Central nervous system

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Medicines Formulary – Central Nervous System, Version 8a
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1. Sleep disorders

**CSM advice on benzodiazepines**
Benzodiazepines should be used to treat insomnia only when it is severe, disabling or subjecting the individual to extreme distress.

For transient insomnia, only one or two doses of a hypnotic should be given. For short-term insomnia, a hypnotic may be useful but should not be given for more than three weeks (preferably only one week). Intermittent use is desirable. Chronic insomnia is rarely benefited by hypnotics. Tolerance can occur within 3 to 14 days and long-term efficacy is not guaranteed. Dependence can occur if treatment is continued for more than a few weeks.

**Zopiclone** 7.5mg orally at bedtime, elderly 3.75mg at bedtime

*Or*

**Temazepam** 10mg orally at bedtime (maximum dose, in exceptional circumstances, 40mg daily, for elderly patients the maximum is 20mg daily)

**NOTE:** If prescribed in hospital, ensure hypnotics are prescribed for “in-hospital use only”.

If patient experiences adverse effects to zopiclone, consider

**Zaleplon** 10mg, orally, at bedtime, elderly: 5mg at bedtime

*Or*

**Zolpidem** 10mg, orally, at bedtime, elderly: 5mg at bedtime

**NOTE:** If zopiclone is not effective, zaleplon and zolpidem will not be effective either

**NOTE:** Zolpidem and zaleplon should be prescribed by consultant ONLY in line with NICE technology appraisal 77 ([www.nice.org.uk/ta77](http://www.nice.org.uk/ta77))

2. Anxiety or agitation

Treatment for anxiety differs depending on the intended duration of treatment — with benzodiazepines being used for short-term anxiety.

For longer-term treatment, psychological treatment and drug treatment have similar effectiveness and decisions should be based on patient preference.
For psychological treatment, patients can be referred for cognitive behavioural therapy through their GP. For drug treatment, SSRIs are effective across a wide spectrum of anxiety disorders.

For antidepressants and benzodiazepines, there needs to be a specific discussion and monitoring of adverse effects on stopping medication even after as little as a week of continuous treatment.

For information on treating anxiety in patients with dementia, see section 18. Dementia.

1. **Short-term treatment**

**NOTE:** Benzodiazepines are effective anxiolytics but are only indicated for short-term relief (2 to 4 weeks) of anxiety that is severe, disabling or subjecting the individual to unacceptable distress. This distress can occur alone or in conjunction with insomnia or short-term psychosomatic, organic or psychotic illness.

The use of benzodiazepines to treat short-term “mild” anxiety is inappropriate and unsuitable.

First choice
**Diