to stop or reduce. See 4.10c and resources on

the primary care intranet

- **Patients should be advised about the benefits and harms of hypnotics**. For every 13 people aged 60 years or over, treated with a hypnotic:
  - About one person will sleep better. This means that, on average, they will get an extra 25 minutes sleep each night and will wake up once less often every two nights. The hypnotic will have no benefit for the other 12 people
  - About two people will have adverse effects such as drowsiness, fatigue, headaches, nightmares, nausea or GI disturbances.
- Please note **high cost of benzodiazepine liquids** e.g. nitrazepam suspension costs £114 per 70ml (Nov 19)
- Promethazine is sometimes used (prescribed or purchased OTC) as a perceived 'safer' alternative to benzodiazepines in the short-term management of insomnia. It can cause severe anticholinergic effects, particularly in elderly patients and when taking other anticholinergic drugs in combination. Refer to 'Anticholinergic Burden' resources. Prescribers should be aware that use may lead to hangover drowsiness the following day and its sedative effects may diminish after a few days of continued treatment

Cautions

- Clinicians should be mindful of the risks associated with prescribing benzodiazepines and impact of co-prescribed medicines and co-morbidities. The risk of diversion and misuse of prescribing medicines along with illicit use should also be considered
- Withdrawal of hypnotic and anxiolytic drugs should be gradual because abrupt withdrawal may produce confusion, toxic psychosis, convulsions, or a condition resembling delirium tremens
- Hypnotics and anxiolytics should be avoided in older patients if possible. Older patients can become ataxic, confused and are at increased risk of falls and fractures
- All benzodiazepines are capable of being fatal in overdose but are particularly dangerous if combined with other CNS depressants

such as alcohol. Care should be taken when prescribing for patients at high risk of overdose
- Avoid the use of nitrazepam in the elderly as it has a prolonged action and may give rise to residual effects on the following day; repeated doses tend to accumulate
- The use of benzodiazepines in dementia is associated with increased mortality and their use should be a last resort. Insomnia is common in patients with dementia – zolpidem may be a preferred option

4.1.2 Anxiolytics

4.1.2.1 Acute anxiety state

Choice	Drug	Dosage
1st choice	**Non-drug treatment**	
2nd choice	Diazepam tablets 2mg, 5mg	Dose: 2mg three times daily increased if necessary to 15-20mg daily in divided doses; elderly (or debilitated) half adult dose

Prescribing Notes

- The most appropriate first-line treatments for anxiety are self-help strategies, counselling and CBT. See resources e.g. 'Good relaxation guide' on the Patient Zone and the Choice and Medication website
- Benzodiazepines are indicated for the short-term relief (**2-4 weeks only**) of anxiety that is severe, disabling or subjecting the individual to unacceptable distress. The use of benzodiazepines to treat short-term 'mild' anxiety is inappropriate and unsuitable
- Benzodiazepine anxiolytics should not be used as sole treatment for chronic anxiety, and they are not appropriate for treating depression or chronic psychosis

- Treatment should be limited to the lowest possible dose for the shortest possible time
- Diazepam has a medium duration of action and rapid onset. It is the recommended daytime anxiolytic (and issued as pre-medication before surgery and other procedures. See BNF)
- New patients should not be put on a repeat prescription system and existing patients receiving an anxiolytic should be reviewed and offered the chance to stop. See 4.10c and resources on the primary care intranet
- The beta-blocker propranolol may be useful for somatic symptoms of anxiety such as tachycardia, sweating and tremor in performance related anxiety. Please refer to BNF for doses and contraindications etc
- Buspirone has little efficacy as an acute anxiolytic as clinical effect typically takes 2-4 weeks to achieve. However, it is only licensed for short term use, making its place in therapy unclear

Cautions – *Bookmark to box under hypnotics section*

4.1.2.2 Anxiety disorders

Includes generalised anxiety disorder (GAD), panic disorder, social anxiety disorder, obsessive-compulsive disorder (OCD) and post-traumatic stress disorder (PTSD)

Non-pharmacological treatment is the first line intervention in all anxiety disorders

SSRIs are the first line pharmacological drug choice in the management of patients with chronic anxiety disorders. See Section 4.3 (b) – *ADD Link*

Prescribing Notes

- Refer to NICE CG123 Common mental health disorders

- Refer to NICE CG113 Clinical Guideline for Generalised Anxiety Disorder (GAD) and Panic Disorder
- Also refer to NICE CG 159 Social Anxiety Disorders
- Non-pharmacological treatment is the first line intervention in all anxiety disorders
- Treatment options for panic disorder and generalised anxiety disorder include psychological, pharmacological and self-help approaches. Trauma focused psychological therapy is the first line treatment for post-traumatic stress disorder. Choice of treatment in individual cases will usually be determined by patient preference, service availability and the severity of the condition
- Diagnosis and treatment can be difficult. In some cases specialist advice or referral will be necessary
- Benzodiazepines are indicated for the **short term (up to four weeks) relief of severe anxiety***;* long-term use should be avoided
- Treatment with a benzodiazepine in states of anxiety should be limited to the lowest possible dose for the shortest possible time:

Generalised Anxiety Disorder - *ADD Link to 4.3 .2.1)*

- Do not offer a benzodiazepine for the treatment of GAD in primary or secondary care except as a short-term measure during crises
- GAD should be distinguished from acute anxiety state

- Benzodiazepines are associated with a risk of dependence, sedation, accidents and withdrawal symptoms. Antidepressants are preferred

Panic Disorder – *ADD Link to 4.3.2.2*
- Benzodiazepines should not be used to treat panic disorder

Post-Traumatic Stress Disorder – *ADD Link to 4.3..2.3*
- Benzodiazepines are probably ineffective

Obsessive Compulsive Disorder – *ADD Linkto 4.3 .2.4*
- Benzodiazepines are only useful in reducing associated anxiety; only careful short-term use is supported by NICE

4.1.3 Barbiturates

Prescribing Notes

- Barbiturates (controlled drugs) should only be prescribed to patients already taking them, who have severe intractable insomnia, when attempts to discontinue treatment have been unsuccessful. **New patients should not be started on barbiturates**
- Barbiturates are used in the treatment of epilepsy and anaesthesia (see BNF)

4.2 Drugs used in psychoses and related disorders

General notes

- Refer to NICE CG 178 for the treatment and management of psychosis and schizophrenia in adults
- Refer to NICE CG 120 for the assessment and management of psychosis with coexisting substance misuse

4.2.1 Antipsychotic drugs

Prescribing Notes

Antipsychotics for the treatment of schizophrenia should be initiated by a psychiatrist. Contact appropriate psychiatric services

- Do not start antipsychotic medication for a first presentation of sustained psychotic symptoms in primary care unless it is done in consultation with a consultant psychiatrist
- Modified release(MR) preparations of quetiapine should be reserved for patients with compliance issues
- Some patients may be suitable for switching to quetiapine immediate release once stabilised on quetiapine MR
- Where quetiapine MR is necessary, Biquelle XL® is the recommended cost-effective choice (**prescribe by brand**)
- Clozapine is the drug of choice for treatment resistance. It requires monitoring and is a red list drug that should not be prescribed in primary care. However, it is important that clinically important medication such as clozapine is added to the patient's record. Method varies depending on GP clinical system e.g. add the drug as 'issued but not printed' or enter drug source as 'issued outside the practice or secondary care'. See Specialist Medicines Supplement for further information

- Clozapine and olanzapine are metabolised principally via CYP1A2 therefore clearance is increased in smokers. People who stop or reduce their smoking may require a dose reduction. Refer to SPS website or further details.
- For patients taking clozapine who are intending to stop smoking, specialist advice should be sought to ensure the patient's safety
- GPs and other primary healthcare professionals should monitor the physical health of people with psychosis or schizophrenia when responsibility for monitoring is transferred from secondary care, and then at least annually.

Maintenance treatment

- Patients should remain on the antipsychotic which controlled their symptoms unless symptoms return or side-effects are intolerable; the dose should be monitored and reviewed regularly with specialist advice and over time might be reduced
- Specialist advice should be sought before discontinuing antipsychotics due to the risk of relapse. Current evidence states that patients presenting with first episode of acute functional psychosis should ideally remain on antipsychotics for a minimum of one year

4.2.1.1 Management of agitation and aggression

- Management depends on the underlying cause and consideration should always be given to physical illness or an acute confusional state.
- For patients with BPSD see (*add link to 4.11.1*)
- Arrange for urgent assessment by Mental Health Services. Consider use of the Mental Health Order if appropriate
- Refer to NICE NG10 Violence and aggression
- **NOTE:** Whilst the NICE Guidance does cover violence and aggression in primary care settings, the focus is on avoiding violence, prevention, de-escalation and breakaway techniques. In situations of

high risk, staff should remove themselves from the situation and, if there is immediate risk to life, contact the police

4.2.3 Mood stabilising drugs

4.2.3.1 Treatment of the acute phase of mania

Prescribing Notes

- Refer all people in a hypomanic or manic episode for specialist mental health assessment. Contact a mental health specialist for advice on initial management while the person is waiting to be seen in secondary care. An antipsychotic may sometimes be recommended in the interim
- Primary treatment for hypomania or mania is usually with an antipsychotic agent. See NICE CG 185 Bipolar disorder http://www.nice.org.uk/guidance/cg185
- If the person is already taking lithium, check plasma lithium levels to ensure they are within therapeutic range and to check concordance
- Consider stopping antidepressant (on specialist advice)
- Modified release preparations of quetiapine should be reserved for patients with compliance issues

4.2.3.2 Maintenance treatment of bipolar disorder with mood stabilisers

Prescribing Notes

- Therapy should be initiated by a psychiatrist and only following medical examination and careful assessment of risk/benefit
- See NICE CG 185 Bipolar disorder http://www.nice.org.uk/guidance/cg185
- The Lithium Shared Care Guideline and Lithium Care Pathway should be consulted for advice on appropriate patient management including monitoring requirements and responsibilities

Women of childbearing potential

- Women receiving mood stabilisers must be warned to obtain

pre-conception advice if they plan to become pregnant; the risk of relapse following withdrawal of mood stabilisers must be balanced against their established teratogenic potential which should be fully discussed with the patient. Psychiatric advice should be sought regarding the most appropriate management of individual patients. Advice is normally weighted towards stopping mood stabilisers and maintaining the patient on an antipsychotic if necessary

- Valproate medicines (Epilim▼, Depakote ▼) are contraindicated in women and girls of childbearing potential unless conditions of Pregnancy Prevention Programme are met. For further information see MHRA. All patients should be under the management of a specialist and have an annual review

4.3 Antidepressant drugs

4.3.1For mild, moderate and severe depression

Please note antidepressants are not routinely recommended for the initial treatment of MILD depression because the risk-benefit ratio is poor

Non pharmacological treatment is a preferable 1st line option for most people

Choice	Drug	Dosage
1st choices	Citalopram tablets 10mg, 20mg, 40mg	Dose: Citalopram tablets: depressive illness, 20mg once daily, increased if necessary in steps of 20mg daily at intervals of 3-4 weeks; max 40mg daily (**Elderly** over 65 years, 10–20mg once daily, max 20mg daily)
	Or	
	Fluoxetine capsules 20mg	Dose: Major depression, 20mg once daily increased after 3-4 weeks if necessary, and at appropriate intervals thereafter; max 60mg once daily (**Elderly** usual max 40mg once daily but 60mg can be used)
	Or	
	Sertraline tablets 50mg, 100mg	Dose: Depressive illness, initially 50mg daily, increased if necessary by increments of 50mg at intervals of at least 1 week to max 200mg; usual maintenance dose 50mg daily

Prescribing Notes

- Refer to NICE CG90 Depression in adults
- Antidepressants are not routinely recommended for the initial treatment of mild depression because the risk-benefit ratio is

poor. Antidepressants can be considered for people with
    - a history of moderate to severe depression
    - people with subthreshold depressive symptoms that have persisted for a long period (typically at least 2 years)
    - mild depression that is complicating the care of a chronic physical health problem
- If previous treatment with any antidepressant has been successful it should be considered again for treatment of recurrence
- SSRIs are better tolerated than tricyclic antidepressants (TCAs). They are first choice because of reduced toxicity in overdose and, for most patients, a better adverse effect profile
- If a TCA is required:
    - Trimipramine should not be routinely prescribed due to availability of more cost-effective TCAs (trimipramine 25mg TDS costs over £600, DT Nov 19)
    - Dosulepin is not recommended because it has a high chance of causing heart problems, is toxic in overdose and there are other anti-depressants available which are safer to use. **Dosulepin should not be initiated in primary care for any indication and existing patients should be reviewed for suitability for switching to a safer agent.** This may require consultation with a specialist. Dosulepin should not be stopped abruptly unless serious side effects have occurred. Refer to Medicines Management March 2018 newsletter for further information
- Antidepressants all have a delayed onset of action and substantial effects may not be achieved for at least 2-4 weeks
- Advise people to be vigilant for worsening depressive symptoms and suicidal ideas, particularly when starting and changing medications
- Treatment for a first depressive episode should normally be continued, at the dose that brought about remission, for at least 6 months after response (and often up to one year)
- After recurrent or resistant depressive episodes, consider continuing treatment for up to 2 years. Some patients may

require life-long treatment at therapeutic doses

- For doses of fluoxetine 60mg it is more cost-effective to prescribe this dose as 3 x 20mg capsules
- Sertraline is the SSRI of choice in Coronary Heart Disease (CHD); more data exists for sertraline in a population with pre-existing heart disease than the other SSRIs. It has a lower propensity for interactions
- Liquid formulations should be reserved for patients who are unable to swallow tablets. 'Specials' should be avoided and licensed medicines used where possible, e.g. it may be appropriate to switch to a different medicine (fluoxetine liquid may be a suitable alternative to sertraline tablets). Refer to resources on Specials
- Although there is evidence that St John's Wort may be of benefit in mild or moderate depression, practitioners should not prescribe or advise its use by people with depression because of uncertainty about appropriate doses, persistence of effect, variation in the nature of preparations and potential serious interactions with other drugs (including oral contraceptives, anticoagulants and anticonvulsants)

Cautions

- The elderly are generally more sensitive to all side-effects of antidepressants
- All antidepressants may be associated with a discontinuation syndrome and, if taken continuously for 6 weeks or longer, should be withdrawn gradually unless a serious adverse effect has occurred
- Due to the risk of gastrointestinal bleeding, SSRIs should be avoided if possible, or used with caution, in patients aged over 80 years, those with prior upper gastrointestinal bleeding, or in those also taking aspirin or another NSAID
- SSRIs can cause sleeplessness and GI/anorexic problems in older patients. Mirtazapine has often a better profile due to sleep effects

and increased appetite. This can avoid the need for night sedation

- Hyponatraemia (usually in the elderly) has been associated with all types of antidepressants; however it has been reported more frequently with SSRIs. Hyponatraemia should be considered in all patients who develop drowsiness, confusion, or convulsions while taking an antidepressant
- TCAs are cardiotoxic in older people and are contraindicated in patients with dementia
- Caution on concurrent use of amitriptyline (e.g. for neuropathic pain) with other antidepressants. When amitriptyline is co-prescribed with another antidepressant the maximum daily dose of amitriptyline is 25mg
- Dosulepin (dothiepin) and doxepin are not recommended due to their association with ischaemic heart disease, cardiac arrhythmias and fatalities following overdose
- Citalopram and escitalopram are associated with dose-dependent QT interval prolongation and should not be used in those with: congenital long QT syndrome; known pre-existing QT interval prolongation; or in combination with other medicines that prolong the QT interval. See (https://www.gov.uk/drug-safety-update/citalopram-and-escitalopram-qt-interval-prolongation)
- Agomelatine (Valdoxan®) is associated with a dose related risk of hepatotoxicity and liver failure. MHRA Drug Safety Update November 2014 has full details of the advice for healthcare professionals

Comment [e1]: Shared care guideline is in development. Link to SCG when published

4.3.2 Antidepressants for the treatment of anxiety disorders*

*includes generalised anxiety disorder (GAD), panic disorder, social anxiety disorder, obsessive–compulsive disorder (OCD) and post-traumatic stress disorder (PTSD).

For treatment of acute anxiety state, see section 4.1.2.1 – *ADD LINK*

General Notes

- Diagnosis and treatment can be difficult and in some cases

specialist advice or referral will be necessary
- For mild anxiety disorders, consider a period of active monitoring and provide verbal and written information about the condition
- Due to the risk of withdrawal reactions, patients taking paroxetine should not stop the drug suddenly. Cessation of treatment should involve a very gradual downward titration. If intolerable symptoms develop it may be necessary to reinstate the previously prescribed dose and withdraw more gradually
- For doses of fluoxetine 60mg it is more cost-effective to prescribe this dose as 3 x 20mg capsules
- Do not offer St John's Wort or other over-the-counter medications and preparations for anxiety

4.3.2.1 Generalised anxiety disorder (GAD), social anxiety disorder

Choice	Drug	Dosage
1st choice	**Non-pharmacological treatment**	
2nd choice	Sertraline tablets 50mg, 100mg [unlicensed indication]	Dose: Initially 25mg (half a tablet) daily, increased if necessary by increments of 25mg at intervals of at least one week to max 200mg daily

Prescribing Notes

- Refer to NICE CG113 Generalised Anxiety Disorder and Panic Disorder
- GAD should be distinguished from acute anxiety state. Treatment options include psychological, pharmacological and self-help approaches
- NICE state: Do not offer a benzodiazepine for the treatment of GAD in primary or secondary care except as a short term measure during crises
- Refer to NICE GG159 for the management of Social Anxiety

Disorder

4.3.2.2 Panic Disorder

Choice	Drug	Dosage
1st choice	**Non –pharmacological treatment**	
2nd choices	Citalopram tablets 10mg, 20mg, 40mg	Dose: Initially 10mg daily, increased gradually if necessary in steps of 10mg daily, usual dose 20-30mg daily; max 40mg daily (elderly over 65 years, max 20mg daily)
	Or	
	Sertraline tablets 50mg, 100mg	Dose: Initially 25mg (half a tablet) daily, increased after one week to 50mg daily; if response is partial and if drug tolerated, dose increased in steps of 50mg at intervals of at least one week to max 200mg daily

Prescribing Notes

- Refer to NICE CG113 Generalised Anxiety Disorder and Panic Disorder
- Treatment options include psychological, pharmacological and self-help approaches
- In panic disorder, symptoms frequently get worse before they get better after starting a SSRI
- Most patients will require a SSRI for 6–12 months before the gradual discontinuation of treatment

4.3.2.3 Post -Traumatic Stress Disorder

Choice	Drug	Dosage
1st choice	**Non-pharmacological treatment**	
2nd choices	Sertraline 50mg, 100mg tablets	Dose: Initially 25mg daily for 1 week, then increased to 50mg daily, then increased in steps of 50mg at intervals of at least 1 week if required, increase only if response is partial and if drug is tolerated; max 200mg per day
	Or Venlafaxine MR (Vensir® XL) **[unlicensed]**	Dose: Initially 75mg once daily, increased if necessary up to 225mg once daily. Dose to be increased at intervals of at least 2 weeks; maximum 225mg per day

Prescribing notes

- See NICE NG116 Post-traumatic stress disorder
- Trauma focused psychological therapy is the first line treatment for PTSD. Choice of treatment in individual cases will usually be determined by patient preference, service availability and the severity of the condition. Evidence on the pharmacological treatment of PTSD is limited
- Response to SSRIs is usually seen within 8 weeks, but can take up to 12 weeks. Treatment should be continued for at least six

months and probably longer

- Antipsychotics such as risperidone can be considered for patients with disabling symptoms and behaviours that have not responded to other drug or psychological treatments. Antipsychotic treatment should be started and reviewed regularly by a specialist

4.3.2.4 Obsessive compulsive disorder (OCD)

Choice	Drug	Dosage
1st choice	**Non-pharmacological treatment**	
2nd choices	Citalopram tablets 10mg, 20mg, 40mg [unlicensed indication]	Dose: 20mg one daily. If necessary increase the dose gradually up to a maximum of 40mg once a day (20mg in the **elderly** and in those with reduced hepatic function)
	Or	
	Fluoxetine capsules 20mg	Dose: 20mg once daily; if inadequate response after 2 weeks increase gradually to max 60mg once daily (**elderly** usual max 40mg once daily but 60mg can be used)
	Or	
	Sertraline tablets 50mg, 100mg	Dose: Initially 50mg daily, increased if necessary in steps of 50mg at intervals of at least one week; max 200mg daily

Prescribing notes

- Refer to NICE CG 31, Obsessive compulsive disorder (OCD)
- The licensed doses of SSRIs in OCD are generally higher than doses used for the treatment of depression
- Improvement of OCD may not be apparent for 12 weeks. Treatment should be continued for at least 12 months. Long-term maintenance is often necessary.
- Clomipramine and SSRIs have proven efficacy in OCD but clomipramine is associated with more adverse effects

Cautions – *ADD bookmark to cautions box under depression section*

4.4 CNS stimulants and drugs used for attention deficit hyperactivity disorder

4.4.1 Narcolepsy

Choice	Drug	Dosage
1st choice **For information** **Specialist initiation only**	Modafinil tablets 100mg	Dose: Initially 200mg daily either in 2 divided doses morning and at noon or as a single dose in the morning, dose adjusted according to response to 200-400mg daily in 2 divided doses or as a single dose; **elderly** initiate at 100mg daily

Prescribing Notes

- Modafinil is an amber list drug and should be initiated by a specialist
- Supervision should remain the responsibility of hospital staff for the first three months or until objective evidence of effectiveness has been provided
- Dependence with long-term use of modafinil cannot be excluded
- Dexamfetamine sulphate or methylphenidate hydrochloride may be prescribed by specialists when modafinil is ineffective

Comment [e2]: Link to information sheet from red/amber once published

4.4.2 Attention deficit hyperactivity disorder (ADHD) in adults

Choice	Drug	Dosage
1st choice **For information** **Specialist initiation only**	Delmosart ® (methylphenidate) 18mg, 27mg, 36mg, 54mg prolonged-release tablets	Dose: See BNF for dosing [Initiation unlicensed in adults]
2nd choice **For information** **Specialist initiation only**	Methylphenidate standard release tablets 5mg, 10mg, 20mg	Dose: See BNF for dosing [Initiation unlicensed in adults]

Prescribing Notes

- Refer to NICE NG87 ADHD guidance
- Lisdexamfetamine or methylphenidate are the first line pharmacological treatments for adults with ADHD. Refer to NICE for details of other treatment options
- Methylphenidate and lisdexamfetamine are amber list drugs and should only be initiated by a specialist with expertise in ADHD- see Shared Care Guidelines
- Modified-release preparations of methylphenidate should be prescribed by brand. GPs should prescribe the brand of methylphenidate that has been recommended by the specialist. Delmosart® is the recommended cost effective brand of choice (CEC) for those preparations that are bioequivalent to the originator brand Concerta® XL (i.e. for strengths 18mg, 27mg, 36mg and 54mg)

4.5 Drugs used in the treatment of obesity

4.5.1. Anti-obesity drugs acting on the gastrointestinal tract

Choice	Drug	Dosage
1st choice	**Non-pharmacological treatment - diet and lifestyle changes**	
2nd choice	Orlistat capsules 120mg	Dose: 120mg taken immediately before, during, or up to 1 hour after each main meal (max 120mg 3 times daily); max period of treatment 2 years. Omit dose if meal is missed or contains no fat

Prescribing Notes

- Refer to NICE CG189 Obesity: identification, assessment and management of overweight and obesity in children, young people and adults https://www.nice.org.uk/guidance/cg189
- Pharmacological treatment should be considered only after dietary, exercise and behavioural approaches have been started and evaluated
- Drug treatment may be considered in patients as part of an overall treatment plan for managing obesity, who have a BMI ≥30kg/m^2 or BMI ≥28kg/m^2 plus associated risk factors
- Patients should be informed that drug therapy will be discontinued after 3 months if they fail to lose 5% of their initial body weight since starting drug treatment (less strict goals may be appropriate for people with type 2 diabetes). Further courses should only be considered after a suitable period and patients should again demonstrate the ability to lose weight on a suitable diet
- Continue for longer than 12 months (usually for weight maintenance) only after discussing potential benefits and

limitations with the patient

- Common side-effects with orlistat may be limited by dietary compliance (i.e. decreased fat intake)
- Orlistat (60mg and 120mg) has been linked to cases of oxalate nephropathy and pancreatitis. Interactions with levothyroxine and epileptic drugs have also been reported (MHRA, Drug Safety Update February 2010) https://www.gov.uk/drug-safety-update/orlistat-safety-update
- Orlistat is available to buy over the counter (OTC) from pharmacies, under the brand name alli®. It is licensed for those with a BMI >28kg/m^2, and is available as 60mg capsules

Cautions

- Orlistat (60mg and 120mg) has been linked to cases of oxalate nephropathy and pancreatitis. Interactions with levothyroxine and epileptic drugs have also been reported (MHRA, Drug Safety Update February 2010) https://www.gov.uk/drug-safety-update/orlistat-safety-update

4.6 Drugs used in nausea and vertigo

For migraine (see section 4.7.4- *ADD LINK*)

4.6.1 Drugs for the short-term treatment of nausea and vomiting

Choice	Drug	Dosage
1st choice	Prochlorperazine tablets 5mg	Dose: Nausea and vomiting, acute attack, 20mg initially then 10mg after 2 hours; prevention 5-10mg 2-3 times daily
	3mg tablets (buccal) Reserve buccal tablets for active vomiting	1-2 tablets twice daily; tablets are placed high between upper lip and gum and left to dissolve **Short-term use only**
	Or	
	Domperidone tablets 10mg; suspension 5mg/5ml	Dose: 10mg up to 3 times daily; max 30mg daily **Max length of treatment 1 week - see restrictions below** (add bookmark)
	Or	
	Metoclopramide tablets 10mg; oral solution 5mg/5ml; injection 5mg/ml	Dose: Orally, or by intramuscular or intravenous injection, 10mg (5mg in 15-19 year olds under 60kg) three times daily **Max length of treatment 5 days - see restrictions below** *(add bookmark)*

Prescribing Notes

- Metoclopramide is associated with neurological effects such as short-term extrapyramidal disorders and tardive dyskinesia. These side-effects usually occur in the young (especially girls and young women) and the very old; it is best avoided, if possible, in patients under 20 years old
- Metoclopramide should only be prescribed for short-term use (up to 5 days) for prevention of postoperative nausea and vomiting; radiotherapy-induced nausea and vomiting; delayed (but not acute) chemotherapy-induced nausea and vomiting; and symptomatic treatment of nausea and vomiting, including that associated with acute migraine (where it may also be used to improve absorption of oral analgesics). For further information click https://www.gov.uk/drug-safety-update/metoclopramide-risk-of-neurological-adverse-effects
- Long-term metoclopramide and prochlorperazine may cause tardive dyskinesia in the elderly
- Domperidone does not cross the blood brain barrier; it is less likely than metoclopramide and prochlorperazine to cause sedation or dystonic reactions
- Domperidone is associated with a small risk of serious cardiac side effects. Its use is now restricted to the relief of symptoms of nausea and vomiting and the dosage and duration of use have been reduced. Treatment should generally only be given for up to one week. Domperidone is contraindicated in those with underlying cardiac conditions and other risk factors. Risks are higher in people older than 60 years. For further information click https://www.gov.uk/drug-safety-update/domperidone-risks-of-cardiac-side-effects
- Note that cyclizine has potential for abuse

4.6.1.1Motion sickness

Choice	Drug
1st choice	Advise patients that medication can be purchased over-the-counter (OTC)

Prescribing Notes

- Anti-emetics should be given to prevent motion sickness rather than after nausea or vomiting develop
- The most effective drug for the prevention of motion sickness is hyoscine hydrobromide (available OTC). The sedating antihistamines are slightly less effective against motion sickness but are generally better tolerated than hyoscine
- Domperidone, metoclopramide and $5HT_3$ receptor antagonists are ineffective in motion sickness

Nausea and vomiting associated with cytotoxic chemotherapy

See chapter 8 of the BNF

Nausea and vomiting in palliative care

See Palliative Care resources

4.6.2 Drugs for the treatment of labyrinthine vertigo

Choice	Drug	Dosage
1st choice	Cinnarizine tablets 15mg Or Prochlorperazine tablets 5mg; syrup 5mg/ml	Dose: 15-30mg three times daily Dose: 5mg three times daily, gradually increased if required to 30mg daily in divided doses, and reduced after several weeks to 5-10mg daily

Prescribing Notes

- These products are only effective for labyrinthine vertigo
- Prochlorperazine buccal tablets may be a suitable alternative for patients who are vomiting

4.6.3 Treatment of Ménière's disease

- Prochlorperazine or cinnarizine may be used short–term for the acute treatment of Ménière's disease
- Betahistine and thiazide diuretics should be reserved for prophylaxis in patients with a proven diagnosis of Ménière's disease

Caution

- Prochlorperazine should not be prescribed for "dizziness" in older patients due to the risk of drug-induced parkinsonism, postural hypotension and mental confusion
- Prolonged use of cinnarizine in the treatment of labyrinthine vertigo

can cause tremor

- Betahistine use may delay labyrinthine rehabilitation
- Patients prescribed drugs for the treatment of nausea and vertigo should be reviewed regularly and medicines which are not of benefit should be stopped

4.7 Analgesics

For NSAIDs, musculoskeletal and joint pain (including gout), see Chapter 10 – (*ADD LINK*)

For dysmenorrhoea, see Chapter 7 – ADD LINK

4.7.1 General management of acute pain

4.7.1.1Non-opioid and compound analgesics

Choice	Drug	Dosage
1st choice	*Consider* Pain Self-Management	
	Paracetamol tablets 500mg	Dose: 0.5-1g every 4-6 hours; max 4g daily
2nd choice	Consider NSAID	see 10.1.1 (add link)
	Consider addition of codeine 15mg tablets *Prescribe codeine separately from paracetamol to give flexibility*	Dose: 15mg-60mg every 4-6 hours; up to four times daily *Keep dose as low as possible*
Reserve	Co-codamol 8/500 tablets (codeine 8mg with paracetamol 500mg)	Dose: Co-codamol 8/500, 1-2 tablets every 4-6 hours; max 8 tablets daily
	Co-codamol 15/500 tablets (codeine 15mg with paracetamol 500mg)	Dose: Co-codamol 15/500, 1-2 tablets every 4-6 hours; max 8 tablets daily
	Co-codamol 30/500 tablets (codeine 30mg with paracetamol 500mg)	Co-codamol 30/500, 1-2 tablets every 4-6 hours; max 8 tablets daily

Prescribing Notes

- See HSCB implementation support tool for prescribing in acute pain *(add link)*
- Encourage self-care / advice from community pharmacist for minor self-limiting conditions and OTC purchase of simple analgesics as appropriate.
- Before prescribing, ask if the person is taking any OTC medicines and remind them not to 'top up' prescription medicines with pain relievers bought OTC – seek advice from a doctor or pharmacist and see NI Patient Zone resources
- Consider need for non-drug interventions e.g. referral to physiotherapy
- Paracetamol taken regularly appears to be as effective as co-codamol 8/500 with less side-effects
- Management of postoperative pain should follow **hospital acute pain guidelines**
- Codeine is metabolised to morphine to have its analgesic effect e.g. 30mg codeine = 3mg morphine. Codeine is ineffective in approximately 10% of patients who are unable to convert it to morphine. Consider an alternative analgesic in these people
- In acute pain use opioids for **short periods only** (3 days or less is usually enough and over 7 days is rarely needed)
- Inform patients about potential harms and risks of dependence with long term use
- Co-codamol capsules are high cost and should not be prescribed

Cautions

- Some patients may be at increased risk of experiencing toxicity at therapeutic doses of paracetamol, particularly those with a body-weight under 50 kg and those with risk factors for hepatotoxicity. Clinical judgement should be used to adjust the dose of oral and intravenous paracetamol in these patients
- Each effervescent tablet can contain a sodium content of up to 400mg. Persons on a low sodium diet should be aware of this if they wish to take effervescent tablets as a daily intake can exceed 3g sodium per day. Effervescent tablets are significantly more

expensive that tablets / caplet preparations

- Codeine should not be used by breastfeeding mothers because it can pass to the baby through breast milk and potentially cause respiratory depression.
- Before prescribing any opioid, including codeine, be aware that some patients are at higher risk of developing dependence or addiction. Assess risk e.g. previous history of substance misuse, use of concurrent sedatives or alcohol use. For information on 'acute pain management for drug misusers' click here *(add link)*. Acute pain requires full analgesic management in patients dependent on opioids

4.7.1.2 Opioid analgesics

Choice	Drug	Dosage
1st choice **For acute management of severe pain before hospital admission**	**Morphine** Morphine immediate release tablets 10mg, 20mg 50mg; oral solution 10mg/5ml; 100mg/5ml; modified-release tablets, capsules; injection (see BNF)	Dose: Morphine – see BNF for dosage. Morphine preparations should be prescribed by brand name

Prescribing Notes

- Morphine should be given parenterally when possible for acute severe pain. The first dose of intravenous morphine should be given slowly, titrated to effect, and respiratory rate monitored. For use of naloxone, see BNF
- Patients may be discharged following surgery on **strong opioid analgesics**. Treatment should be for short duration and patients should be reviewed before further medication is prescribed by primary care. Where necessary secondary care specialist(s) should be contacted about the treatment plan or patient's reported pain

4.7.2 Chronic non-malignant pain

General Prescribing Notes

- Use in conjunction with 'HSCB Prescribing for Chronic Non-Malignant Pain – Implementation Support Tool' *(add link)*. This includes further important points for managing chronic pain
- The psychological and social aspects of pain must not be overlooked in the management of chronic pain. Coping strategies can be found within www.paintoolkit.org
- See MyNI pain management and live well with pain websites for useful information and resources for patients and clinicians
- If analgesics are commenced regular review to gauge the efficacy is essential. Prescribers are reminded that it is estimated that opioids are effective for only 1 in 10 people with chronic pain
- Consider signposting/referral:
    - To the Physical activity Referral Scheme (PARS). GP practices and other relevant HSC staff can refer using PARS specific protocols generated through CCG
    - To relevant support groups e.g.Versus Arthritis NI
    - To your local Healthy Living Centre (HLC). Some centres provide pain support programmes. Contact your local HLC to find out about the services they offer
    - To access additional services, e.g. Pain Clinic
    - To relevant specialist if the patient does not respond to ≤90mg morphine equivalent
      Note: all opioids recommended by specialists should be accompanied by a clear management plan including arrangements for review, which has also been discussed with the patient

Choice	Drug	Dosage
1st choice	**Non-pharmacological management**	
	Paracetamol tablets 500mg	Dose: 0.5-1g every 4-6 hours; max 4g daily
	Plus/Or NSAID	see 10.1.1 (add link)
2nd choice	Consider addition of codeine 15mg tablets prescribed separately to paracetamol	Dose: 15mg-60mg every 4-6 hours; up to four times daily *Lowest dose that achieves goals. Max 4 weeks codeine*

Stop codeine and consider modified release preparations in table below:

- If codeine not tolerated, there is no improvement or goals not achieved
- To maintain goals beyond 4 weeks codeine treatment

Continue regular paracetamol +/or NSAID

Choice	Drug	Dosage
3rd choice	Tramadol MR +/- NSAID / Paracetamol **Maxitram® is the recommended cost-effective choice (prescribe by brand)**	Dose of tramadol MR: 50mg twice daily, increased if necessary to 100mg twice daily, maximum 200mg twice daily. Titrate to lowest effective dose that achieves agreed goals of treatment
	Or Buprenorphine patch (as a sole agent) **Butec® patches are the recommended cost-effective choice (prescribe by brand)**	Titrate to lowest effective dose that achieves agreed goals of treatment
	Butec® patches, '5' patch (releasing 5 micrograms/ hour), '10' patch (releasing 10 micrograms/hour), '15' patch (releasing 15 micrograms/hour), '20' patch (releasing 20 micrograms/hour)	Dose of Butec®: Initially one '5micrograms/hour' patch; apply to dry, non-irritated, non-hairy skin on upper torso, removing after 7 days and siting replacement patch on a different area (avoid same area for at least 3 weeks)

Prescribing Notes

- Set goals with the patient before starting any medication. The primary aim of treatment should be to improve function and quality of life. Pain reduction of 30% and a positive impact on daily life is a realistic goal (not 100% pain relief)
- In chronic non-malignant pain the long-term use of opioids has many implications. See Faculty of Pain Medicine website for resources to support patients and healthcare professionals and the NI Formulary Patient Zone
- Prescribers should exercise caution before increasing to an oral morphine equivalent (OME) >50mg per day (e.g. tramadol 200mg/day has an OME of 40mg/day) and document reasons for increasing above this dose
- **Oral morphine /codeine equivalence** should be considered to ensure the dosage is safe and appropriate, e.g. Butec® 10

(buprenorphine 10micrograms/hr) is equivalent to ~240mg of oral **codeine** daily. Caution re incomplete cross tolerance *(ADD JUMP TO CAUTIONS)* if switching between opioids

- **Buprenorphine patches** should be prescribed by brand name
- Butec® patches are replaced every 7 days
- Opioids have the potential to impair driving and anyone who is adversely affected must not drive. If a patient has a condition or is undergoing treatment that could impair their fitness to drive, healthcare professionals should advise them on their legal requirement to notify the DVA. Discuss with the patient and document - for further details see driving information in the Opioid Prescribing for Chronic Pain Resource Pack

Cautions

- Some patients may be at increased risk of experiencing toxicity at therapeutic doses of paracetamol, particularly those with a body-weight under 50 kg and those with risk factors for hepatotoxicity. Clinical judgement should be used to adjust the dose of oral and intravenous paracetamol in these patients
- The use of opioids should be reviewed regularly, preferably face to face and with the same clinician; this should be at least monthly in the first six months after stable dosing has been achieved. Frequency of review thereafter can be clinically determined by the complexity of the case, but should be at least biannually
- Patients must be aware of the signs and symptoms of opioid sensitivity/toxicity - i.e. trouble breathing, tiredness, extreme sleepiness, inability to think, walk, or talk normally and feeling faint, dizzy, or confused. If toxicity is suspected advise patients to seek medical attention immediately
- Older patients are particularly susceptible to respiratory depression and constipation secondary to opioids
- Incomplete cross-tolerance is where there is tolerance to a currently administered opioid that does not extend completely to other opioids, if the patient's medication is switched. It may mean that a lower dose of the new opioid is required. It is therefore recommended that a 25-50% reduction of the calculated dose of the new opioid should occur to allow for this. The new regimen

should then be re-titrated according to patient response. The patient should be monitored closely, especially at higher doses

- Tramadol has been reclassified as a Schedule 3 CD following an increased number of reports involving tramadol and the significant harm when misused including death
- Patients / carers must be informed about the safe use of transdermal opioid preparations
- In severe opioid toxicity, consider reversal of respiratory depression using naloxone (see BNF)
- Never prescribe more than one opioid long-term e.g. codeine and tramadol.
- Where possible, avoid co-prescribing other CNS depressants e.g. benzodiazepines or gabapentinoids with opioids. If co-prescribing cannot be avoided, exercise extreme caution due to the increased risk of serious side effects e.g. respiratory depression
- Patients taking enzyme inducing or inhibiting medicines may demonstrate an altered response to some opioid medications and doses may need to be adjusted – refer to BNF for information on specific drug combinations

4.7.3 Neuropathic pain

Neuropathic pain (except trigeminal neuralgia*)

Choice	Drug	Dosage
1st choice	Amitriptyline tablets 10mg, 25mg, 50mg; oral solution 10mg/5ml, 25mg/5ml, 50mg/5ml	Dose: Start at 10mg and titrate by 10mg a week until 70-75mg daily is reached (as a single dose in the evening) [unlicensed]
2nd choice	Gabapentin capsules 100mg, 300mg, 400mg	Dose: Start at 300mg at night (100mg [unlicensed] if the patient very frail or susceptible to sedative medications). Titrate up in steps of 300mg daily (with total given in 3 divided doses) according to side effects/response, to a usual max of 1.8mg daily (note licensed max 3.6g daily but if no substantial improvement at 2.4mg, increasing the dose further is unlikely to be of benefit)
3rd choice	Duloxetine capsules 30mg, 60mg Or	Dose: Start at 30mg daily and titrate up to 60mg daily. A lower starting dose may be appropriate in some people. Nausea is common on initiation but may resolve on continued treatment

	Pregabalin capsules 25mg, 50mg, 75mg, 100mg, 150mg, 200mg, 225mg, 300mg	Start at 75mg at night. This can then be titrated according to side effects to a maximum of 600mg daily in two divided doses. A more conservative dose schedule may be considered in the elderly (e.g. initially 25mg twice daily [unlicensed]).

*** Carbamazepine is first choice for trigeminal neuralgia**

Prescribing Notes

- See HSCB 'Management of Non-Malignant Neuropathic Pain'
- See NICE CG173 Neuropathic pain- pharmacological management
- See NICE NG59 Low back pain and sciatica
- Use of validated tools e.g. DN4 or Leeds Assessment of Neuropathic Symptoms (LANSS) can help to identify neuropathic pain
- **Pregabalin and gabapentin can lead to dependence and may be misused or diverted. Click here for further advice (*add link)*. From 1st April 2019, gabapentin and pregabalin have been reclassified as schedule 3 controlled drugs – click here for further advice**
- Gabapentin tablets are more expensive than the capsules. When prescribing, use the most cost effective strength and formulation
- Lidocaine 5% medicated plaster may be used topically for the treatment of post-herpetic neuralgia, in those patients who are intolerant of first-line systemic therapies or where these therapies have been ineffective. See Regional Guidance for further details "Lidocaine plaster- recommendations for primary and secondary care use in non-specialist settings"
- Tapentadol MR may be recommended as a sole agent for mixed (neuropathic/nociceptive) pain in a **specialist setting** only
- If treatment, with regular assessment, is unsuccessful then referral

for specialist advice is recommended

Cautions

- Amitriptyline should be used with caution in the elderly and patients with glaucoma or prostatic hypertrophy. In the older patient, higher doses of amitriptyline are particularly likely to cause anticholinergic effects such as postural hypotension, sedation, confusion, dry mouth, urinary retention and constipation and should therefore be avoided. Gabapentin may be a safer option for neuropathic pain in these patients. Full details of amitriptyline cautions are available in the BNF
- Caution on concurrent use of amitriptyline with other antidepressants. When amitriptyline is co-prescribed with another antidepressant the maximum daily dose of amitriptyline is 25mg
- In patients with a reduced eGFR, see BNF for dosing directions for initiating and titration of both gabapentin and pregabalin
- Avoid co-prescribing CNS depressants e.g. benzodiazepines or gabapentinoids with opioids due to the increased risk of serious side effects e.g. respiratory depression
- Duloxetine has been associated with an increase in blood pressure and cases of hypertensive crisis have been reported. BP monitoring is recommended in patients with known hypertension and/or other cardiac disease, especially during the first month of treatment. Duloxetine is contraindicated in patients with uncontrolled hypertension. See SPC for further details

4.7.4 Antimigraine drugs

4.7.4.1Treatment of acute migraine attack

- **Offer combination therapy** with an oral triptan and an NSAID, or an oral triptan and paracetamol

Choice	Drug	Dosage
1st choice	Ibuprofen tablets 200mg, 400mg, 600mg Or Paracetamol tablets 500mg; soluble tablets **Plus** oral triptan (see choice below)	Dose: 400 mg to 600 mg every 4-6 hours, no more than four doses in 24 hours. Dose: 1 g every 4–6 hours, no more than four doses in 24 hours
1st choice triptan	Sumatriptan tablets 50mg, 100mg	Dose: 50-100mg as soon as possible after onset of headache; dose may be repeated after not less than 2 hours if migraine recurs; max 300mg in 24 hours

- **If monotherapy is preferred**, offer an oral triptan, or NSAID or aspirin (900mg every 4-6 hours when necessary up to a max 4g daily), or paracetamol
- **Consider adding an anti-emetic** (see notes below) even in the absence of nausea and vomiting

Prescribing Notes

- Refer to NICE CKS Migraine or BASH Guidelines for more comprehensive information
- Mild infrequent migraines can be treated with over the counter medicines. Analgesics and a number of combination medicines

(analgesic plus antiemetic) are available to purchase

Standard Analgesics / NSAIDs

- Most patients with true migraine have gastric stasis during an acute attack. Soluble/dispersible tablets are particularly useful in migraine as they are absorbed quickly and have a more rapid effect than non-dispersible tablets
- Paracetamol suppositories or diclofenac suppositories (off label) may be useful for pain relief if vomiting occurs during migraine
- Do NOT use ergots or opioids
- Chronic overuse of acute treatments may cause **Medication Overuse Headache (MOH)**. Chronic overuse of analgesics should therefore be avoided
    - Triptan, opioids and combination analgesics are likely to result in the development of MOH more rapidly (treatment taken on 10 days or more per month) compared to simple analgesics such as paracetamol (treatment taken on 15 days or more per month)
    - GPs can guide patients by suggesting use of rescue medication on no more than 2 days per week on average.
- Some patients may be at increased risk of experiencing toxicity at therapeutic doses of paracetamol, particularly those with a body-weight under 50 kg and those with risk factors for hepatotoxicity. Clinical judgement should be used to adjust the dose of oral and intravenous paracetamol in these patients

Anti-emetics

- Consider adding an anti-emetic such as metoclopramide or prochlorperazaine (see section 4.6 – *ADD JUMP*)
- Anti-emetics have an independent action on migraine, so can be considered even if nausea or vomiting are not present
- If vomiting restricts oral treatment, consider buccal prochlorperazine tablets
- Metoclopramide can cause acute dystonic reactions especially in patients under 20 years of age. It can be prescribed for short

term use (**up to 5 days**) for the symptomatic treatment of nausea and vomiting associated with acute migraine (where it may also be used to improve absorption of oral analgesics). Click here for further information

Triptans

- Medication should be taken as early as possible after migraine headache starts, but not during the aura phase. Headache recurrence within the first 24 hours can be treated with a second dose
- Sumatriptan 50mg is recommended as first line choice. The 100mg dose has more adverse effects and is only marginally more effective
- If the first dose of a triptan fails to help, alternative medication should be considered
- If treatment with sumatriptan proves to be inadequate, assess compliance and consider:
    - Increasing to a dose of sumatriptan to 100mg (if not used already)
    - Other triptans should be offered if sumatriptan fails. Patients have a variable response to triptans and it is worth sequencing through the triptans to find the most effective treatment
    - If vomiting restricts oral treatment, a non-oral formulation, such as intranasal spray or subcutaneous injection should be considered
    - Subcutaneous sumatriptan should be considered in severe migraine or where vomiting precludes oral treatment or where other formulations have been ineffective
- Sumatriptan 50mg tablets are available over-the-counter to buy from pharmacies and patients should be asked about any OTC triptan use
- Overuse of triptans (use on more than 2 days per week) should be discouraged due to the risk of medication overuse headache

Cautions

- Triptans should not be given to people with uncontrolled hypertension, coronary heart disease, cerebrovascular disease or coronary vasospasm

4.7.4.2 Migraine prophylaxis

Choice	Drug	Dosage
1st choice	Propranolol tablets 10mg, 40mg, 80mg, 160mg Propranolol m/r capsules 80mg, 160mg	Dose: Initially, 80mg daily (either 40mg twice a day or 80mg modified-release once a day). The dose may be increased to 160mg daily, and subsequently to 240mg daily if necessary (either in divided doses or as a single modified release dose)
2nd choice	Topiramate tablets 25mg, 50mg, 100mg **Highly effective contraception is required prior to initiation in women of child-bearing age**	Dose: Initially 25mg at night for 1 week then increase in steps of 25mg at weekly intervals based on clinical response; usual dose 50-100mg daily in 2 divided doses; usual max 100mg daily (NB withdraw topiramate gradually)

Prescribing Notes

- Refer to NICE Clinical Knowledge Summaries Migraine for more comprehensive information including further preventative treatment choices http://cks.nice.org.uk/migraine
- The aim of preventive treatment is to reduce the frequency, severity and duration of attacks and avoid medication-overuse

headache (MOH)

- Consider preventive treatment if:
    - Migraine attacks are having a significant impact on quality of life and daily function e.g. occurring frequently (more than 1 attack per week on average) or are prolonged and severe despite optimal treatment
    - The person is at risk of MOH due to frequent use of acute drugs
    - Standard analgesia and triptans are contraindicated or ineffective
- It is essential to rule out MOH before preventive treatment is initiated. If MOH is suspected then the appropriate management is drug withdrawal rather than prevention
- Propranolol is suitable for people with coexisting hypertension or anxiety. It is not suitable for people with asthma, COPD, peripheral vascular disease or uncontrolled heart failure
- Advise women and girls of childbearing potential that topiramate is associated with a risk of fetal malformations and can impair the effectiveness of hormonal contraception. Ensure suitable contraception is offered –see FSRH
- If both topiramate and propranolol are ineffective (after two months of therapy at the target dose) or are unsuitable, refer to NICE CKS Migraine or BASH Guidelines for information on other drug treatment options including amitriptyline and candesartan. If there is no benefit with an adequate trial of 3 prophylactic medicines and withdrawal of overused medication, consider referral to headache services for further management
- Treatment is considered to have failed if there is lack of response to the highest tolerated dose after 8-12 weeks of treatment
- Prophylaxis should be given for approx. 6 months, then consider gradual drug withdrawal
- Pizotifen and clonidine have been widely used for many years but with little clinical trials evidence of efficacy. They should now be superseded

Cautions

- Prescribe with caution in people at risk of metabolic acidosis
- Topiramate has been associated with acute myopia with secondary angle-closure glaucoma, typically occurring within 1 month of starting treatment. Seek specialist advice and stop topiramate as rapidly as feasible

4.7.4.3 Drug treatment of cluster headache

(a) Acute attacks

Choice	Drug	Dosage
1st choice	Sumatriptan subcutaneous injection 6mg/0.5ml syringe	Dose: By subcutaneous injection, 6mg as soon as possible after onset (patient not responding should not take second dose for same attack); dose may be repeated once after not less than 1 hour if headache recurs; max 12mg in 24 hours

Prescribing Notes

- NICE Clinical Guideline 150 entitled “Diagnosis and management of new onset headaches in young people and adults” was published in September 2012 http://publications.nice.org.uk/headaches-cg150
- Cluster headache management is usually better left to experienced specialists who see this disorder frequently
- Analgesics have no place in treating cluster headache. Ergotamine tartrate, and all orally-administered triptans are of no use as acute therapy

- High flow oxygen (100% at 7-12 L/min for 10-15 minutes at onset of attack) is a useful addition to subcutaneous sumatriptan. The oxygen is administered through a high flow regulator and tight fitting mask. A tight fitting non-rebreathing mask should be used. Information on availability of suitable masks and loan of appropriate regulator equipment is available from www.ouchuk.org
- During a cluster, patients may suffer more than one attack daily and require up to 2 doses of sumatriptan in a 24 hour period
- Patients with cluster headache may need to use up to 2 doses of sumatriptan per day throughout their cluster bout. Therefore triptan use should not be restricted to 2 days per week as recommended for migraine
- If sumatriptan injections are unacceptable consider zolmitriptan nasal spray

(b) Prophylaxis

Choice	Drug	Dosage
1st choice	Verapamil tablets 40mg, 80mg, 120mg, 160mg [unlicensed indication; under specialist supervision]	Dose: 240-960mg daily in 3-4 divided doses. A baseline ECG should be performed before initiating treatment, and repeated with each dose escalation over 80mg twice daily

Prescribing Notes

- NICE Clinical Guideline 150 entitled “Diagnosis and management of new onset headaches in young people and adults” was published in September 2012 http://publications.nice.org.uk/headaches-cg150
- Prophylaxis is indicated during a cluster of attacks (approximately 1-3 months) and should be withdrawn one month after headaches cease
- Most patients will require specialist advice

4.8 Anti-epileptics

Prescribing of Anti-epileptic Drugs

Different anti-epileptic drugs (AEDs) vary considerably in their characteristics, which influences the risk of whether switching between different manufacturers' products of a particular drug may cause adverse effects or loss of seizure control. AEDs have been divided into three risk-based categories to help healthcare professionals decide whether it is necessary to maintain continuity of supply of a specific manufacturer's product. Please refer to MHRA https://www.gov.uk/drug-safety-update/antiepileptic-drugs-updated-advice-on-switching-between-different-manufacturers-products

4.8.1 Control of epilepsy

(a) Pharmacological treatment of focal seizures, evolving / not evolving to bilateral tonic clonic seizure (previously termed with and without secondary generalisation)

1st choice	Lamotrigine tablets 25mg, 50mg, 100mg, 200mg	Dose: See BNF
2nd choice	Levetiracetam tablets f/c 250mg, 500mg, 750mg, 1g; oral solution 100mg/ml; Or Oxcarbazepine tablets 150mg, 300mg, 600mg Or	Dose: See BNF Dose: See BNF

	Carbamazepine m/r tablets 200mg, 400mg; Carbamazepine liquid 100mg/5ml; Carbamazepine suppositories 125mg, 250mg Or Sodium valproate tablets e/c 200mg, 500mg; m/r 200mg, 300mg, 500mg; oral solution 200mg/5ml; **[NB Sodium valproate is contraindicated in women and girls of childbearing potential unless conditions of Pregnancy Prevention Programme are met – see MHRA**	Dose: See BNF Dose: See BNF

(b) Pharmacological treatment of generalised (tonic-clonic, absence, myoclonic, tonic, clonic, atonic) and unclassified seizures

1st choice	Lamotrigine tablets 25mg, 50mg, 100mg, 200mg Or Sodium valproate tablets e/c 200mg, 500mg; m/r 200mg, 300mg, 500mg; oral solution 200mg/5ml; injection 100mg/ml; intravenous injection 400mg (powder and solvent for solution for injection vials) **[NB Sodium valproate is contraindicated in women and girls of childbearing potential unless conditions of Pregnancy Prevention Programme are met – see MHRA**	Dose: See BNF Dose: See BNF
2nd choice	Levetiracetam tablets f/c 250mg, 500mg, 750mg, 1g; oral solution 100mg/ml; concentrate for intravenous infusion 100mg/ml Or Topiramate tablets 25mg, 50mg, 100mg, 200mg	Dose: See BNF Dose: See BNF

Prescribing Notes

General Information

- Refer to NICE CG137 'The epilepsies: diagnosis and management of the epilepsies in adults and children in primary and secondary care'
- The AED treatment strategy should be individualised according to the seizure type, epilepsy syndrome, co-medication and co-morbidity, the young person or adult's lifestyle, and the preferences of the person and their family and/or carers as appropriate
- Sudden Unexpected Death in Epilepsy (SUDEP) risk can be actively reduced by identifying high risk individuals in primary care; such as those who pick up prescriptions erratically, alcohol or substance misuse, convulsive seizures, drug-resistant epilepsy (not seizure free after two appropriately selected, well tolerated drugs, at top dose range) Refer to the Epilepsy Action Women and Epilepsy guidance for advice on topics including contraception and pre-pregnancy planning
- Certain AEDs carry a risk of teratogenicity. Never stop AEDs acutely upon finding out a woman is pregnant; specialist discussion is required. Teratogenic risk is dependent on several factors, most notably dose and AED choice. Hence the importance of appropriate contraception – see FSRH website
- Valproate medicines (Epilim▼, Depakote ▼) are contraindicated in women and girls of childbearing potential unless conditions of Pregnancy Prevention Programme are met. For further information see MHRA Drug Safety Update April 2018. All patients should be under the management of a specialist and have an annual review
- The dose of AED may need to be adjusted in women who commence or stop oral contraceptives, or who become pregnant while taking AEDs - see FSRH website
- Many AEDs are hepatic enzyme-inducing agents, in particular carbamazepine, phenytoin, phenobarbital, oxcarbazepine, eslicarbazepine acetate and topiramate. Hepatic enzyme-

inducing agents interact with a range of medicines, including:
    - AEDs which induce hepatic enzymes may impair the efficacy of oral contraceptives; see BNF for details
    - Sudden withdrawal of these drugs may decrease the rate at which warfarin is metabolized and put a patient taking a combination of these drugs at an increased risk of bleeding
- Liquid formulations and dispersible or chewable tablets are more expensive than standard tablets. Standard tablet formulations (m/r or e/c included) should be prescribed where possible
- If using carbamazepine, offer controlled-release carbamazepine preparations as they are better tolerated

Initiation of pharmacological treatment

- AED therapy should only be started once the diagnosis of epilepsy is confirmed, except in exceptional circumstances
- In considering patients with suspected seizures; the appropriate pathway is either via ED, via local first seizure clinic, or via named neurologist who may have them under review
- Routine plasma drug level monitoring is generally unnecessary unless side-effects/toxicity are suspected or non-compliance is suspected
- Abnormal blood parameters occur with a number of AEDs. Routine bloods should be checked at baseline, after initiation of a new AED and periodically thereafter (every 1-2 years)
- Gradual withdrawal of antiepileptic drugs can be considered with caution, for some patients, after a prolonged period of seizure freedom (at least 2 years) but note implications for driving. Specialist advice should always be sought to estimate the individual risk of seizure recurrence on withdrawal of AED treatment

AED polytherapy

- If a patient is still having ongoing seizures discuss with the specialist epilepsy team

4.8.2 Drugs used in status epilepticus

Step 1 (in community)

1st choice	Midazolam buccal liquid	Dose: As per individualised patient protocol (administered by trained individuals) **NB prescribe by brand name to reduce risk of confusion between different preparations.**
2nd choice	Diazepam rectal solution 10mg/2.5ml	Dose: Usually 10mg, or as per individualised patient protocol This is 2nd choice due to lower social acceptability and lower efficacy of this option for most patients.

Step 2 (in hospital)

1st choice (reduced doses of benzodiazepines should be administered in hospital if they have already been administered to the patient prior to admission. This is at clinician discretion)	Lorazepam injection 4mg/ml	Dose: By intravenous injection (into large vein), 4mg repeated once after 10 minutes if necessary (The combined total dose should not exceed 0.1mg/kg)

	Or Diazepam injection (emulsion) 5mg/ml (Diazemuls®) Or Midazolam buccal liquid **N.B. to be used only when IV access not available**	 Dose: By slow intravenous injection, 10mg at a rate of 1ml (5mg) per minute, repeated once after 10 minutes if necessary (Max dose 20mg in total) Dose: As per individualised patient protocol

Step 3 (in hospital)

1st choice The first choice for the next drug agent used in convulsive status epilepticus should be guided by the local trust	Phenytoin sodium injection 50mg/ml Or	Dose: See BNF or product literature

	Levetiracetam Or Sodium Valproate **Avoid Sodium Valproate if suspect mitochondrial epilepsies – can be fatal** **[NB Sodium valproate is contraindicated in women and girls of childbearing potential unless conditions of Pregnancy Prevention**	Dose: See BNF or product literature Dose: See BNF or product literature

	Programme are met – see MHRA	

Step 4

Admit to ICU/ITU

- Pharmacological management is with anaesthetic agents and ideally will be guided with ICU and neurology input.

Prescribing Notes

- Convulsive status epilepticus is a medical emergency, which can be life-threatening.
- It is operationally defined based on timeframes of when to start treatment. It is a seizure episode which lasts for more than 5 minutes or a series of shorter seizures which take place without the patient regaining consciousness between seizures lasting 5 minutes

Community

- The initial episode of convulsive status epilepticus should be treated with buccal midazolam if available and an ambulance should be called
- Give immediate emergency care and treatment if prolonged (lasting 5 minutes or more). Some care plans may have a provision in acute repetitive seizures for midazolam administration
- Treatment should be administered by trained clinical personnel or, if specified by an individually agreed protocol drawn up with the specialist, by family members or carers with appropriate training

Hospital

- A second dose of benzodiazepine drug may be given if resuscitation facilities are available. Do not exceed specified

maximum doses.

- For non-benzodiazepine IV drug infusions used as second line treatment (e.g. phenytoin, levetiracetam) the choice between these agents is based on expert opinion. Phenytoin is used most commonly. The essential aspect is to give the correct mg/kg dose in a timely manner
- If status epilepticus continues beyond 30 minutes (refractory status epilepticus), the patient will need urgent assessment for admission to ICU
- Note that lorazepam should be refrigerated to ensure product stability.
- Clobazam may be prescribed to prevent status epilepticus in patients with a previous history of status epilepticus or in those who are known to be at risk of a seizure cluster. It may also be prescribed for those whose seizures occur relatively predictably at certain times e.g. during menstruation or intercurrent infections. Prescriptions should be endorsed ‘SLS’

4.9 Drugs used in parkinsonism and related disorders

General Notes

- Refer to NICE NG71 Parkinson's disease in adults and BMJ visual summary
- Refer to COMPASS therapeutic notes on the management of Parkinson's disease
- Refer to Parkinson's UK for patient information and support
- Specialist advice should precede initiation and adjustment of drug therapy
- Could this be drug-induced parkinsonism? Most common causative agents are **antipsychotics** (typical e.g. haloperidol more likely than atypical to cause parkinsonism) and **anti-emetics** (prochlorperazine, metoclopramide, cyclizine)
- Tailor treatment to optimise patients' functional goals
- It is not possible to identify a universal first choice drug therapy for either early Parkinson's Disease (PD) or for adjuvant drug therapy for later PD
- Levodopa, non-ergot derived dopamine agonists, or monoamine-oxididase-B inhibitors can be prescribed for initial treatment in early PD. Therapy with two or more anti-parkinsonian drugs may be necessary as the disease progresses
- Patients with PD should be supported to get their medication 'on time', and this is particularly relevant in situations where they are not self-medicating (e.g. hospital admission).See Parkinson's UK 'Get It On Time' campaign for further details and resources
- Dopamine replacement therapy should not be stopped suddenly, e.g. on admission to hospital. These medications are not optional and are essential for the patients' wellbeing
- Dopamine agonists, and less commonly levodopa, may cause **impulse control disorders** (pathological gambling/shopping, hypersexuality). Patients and carers should be advised in advance of these potential adverse effects (see MHRA and Parkinson's UK patient information leaflet)

- Patients who drive must inform the DVA

Cautions

- Patients who have suffered excessive sedation or sudden onset of sleep with dopaminergic drugs (levodopa and dopamine agonists) should refrain from driving or operating machines until those effects have stopped recurring. In some individuals, these drugs may cause wakefulness and should be avoided in the evening

4.9.1 Dopaminergic drugs used in parkinsonism

- Levodopa, dopamine agonists, or MAO-B inhibitors are all first-choice options for initial pharmacotherapy in early Parkinson's Disease.
- In later stages of Parkinson's Disease, levodopa, dopamine agonists, MAO-B inhibitors, or COMT inhibitors are all options.

4.9.1.1 Dopamine receptor agonists

Choice	Drug	Dosage
1st choice Oral preparations	Ropinirole tablets 250 micrograms, 500 micrograms,1mg, 2mg, 5mg; Ropinirole tablets m/r 2mg, 4mg, 8mg (**Spiroco XL**® is a cost-effective choice - **prescribe by brand**) Or Pramipexole tablets 88 micrograms, 180micrograms, 350micrograms, 700micrograms; pramipexole tablets m/r 260micrograms, 520 micrograms, 1.05mg, 1.57mg, 2.1mg, 2.62mg, 3.15mg Strengths stated in terms of pramipexole **base**	Dose: See BNF - seek specialist advice Dose: See BNF - seek specialist advice Dose: See BNF - seek specialist advice
Transdermal preparations **Specialist initiation**	Rotigotine transdermal patches 1mg/24 hours,2mg/24 hours, 3mg/24 hours, 4mg/24 hours, 6mg/24 hours, 8mg/24 hours	Dose: See BNF - seek specialist advice

Prescribing Notes

- Ropinirole or pramipexole can be used as monotherapy or adjunctive therapy with levodopa
- Rotigotine patches may be useful in patients with complicated oral regimes and in those with delayed gastric emptying or swallow problems or where there are predominant nocturnal symptoms
- Ergot derivatives (bromocriptine, cabergoline and pergolide) are no longer recommended. They have rarely been associated with pulmonary, retroperitoneal, pericardial and valvular fibrotic reactions and require regular clinical monitoring – see MHRA
- Dopamine receptor agonists are emetogenic. Nausea will often settle over time as tolerance occurs. If nausea is persistent or severe:

- Do not use metoclopramide or prochlorperazine
- Domperidone can be prescribed, reducing or stopping it when the nausea or vomiting settles. Domperidone is associated with a small increased risk of serious cardiac side effects. Its use is now restricted to the relief of symptoms of nausea and vomiting and the dosage and duration of use have been reduced. Treatment should generally only be given for up to one week. Domperidone is now contraindicated in those with underlying cardiac conditions and other risk factors. Risks are higher in people older than 60 years. For further information see MHRA

- When used as adjunctive therapy, dopamine receptor agonists can exacerbate levodopa-induced adverse effects
- All dopamine receptor agonists can cause postural hypotension and neuropsychiatric adverse effects
- Apomorphine is a powerful dopamine receptor agonist that must be given subcutaneously, either by infusion or on an "as required" basis. It is approved for use under a shared care guideline
- Amantadine is not a first choice treatment but it may be an option for some patients where dyskinesia is not adequately managed by other therapies. Not all patients respond to amantadine and it may have only a mild effect. However, it can cause a range of side effects including psychiatric effects e.g. hallucinations and insomnia (do not prescribe at night). Abrupt discontinuation should be avoided

(a) 4.9.1.2Levodopa

Choice	Drug	Dosage
1st choice	Co-beneldopa (Madopar®) containing levodopa and benserazide Or Co-careldopa (Sinemet®) containing levodopa and carbidopa	Dose: See BNF - seek specialist advice Dose: See BNF - seek specialist advice

Prescribing Notes

- To reduce the risk of nausea, start with a low dose and build up slowly. Levodopa should not be withdrawn abruptly. It may colour urine red
- Levodopa is a useful first line drug for older/frailer patients to optimise control faster
- Levodopa containing preparations are normally prescribed as their individual components, however, be aware that the total dose is sometimes referred to e.g. Madopar 50mg/12.5mg as Madopar 62.5mg
- Co-beneldopa (Madopar®) and co-careldopa (Sinemet®) are used equally and there is no evidence of benefit of one over the other
- Dispersible Madopar® may be useful where rapid absorption is desired, for example first thing in the morning. Patients should be advised to dissolve in plenty of water; often an inactive sediment remains in the glass
- Modified-release formulations of levodopa are not recommended for initiation of therapy. They may be useful for nocturnal immobility and rigidity e.g. some patients are prescribed a modified release preparation at night and immediate release preparations during the day
- For driving advice, see general notes (cautions)

4.9.1.3Monoamine-oxidase-B (MAOB) inhibitors

Choice	Drug	Dosage
1st choice	Rasagiline tablets 1mg	Dose: See BNF - seek specialist advice
2nd choice	Selegiline tablets 5mg, 10mg; oral lyophilisate 1.25mg	Dose: See BNF - seek specialist advice

Prescribing Notes

- MAOB inhibitors can be used as monotherapy in early Parkinson's disease to improve motor symptoms and delay the need for levodopa
- MAOB inhibitors may be used as an adjunct to levodopa in later Parkinson's disease for 'end-of-dose' fluctuations

Cautions

- The combination of MAOB inhibitors and antidepressants can increase the risk of serotonin syndrome. However, depression is commonly associated with PD and SSRIs are often used for its management. According to the literature, serotonin syndrome occurs rarely and this combination is sometimes used **under specialist advice**. Recommended doses should not be exceeded and SSRI dose should be kept at the lower end of the therapeutic range. Among the SSRIs, citalopram and sertraline may be preferred. Healthcare professionals should remain vigilant to this potential complication

(b) 4.9.1.4 Dopamine enzyme inhibitors / catechol-O-methyltransferase inhibitors (COMT inhibitors)

Choice	Drug	Dosage
1st choice	Entacapone tablets 200mg	Dose: See BNF - seek specialist advice
2nd choice	Tolcapone 100mg tablets	Dose: See BNF and Shared Care Guideline - seek specialist advice

Prescribing Notes

- A triple combination preparation of levodopa, caridopa and entacapone may be suitable for patients requiring entacapone who are having problems with concordance. Prescribe by **brand** - Sastravi® and Stanek® are currently the 'branded generic' combination preparations with the lowest acquisition cost
- Due to the risk of hepatotoxicity, tolcapone should be prescribed under specialist supervision only, when other COMT inhibitors combined with co-beneldopa or co-careldopa are ineffective or not tolerated. LFT monitoring is required (see shared care guideline)
- The levodopa dose may need to be adjusted when a COMT inhibitor is initiated
- Tolcapone should only be continued beyond three weeks if there is substantial improvement in symptom control

4.9.2 Antimuscarinic drugs used in parkinsonism

Choice	Drug	Dosage
1st choice	Procyclidine tablets 5mg	Dose: See BNF - seek specialist advice
	Or	
	Trihexyphenidyl hydrochloride tablets 2mg, 5mg	Dose: See BNF - seek specialist advice

Prescribing Notes

- Antimuscarinics are sometimes used as a first line therapy in **young onset** Parkinson's Disease under specialist supervision, but not generally recommended in older patients – see Cautions

- Antimuscarinics may occasionally be useful in patients with tremor which is unresponsive to other drugs, on the advice of a specialist
- Procyclidine is mainly used in the management of drug-induced parkinsonism
- Tardive dyskinesia is not improved by antimuscarinic drugs and may be made worse

Cautions

- Antimuscarinics may cause cognitive impairment and urinary retention. They should be avoided in older patients
- Antimuscarinics are not generally recommended for use in Parkinson's Disease because of toxicity in the elderly and the risk of aggravating dementia
- Abrupt withdrawal of antimuscarinics should be avoided

Essential tremor

Choice	Drug	Dosage
1st choice	Propranolol tablets 10mg, 40mg, 80mg, 160mg; capsules m/r 80mg, 160mg	Dose: Essential tremor: initially 40mg 2-3 times daily, increased if necessary; maintenance 80-160mg daily 'As required' use may be appropriate (see notes below)

Prescribing Notes

- Propranolol may be used on an 'as required' basis e.g. where tremor is troublesome in stressful situations e.g. social events or work engagements
- The continued benefit of treatment with a beta blocker should be reviewed
- Primidone may be useful for essential tremor in patients unable

to take beta-blockers due to, for example, asthma, bradycardia or peripheral vascular disease, although primidone can be poorly tolerated e.g.due to somnolence

Cautions

- Beta-blockers should usually be avoided in patients with a history of asthma, bronchospasm or a history of obstructive airways disease

4.9.4 Management of dementia in Parkinson's disease

Choice	Drug	Dosage
1st choice	Non drug treatment – see Prescribing Notes	
2nd choice	Cholinesterase inhibitor [off-label] See section 4.11 (*add jump*)	

Prescribing Notes

- Other causes of cognitive impairment should first be ruled out before considering drug treatment, e.g. infection, dehydration, constipation, electrolyte imbalance or adverse drug reaction Consider safely reducing or discontinuing (on specialist advice if necessary) any drugs that may be causing or exacerbating cognitive impairment, including:
  - Drugs with an antimuscarinic action, including tricyclic antidepressants, tolterodine, promethazine and oxybutynin
  - H_2-receptor antagonists such as ranitidine
  - Benzodiazepines
  - Amantadine
  - Dopamine agonists
- Cholinesterase inhibitors have been shown to improve cognition, delusions and hallucinations in patients with DLB (which has similarities to PD). However, motor function may deteriorate
- Memantine may be considered if cholinesterase inhibitors are not tolerated or contra-indicated [off-label]

4.10 Drugs used in substance dependence

Substitute Prescribing is a highly specialised service and treatment should only be initiated by those who have the appropriate training and expertise. National and local protocols/ guidelines should be used when providing this service. It is good practice to involve Substance Misuse Liaison Service and the Prescribing Drug Service

Key resources:

- "Drug Misuse and Dependence – Guidelines on Clinical Management" (Department of Health, 2017)
- See 'Harm Reduction Services' on BSO website for further information e.g. supplementary guidance for community pharmacists and information on Take Home Naloxone

Notes on the most commonly used drugs for ongoing substitute prescribing treatment are included for **information purposes only.** Detailed prescribing guidance is outside the scope of the NI Formulary

4.10.1Opioid maintenance prescribing

Choice	Drug	Dosage
For information only: Usual drugs prescribed for substitute prescribing	Buprenorphine sublingual tablets 400micrograms, 2mg, 8mg	Dose: Dose will be titrated depending on the individual patient (max. 24mg daily); withdraw gradually; see BNF for further details
	Or Espranor® (buprenorphine oral lyophilisate) 2mg, 8mg Espranor oral lyophilisate has diffferent bioavailablility to other buprenorphine products and is not interchangeable with them - consult product literature before switching between products	Dose: Dose will be titrated depending on the individual patient (max 18mg daily); withdraw gradually; see BNF for further details
Reserve Suboxone® for when there is a risk of dose diversion for parenteral administration	Or Suboxone® (buprenorphine 2mg / naloxone 500micrograms; buprenorphine 8mg / naloxone 2mg; buprenorphine 16mg / naloxone 4mg) sublingual tablets	Dose dependent on individual patient (max 24mg buprenorphine daily).Titrate gradually upwards with daily supervised consumption until at least **2 weeks** after stable dose reached; see BNF for further details
	Or Methadone oral solution 1mg/ml	Dose: Dose will be titrated depending on the individual patient but the maintenance dose range is 60-120mg daily. Do not start (or re-start after a break) above 30mg methadone daily. Titrate gradually upwards with daily supervised consumption until at least 2 weeks after stable dose reached

Prescribing Notes

General Information

- Supervised self-administration of medication by pharmacists optimises compliance and minimises leakage into the illicit market. However, safety must be balanced against the need to provide a patient-centred approach when considering requests for increased take-home doses. Ideally new patients should be started on a supervision regime of at least 6 days per week for a minimum of three months. After 3 months of supervised consumption an assessment of the patient's stability should be undertaken
- Patients who miss 3 consecutive days or more of their regular prescribed dose of opioid substitution therapy are at risk of overdose because of loss of tolerance. Community pharmacists must contact the keyworker after the patient has missed 2 consecutive doses. Prescribers may wish to consider reducing/stopping opioid substitution therapy if a patients has missed more than three days. If the patient misses 5 or more days of opioid substitution therapy, an assessment of illicit drug use is also recommended before restarting substitution therapy; this is particularly important for patients taking buprenorphine because of the risk of precipitated withdrawal
- Use methadone 1mg/ml. The stronger formulation (10mg/ml) should not be used
- Methadone tablets should not be used routinely for opioid maintenance prescribing. They are occasionally prescribed in exceptional circumstances for patients travelling abroad
- When administering Espranor®, the oral lyophilisate should be removed from the pack with dry fingers – any contact with moisture will result in disintegration of the wafer
- Caution is required in prescribing medications for patients who attend out of hours or emergency department (ED) stating they have not had their usual supply of methadone or buprenorphine that day
- Adjunctive therapy may be required for the management of

opioid withdrawal symptoms. Loperamide may be used for the control of diarrhoea; mebeverine for controlling stomach cramps; paracetamol and NSAIDs for muscular pains and headaches; metoclopramide or prochlorperazine may be useful for nausea or vomiting (see BNF for further details). Note potential for abuse with:

  - Loperamide- there has been increasing usage of high doses of oral loperamide to achieve a “high” or to overcome the symptoms of opiate withdrawal. Serious cardiovascular events, including fatalities have been reported in association with large overdoses of loperamide – see MHRA
  - Hyoscine – misuse of hyoscine (Buscopan®) has been reported, particularly in prisons. Crushing and smoking hyoscine releases scopolamine, a known hallucinogen. Prescribers are advised to use an alternative medication where treatment is indicated e.g. mebeverine

- All medications, in particular methadone, should be stored in a child secure area

Hospital admission of people who misuse drugs

- Good communication between hospital and community is essential for safe patient care. Patients will usually have a named keyworker and a named pharmacy. They will be receiving treatment from their own GP, a specialist GP provider, or local drug treatment services
- It is not recommended to dispense methadone or buprenorphine as ‘take home’ medicines to avoid any risk of ‘double prescribing’ – refer to local trust policy
- Drug misusers may be admitted to hospital for treatment of conditions common to other patients or directly related to their drug misuse. In either case, hospital medical staff should take proper account of any drug misuse and any treatment being provided in the community
- Pregnant women dependent on opioids should be jointly

managed by their obstetrician and the OST team

Acute pain management for people who misuse drugs

- Contact the relevant pain control team for advice
- Drug misusers in pain will have needs for pharmacological and other interventions similar to non-drug users
- Acute pain requires full analgesic management in patients dependent on opioids. These patients may have a lower tolerance of pain together with a higher tolerance of opioid analgesic effects
- If pain is mild to moderate, non-opioid analgesia (as used in the general population) is the initial treatment of choice together with appropriate education and advice
- For more severe pain, if opioid analgesia is indicated, the treatment will depend on whether the patient is taking full agonist opioids such as methadone, partial agonist opioids such as buprenorphine, or opioid antagonists such as naltrexone. If the patient is dependent on full agonists the opioid pain relief should be in addition to the usual opioid treatment dose and the amount of pain relief medication titrated against pain while monitoring respiratory function. Sub-therapeutic doses should be avoided
- Splitting the dose of methadone in order to control pain is occasionally done for some patients taking methadone (e.g. from once daily to twice daily). If the patient is dependent on a partial agonist, such as buprenorphine, specialist advice should be sought but, if the buprenorphine is continued, especially high doses of full agonist opioids will be required initially, with careful monitoring and anticipated dose reduction in the subsequent 36 to 72 hours
- Opioid antagonists such as naltrexone will render opioid analgesia ineffective
- It is important to be extremely careful when prescribing additional drugs such as sedatives or gabapentinoids. It may be necessary, in some cases, to contact the relevant pain control team for further advice on improving pain control

- Chronic pain management can be complex and requires good joint working arrangements as well as specialist knowledge. Chronic pain management for patients who are receiving substitute prescribing for drug misuse is not covered in the NI Formulary; information sources include "Drug Misuse and Dependence – Guidelines on Clinical Management" (Department of Health, 2017)

4.10.2 Opioid detoxification

Opioid detoxification refers to a process of achieving abstinence rapidly. Patients who detox as a process of being excluded from treatment or who fall out of treatment or who undergo premature detoxification have particularly poor outcomes. As such, opioid detoxification should only take place under the supervision of those specialist teams outlined above and is beyond the scope of the NI Formulary

Naltrexone is an opioid antagonist which can be initiated under specialist advice to support abstinence from opioids. It must not be commenced until the patient is opioid free for 7-10 days.

Naloxone is also used as the emergency antidote for overdoses caused by heroin and other opioids. Naloxone is a prescription-only-medicine (POM) but regulations enable drug services to supply it without a prescription. And anyone can use it to save a life in an emergency. See link for further details

4.10.3 Benzodiazepines addiction and withdrawal

Choice	Drug	Dosage
1st choice	Diazepam tablets 2mg, 5mg, 10mg	Dose: See prescribing notes and suggested protocol below

Prescribing Notes

Polydrug users

- Benzodiazepines have their own potential for misuse and dependence and are often taken in combination with opiates or stimulants. Many drug misusers misuse benzodiazepines but the majority do not require long-term replacement prescribing or high doses. For those who are benzodiazepine dependent, sudden cessation in their use can lead to a recognised withdrawal state
- Good assessment and care planning and adherence to local protocols are prerequisites for considering prescribing benzodiazepines. Prescribing benzodiazepines to drug misusers requires competencies in this form of treatment and appropriate supervision. It is therefore more likely to be considered an appropriate approach in secondary care rather than in primary care
- Only very rarely should doses of more than 30mg diazepam equivalent per day be prescribed

General advice on Benzodiazepine Withdrawal

- Dosage should generally be tapered gradually in long-term benzodiazepine users. Abrupt or over-rapid withdrawal, especially from high dosage, can give rise to severe symptoms
- Benzodiazepine withdrawal should be flexible and carried out at a reduction rate that is tolerable for the patient. The rate should depend on the initial dose of benzodiazepine, duration of use, and the patient's clinical response. Short-term users of benzodiazepines (2-4 weeks only) can usually taper off within 2-4 weeks. However, long-term users should be withdrawn over a much longer period of several months or more
- For people withdrawing from short-acting drugs it is advisable to switch to a long-acting benzodiazepine such as diazepam
- Exceptions to the general rule of slow reduction are zolpidem and zalepon. These drugs are eliminated quickly and can generally be stopped abruptly without substitution of a long-acting benzodiazepine. However, caution is advised with high doses or prolonged use. If withdrawal symptoms occur, patients can be given a short course of diazepam starting at about 10mg

daily, decreasing the dose gradually

- It is inappropriate for patients to be prescribed more than one benzodiazepine at the same time. Patients already in receipt of a prescription of more than one type of benzodiazepine should normally be converted to diazepam only
- The majority of patients on therapeutic doses are taking less than 20mg diazepam (or equivalent) daily. Only very rarely should doses of more than 30 mg diazepam equivalent per day be prescribed
- Older people can withdraw from benzodiazepines just as successfully as younger people, even if they have taken the drug for years. There are more compelling reasons why older people should withdraw from benzodiazepines, e.g. risk of falls, confusion

A suggested protocol for withdrawal for prescribed long-term benzodiazepine patients is as follows:

1. Transfer the patient stepwise, one dose at a time, over about a week, to an equivalent daily dose of diazepam[(1)] preferably taken at night. *Please note large doses at night may increase risk of falls or respiratory difficulties so it may be advisable to split doses to twice or three times daily in some cases*

2. Reduce diazepam dose, usually by 1–2 mg every 2–4 weeks (in patients taking high doses of benzodiazepines, initially it may be appropriate to reduce the dose by up to one-tenth every 1–2 weeks). If uncomfortable withdrawal symptoms occur, maintain this dose until symptoms lessen

3. Reduce diazepam dose further, if necessary in smaller steps; steps of 500 micrograms may be appropriate towards the end of withdrawal. Then stop completely

4. For long-term patients, the period needed for complete withdrawal may vary from several months to a year or more

Withdrawal symptoms for long-term users usually resolve within 6–18 months of the last dose. Some patients will recover more quickly, others may take longer. The addition of beta-blockers, antidepressants and antipsychotics should be avoided where possible. Counselling can be of considerable help both during and after the taper

1. Approximate equivalent doses, diazepam 5 mg

≡ alprazolam 250 micrograms

≡ clobazam 10 mg

≡ clonazepam 250 micrograms

≡ flurazepam 7.5–15 mg

≡ chlordiazepoxide 12.5 mg

≡ loprazolam 0.5–1 mg

≡ lorazepam 500 micrograms

≡ lormetazepam 0.5–1 mg

≡ nitrazepam 5 mg

≡ oxazepam 10 mg

≡ temazepam 10 mg

Note – dose equivalents of benzodiazepines are only a guide on the effect of single doses and do not account for dose accumulation effects of long acting benzodiazepines in comparison to shorter acting benzodiazepines

4.10.4) Alcohol dependence

4.10.4.1Acute alcohol withdrawal

General Prescribing Notes

- Refer to NICE pathway on alcohol-use disorders http://pathways.nice.org.uk/pathways/alcohol-use-disorders
- Patients should be assessed to determine if they require in-patient treatment rather than out-patient care (see criteria in NICE CG115)
- Refer to NI Alcohol Use Disorders Care Pathway – management in the acute hospital setting
- Risk factors for complicated withdrawal include very heavy alcohol consumption, history of delirium tremens (DTs) or alcohol withdrawal seizures
- A benzodiazepine should be used in a sufficient dose to produce sedation for the initial 24-48 hours, then gradually withdrawn over 4-5 days, e.g. chlordiazepoxide (oral) 20-40 mg 4 times daily for the initial 24-48 hours then reduce
- Acamprosate is not of value in alcohol withdrawal. It is used in conjunction with psychological management of alcoholism for a selected group of patients under specialist care
- Benzodiazepines have dependence potential. To minimise risk of dependence, administer short-term only. Benzodiazepines should not be prescribed if the patient is likely to drink alcohol concomitantly
- Choice of benzodiazepines:
  - Chlordiazepoxide is first choice oral agent for outpatients and general practice alcohol withdrawal, because it has less abuse potential and ‘street value’ than diazepam
  - Chlordiazepoxide is used for in-patients
  - Diazepam is first choice for in-patients if the parenteral route is required
- Short acting benzodiazepines such as oxazepam or lorazepam may be preferred in those for whom over sedation must be

avoided, in patients with liver disease, COPD or a history of alcohol related DTs and seizures
- For advice on co-existing alcohol and benzodiazepine dependence click here (*ADD JUMP*)
- For people with a significant co-morbid mental health disorder, and those at high risk of suicide – refer to a psychiatrist

Assisted alcohol withdrawal for moderate to severe alcohol dependence

Consider an assisted withdrawal programme if a person drinks >15 units alcohol per day and/or scores ≥20 on AUDIT (Alcohol Use Disorders Identification Test)

Choice	Drug	Dosage
1st choice	Chlordiazepoxide capsules 5mg, 10mg **AND psychosocial support** Prescribe as **capsules** not tablets (high cost 'special')	Dose: 20-40mg four times daily for first 24 to 48 hours, then once stabilised, gradually reduce dose over 4 to 5 days. In severe cases 250mg daily in divided doses

Prescribing Notes

Community-based assisted withdrawal
- See NI Drugs & Alcohol Services directory for information on treatment and support services available across Northern Ireland
- Use fixed-dose drug regimens; start treatment with a standard dose then reduce dose to zero over 7 to 10 days according to a standard protocol
- Initial dose should be based on severity of alcohol dependence and/or regular daily level of alcohol consumption
- Prescribe for instalment dispensing; no more than 2 days medication to be supplied at any time

- A family member/carer should preferably oversee the administration of medication
- Monitor the service user at least every other day, ideally daily for the first 3 days
- Adjust the dose if severe withdrawal symptoms or over-sedation occur

In-patient / residential assisted withdrawal

- Refer to NI Alcohol Use Disorders Care Pathway – management in the acute hospital setting

Co-existing benzodiazepine and alcohol dependence

- Consider in-patient management or secondary care involvement
- Ideally manage with one benzodiazepine, normally chlordiazepoxide (diazepam is an alternative if the patient is already taking), not multiple benzodiazepines
- It may be prudent to seek specialist advice. One option may be to increase the dose of benzodiazepine used for withdrawal: calculate initial daily dose based on requirement for alcohol withdrawal plus equivalent regularly used daily dose of benzodiazepine
    - For example, an option for patients taking concurrent diazepam is to calculate the daily dose based on the summated alcohol and diazepam (equivalent) requirement. The diazepam can then be gradually reduced to assist alcohol withdrawal. This avoids multiple benzodiazepines being prescribed simultaneously
- Community-based withdrawal should last longer than 3 weeks and be tailored to the person's symptoms and discomfort
- In-patient regimens should last for 2 to 3 weeks or longer depending on the severity of benzodiazepine dependence

4.10.4.2Relapse Prevention

Choice	Drug	Dosage
1st choice	Acamprosate (Campral EC®) tablets e/c 333mg **AND a psychological intervention**, e.g. CBT, behavioural therapies, social network and environment-based therapies, or behavioural couples therapy Or Naltrexone tablets 50mg **AND a psychological intervention On specialist advice**	Dose: 18-65 years, 60kg and above, 666mg three times daily; under 60kg, 666 at breakfast, 333mg at midday and 333mg in early evening Dose: 25mg initially then 50mg daily if tolerated
2nd choice	Disulfiram tablets 200mg **AND a psychological intervention On specialist advice**	Dose: 800mg for the first dose, reducing over 5 days to 100-200mg daily; should not be continued for longer than 6 months without review

Prescribing Notes

- Refer to NICE pathway on alcohol-use disorders http://pathways.nice.org.uk/pathways/alcohol-use-disorders
- Treatments for maintenance of abstinence are an adjunct to counselling
- Choice of treatment will be influenced by patient acceptability
- Before prescribing a drug for relapse prevention, conduct a comprehensive medical assessment including baseline urea, electrolytes and liver function tests
- Acamprosate is best suited to supporting abstinence in individuals who are concerned that craving will lead to lapse/relapse. It can be initiated without specialist input
- Acamprosate should be initiated as soon as possible after

alcohol withdrawal and maintained if the patient relapses. Repeated relapsing to heavy drinking indicates non-efficacy. Recommended treatment period is 1 year (it is not licensed for use longer than 12 months)

- Contraindications to acamprosate are severe renal or hepatic impairment and therefore liver and kidney function tests should be performed before commencing treatment. It should be avoided in individuals who are pregnant or breastfeeding
- Short-term treatment with naltrexone may be effective at reducing craving for alcohol
- Disulfiram inhibits alcohol dehydrogenase, leading to acetaldehyde accumulation after drinking alcohol, which can cause extremely unpleasant physical effects. Continued drinking can lead to arrhythmias, hypotension and collapse
- Disulfiram is prescribed for patients who would benefit from a deterrent, particularly if they can nominate a partner who can help them to take it regularly
- Before initiating disulfiram, the clinician must ensure that no alcohol has been consumed for 24 hours. Contraindications to use include, cardiac failure, coronary artery disease, history of cerebrovascular disease, hypertension, liver disease, peripheral neuropathy and history of severe mental illness
- A medical assessment should be undertaken at least every 6 months
- Disulfiram self-administration should be supervised by, for example, a partner or an appropriate nurse, or at a day hospital

Do not:

- Use naltrexone for people taking oral opioids
- Use benzodiazepines as ongoing treatment – use for withdrawal only

Cautions

- Caution needs to be exercised when any benzodiazepines are prescribed in older patients since accumulation may result in over sedation. Oxazepam or lorazepam, as short-acting benzodiazepines, may be preferred in older patients
- Benzodiazepine doses may need to be reduced for young people, older people and those with liver impairment; avoid in severe liver impairment. In mild to moderate liver impairment

consider using lorazepam (unlicensed use) – start at a low dose and monitor liver function carefully

- Before initiating disulfiram, the clinician must ensure that no alcohol has been consumed for 24 hours. Contraindications to use include, cardiac failure, coronary artery disease, history of cerebrovascular disease, hypertension, liver disease, peripheral neuropathy and history of severe mental illness

4.10.4.3Interventions for the reduction of alcohol consumption

Prescribing Notes:

- NICE CG 115 recommends that the first line treatment option in mild alcohol dependence is a psychological intervention
- Nalmefene▼ is recommended by NICE as an option for reducing alcohol consumption. It is important that prescribers are aware of the prescribing requirements outlined by NICE and that nalmefene▼ is only prescribed in line with these to avoid inappropriate prescribing. Refer to https://www.nice.org.uk/guidance/ta325

10.4.4.4 Vitamin supplementation

Oral Prophylaxis

Low risk of Wernicke's Encephaopathy (WE)

Choice	Drug	Dosage
1st choice	Thiamine (vitamin B1) tablets 100mg,	Dose: Oral: 100mg three times daily. Single doses above 100mg do not enhance oral absorption and should be avoided

Prescribing Notes

- Refer to NI Alcohol Use Disorders Care Pathway – management in the acute hospital setting
- Oral thiamine can be considered for those at low risk (mild alcohol dependence with an adequate diet)
- Oral thiamine is indicated for less severe cases while receiving detoxification treatment for 5 to 7 days. Patients who resume drinking or continue to drink and are at risk of malnourishment should be given oral thiamine 50mg or 300mg daily, according to local protocol, on a long-term basis
- Clients undergoing community detoxification should also be considered for parenteral prophylaxis with Pabrinex® because oral thiamine is not adequately absorbed and there is considerable doubt about the usefulness of oral replacement. However, parenteral administration of thiamine is not always possible in the community setting. In this case, low-risk drinkers without neuropsychiatric complications and with an adequate diet should be offered oral thiamine: a minimum of 300mg daily during assisted alcohol withdrawal and periods of high alcohol intake
- Due to lack of evidence, vitamin B complex preparations (Vitamin B compound and Vitamin B compound strong) should not be prescribed for prevention of Wernicke's Encephalopathy (WE) in alcoholism. In rare cases where there might be a justifiable reason for prescribing e.g. medically diagnosed deficiency or chronic malabsorption, Vitamin B compound **strong** and not vitamin B compound should be prescribed as it represents better value for money. For further details see SPS website

Parenteral Prophylaxis

Prescribing Notes

- Parenteral thiamine (Pabrinex®) is indicated for prophylaxis of WE in those at moderate-high risk and for treatment of

suspected or confirmed WE.

- Treatment is given under the care of a specialist and Pabrinex® should usually be administered in hospitals or health centres where facilities for treating anaphylaxis are available
- The following patients should be considered to be at moderate-high risk of Wernicke's Encephaopathy (WE):
    - Patients who are alcohol dependent where there is evidence of malnutrition, physical illness or complicated withdrawal
    - Patients who show evidence of malnourishment or are at risk of malnourishment
    - Decompensated liver disease
    - Attending the Emergency Department or are admitted to hospital with acute illness or injury
    - Homelessness
    - Hospitalised for co-morbidity of another alcohol issue
- Refer to NI Alcohol Use Disorders Care Pathway – management in the acute hospital setting

4.10.5 Cigarette smoking

Choice	Drug	Dosage
1st choice	Behavioural support + nicotine replacement therapy (long-acting) patch 5mg, 10mg, 15mg or 25mg over 16 hours, 7mg, 14mg or 21mg over 24 hours Or Behavioural support + nicotine replacement therapy (short-acting) gum, lozenge, sublingual tablet, mouth spray, nasal spray, inhalator, orodispersible film; nicotine chewing gum 2mg, 4mg,6mg; nicotine lozenges 1mg, 1.5mg, 2mg, 4mg; sublingual nicotine tablets 2mg, nicotine mouth spray 1mg/spray; nicotine nasal spray 500micrograms/spray; nicotine inhalator 15mg/cartridge; nicotine 2.5mg orodispersible film;	Dose: See BNF or product SmPC Dose: See BNF or product SmPC
2nd choice	Varenicline▼ f/c tablets 500 micrograms, 1mg	Dose: Start usually1-2 weeks before target stop date, initially 500 micrograms once daily for 3 days, increased to 500 micrograms twice daily for 4 days, then 1mg twice daily for 11 weeks (reduce to 500 micrograms twice daily if not tolerated); 12 week course can be repeated in abstinent individuals to reduce risk of relapse
3rd choice	Bupropion hydrochloride 150mg m/r, f/c tablets	Dose: Start 1-2 weeks before target stop date, initially 150mg daily for 6 days then 150mg twice daily (max single dose 150mg, max daily dose 300mg; minimum 8 hours between doses); period of treatment 7-9 weeks; discontinue if abstinence not achieved at 7 weeks; consider max 150mg daily in patients with risk factors for seizures and the elderly

Prescribing Notes

General Notes

- Refer to NICE NG92 Stop smoking interventions and services, March 2018 https://www.nice.org.uk/guidance/ng92
- A ‘Pregnancy and NRT’ patient information leaflet is available to support pregnant women who smoke
- Prescribing of NRT should be combined with one to one or group behavioural support
- It should not commence until the patient has decided on a ‘target stop date’
- Initial prescriptions should be issued weekly. Further prescriptions should only be issued if the quit attempt is continued at review and normally not for more than 2 weeks treatment on each occasion. NRT must not be added to repeat prescribing systems
- Symptom control of nicotine withdrawal in hospital in-patients, is the only exception to a ‘target stop date’ being set prior to prescribing NRT
- The use of NRT preparations in an individual who is already accustomed to nicotine introduces few new risks and is widely accepted that there are no circumstances in which it is safer to smoke than to use NRT
- Patients wishing to use a cut down to quit approach should be advised to purchase NRT for this purpose. Refer to NICE PH45 Tobacco: harm-reduction approaches to smoking
- The choice of product should be based on patient preference, patient history, discussion of potential side-effects, consideration of co-morbidities, potential drug interactions and cost
- Professional judgement should be used to consider if a repeat course should be initiated within 6 months of an unsuccessful quit attempt
- Stopping smoking may result in slower metabolism and a

consequent rise in blood levels of drug catalysed by CYP1A2 (and possibly CYP1A1). This is because the inhalation of induction agents such as polycyclic aromatic hydrocarbons has stopped. There are a few drugs for which this is clinically significant, e.g. warfarin, theophylline, olanzapine and clozapine. Refer to SPS website for further details.

- NRT may be prescribed to adolescents (12-18 years) and ideally there should be a referral to a specialist stop smoking service for young people for provision of suitable support

Nicotine Replacement Therapy (NRT)

- If the first cigarette of the day is taken less than 30 minutes after waking, then initiate with a patch providing nicotine over 24 hours, reducing over 8–12 weeks as per product information. If the first cigarette of the day is taken more than 30 minutes after waking, then initiate with a patch providing nicotine over 16 hours, reducing over 8–12 weeks as per product information
- There is no evidence that any particular form of NRT is superior in achieving cessation. Patches provide more stable serum levels and are simple to use. While 24 hour patches may be best for those who experience cravings on first waking, the 16 hour patch can be useful if vivid dreams and insomnia become a problem on the longer-acting patch
- Short-acting NRT preparations are more useful than patches at suppressing acute nicotine cravings. Short-acting NRT preparations allow individuals to more closely control the dose of nicotine delivered and personalise this according to their need
- Side-effects such as hiccups or GI symptoms are more of a problem with buccal administration. Acidic drinks such as coffee, carbonated or fruit drinks should be avoided for at least 15 minutes before gum or lozenges are taken as they can interfere with absorption
- In patients with stable cardiovascular disease, NRT is a lesser risk than continuing to smoke and is therefore recommended

- Consider offering a combination of nicotine patches and another form of NRT (such as gum, inhalator, lozenge or nasal spray) to people who show a high level of dependence on nicotine or who have found single forms of NRT inadequate in the past
- Nicotine releases catecholamines which can affect carbohydrate metabolism. Smokers with diabetes should be advised to monitor the blood sugar levels more closely than usual when attempting to quit smoking (with or without NRT)
- Moderate to severe hepatic impairment and/or severe renal impairment decreases the clearance of nicotine or its metabolites and NRT should be used with caution
- NRT should not be used in combination with varenicline▼ or bupropion

Varenicline▼

- Varenicline should only be prescribed as a component of a smoking cessation support programme in combination with one to one or group behavioural support
- All individuals using varenicline▼ must be regularly reviewed by a trained healthcare professional
- Varenicline▼ should be prescribed for 2 weeks initially and then normally for no more than 2 weeks' supply on each occasion for a total of 12 weeks. It is licensed for a further 12 weeks to maintain abstinence
- Varenicline▼ should not be used in patients under 18 years old or in those that are pregnant or breastfeeding
- Varenicline should be prescribed with caution in patients with a history of cardiovascular disease or psychiatric illness
- Varenicline▼ should be used cautiously in patients with a history of seizures or other conditions that potentially lower the seizure threshold
- Varenicline▼ should not be used in combination with NRT or bupropion

Bupropion

- Bupropion should only be prescribed as a component of a smoking cessation support programme in combination with one to one or group behavioural support
- All individuals using bupropion must be regularly reviewed by a trained healthcare professional
- Bupropion should be prescribed for 2 weeks initially and then normally for no more than 2 weeks treatment on each occasion for a total of 7-9 weeks only
- Although it works in a different way to NRT there is no evidence that using a combination of NRT plus bupropion will give better quit rates than either measure alone, so is not recommended. If the combination is used blood pressure should be monitored weekly
- Bupropion is contra-indicated in patients with a current or previous seizure disorder, diagnosis of bulimia or anorexia nervosa, severe hepatic cirrhosis, history of bipolar disorder, pregnancy, breast feeding, and caution advised in heavy alcohol intake
- Drug interactions are a significant problem with bupropion; see BNF
- Bupropion should not be used in combination with varenicline▼

4.11 Drugs for Dementia

Choice	Drug	Dosage
1st choice cholinesterase inhibitor	Donepezil tablets 5mg, 10mg; orodispersible tablets 5mg, 10mg	Dose: Initially 5mg once daily at bedtime, increased after one month to 10mg daily
2nd choice cholinesterase inhibitors	Galantamine m/r capsules 8mg, 16mg, 24mg **Gatalin XL® is the recommended cost-effective choice (prescribe by brand)** Or Rivastigmine capsules 1.5mg, 3mg, 4.5mg, 6mg; patch 4.6mg/24 hours and 9.5mg/24 hours	Dose: Initially 8mg once daily for 4 weeks increased to 16mg once daily for 4 weeks; maintenance 16-24mg once daily Dose: Orally: initially 1.5 mg twice daily, increased in steps of 1.5 mg twice daily at intervals of at least 2 weeks according to response and tolerance; usual range 3–6 mg twice daily; max. 6 mg twice daily; if treatment interrupted for more than several days, treatment should be retitrated from 1.5 mg twice daily Transdermal: initially 4.6mg/24 hours after a min of 4 weeks and if well tolerated the dose should be increased to 9.5mg/24 hours (see BNF for full details)
In line with NICE guidance	Memantine tablets 10mg, 20mg; treatment initiation pack 7x5mg, 7x10mg, 7x15mg and 7x20mg; oral drops 5mg/actuation	Dose: Initially 5mg once daily, increased in steps of 5mg at weekly intervals; max 20mg daily

Prescribing Notes

- See COMPASS therapeutic notes on the management of dementia
- See NICE NG97 Dementia: assessment, management and support for people living with dementia and their carers, June 2018 and BMJ visual summary
- For people who are not taking an AChE inhibitor or memantine, prescribers should only start treatment with these on the advice of a clinician who has the necessary knowledge and skills. This could include:
    - secondary care medical specialists such as psychiatrists, geriatricians and neurologists
    - other healthcare professionals (such as GPs, nurse consultants and advanced nurse practitioners), if they have specialist expertise in diagnosing and treating Alzheimer's disease.
- Before starting treatment with an AChE Inhibitor check if the patient is taking a bladder anticholinergic. Co-prescribing is not recommended, see newsletter article *(add link)*
- Once a decision has been made to start an AChE inhibitor or memantine, the first prescription may be made in primary care.
- Offer co-prescription of AChE inhibitor and memantine for severe Alzheimer's disease and consider co-prescription in moderate disease
- For people with an established diagnosis of Alzheimer's disease, primary care prescribers may start memantine without taking advice from a specialist clinician
- Starting doses of AChE inhibitors are not therapeutic doses and should be increased as per titration schedule. The dosing schedules in the table above are suggested dosing schedules only
- Do not stop AChE inhibitors because of disease severity alone. However, in patients progressing to very advanced dementia (end of life care), **review the overall benefit of these agents and consider discontinuation**

- If nausea develops after initiation of an AChE inhibitor, reduce the dose and titrate up more slowly
- Donepezil orodispersible tablets are available for patients who have difficulty in swallowing solid oral dose formulations
- Rivastigmine patches may be an appropriate choice of formulation where a trial of oral medicine was poorly tolerated (see BNF notes on switching from oral to transdermal therapy)
- Be aware of the potential for confusion in dosage units with memantine oral solution. Ensure that dose instructions specify the number of milligrams and the corresponding number of pumps required. Pharmacists should counsel patients on how to administer the required dose. Refer to http://www.medicinesgovernance.hscni.net/wpfb-file/medicines_safety_matters_vol4_issue3_nov2014-2-pdf/

4.11 .1 Management of Behavioural and Psychological Symptoms of Dementia (BPSD)

Alzheimer's disease

Choice	Drug	Dosage
1st choice	**Non-drug treatment / watchful waiting**	
2nd choice	Risperidone 500micrograms, 1mg tablets; liquid 1mg/1ml	Dose: Initially 250micrograms once [unlicensed] or twice daily, increased according to response in steps of 250micrograms twice daily on alternate days; usual dose 500micrograms twice daily (up to 1mg twice daily has been required) Note: Some patients will respond to 250micrograms once daily (lower risk of side-effects) [unlicensed]

Prescribing Notes

- A high proportion of people with dementia who have behavioural and psychological symptoms (BPSD) experience significant improvements over four weeks with no specific treatment. Watchful waiting (or 'active monitoring') is the safest and most effective therapeutic approach unless there is severe risk or extreme distress
- If not already receiving treatment, an AChE inhibitor or memantine at maximum tolerated doses should be considered if a non-pharmacological approach is inappropriate or has been ineffective
- Consider a time-limited trial of antipsychotics only if specific interventions have been unsuccessful, and symptoms are causing extreme distress or risk of harm
- If considering an antipsychotic for BPSD, start with a low dose,

titrate slowly and monitor regularly, e.g. to assess changes in target symptoms. Allow sufficient time for each dose titration to take effect – many patients will respond to risperidone 250micrograms daily, 250micrograms twice daily or 500micrograms daily if given time. Review at 6 and/or 12 weeks with a view to discontinuation. Discontinuation should be default except in extreme circumstances. Consider referral to a specialist if symptoms persist

- Antipsychotics should not be used in Lewy Body Dementia without specialist advice
- If there is an atypical response to antipsychotics review the initial diagnosis. If there is a Parkinsonium response review and consider cause of dementia e.g. Lewy Body Dementia v Alzheimer's Disease
- Risperidone is licensed for: short-term treatment (up to 6 weeks) of persistent aggression in patients with moderate to severe Alzheimer's dementia unresponsive to non-pharmacological approaches and when there is a risk of harm to self or others. Other antipsychotics are not licensed to manage BPSD.
- Quetiapine should not be used for BPSD as it is unlikely to be of any benefit
- When stopping an antipsychotic in patients with BPSD:
    - If the person is receiving low dose, proceed directly with discontinuation. Monitor patient and review at two weeks
    - If the person is receiving a higher dose, taper the dose over one month – reduce to half dose for 2 weeks, review at 2 weeks, discontinue after a further 2 weeks
- Refer to the Alzheimer's Society website for information on non-drug treatment and further advice on managing people with BPSD: https://www.alzheimers.org.uk/site/scripts/download_info.php?downloadID=1148
- See PrescQIPP 'reducing antipsychotic prescribing in dementia' toolkit

Cautions

- In the elderly, antipsychotics should be used with caution because of the side-effect profile, including extrapyramidal symptoms, sedation, anticholinergic effects, cardiovascular effects and tardive dyskinesia
- There is a clear increased risk of stroke and a small increased risk of death when antipsychotics (atypical and typical) are used in elderly people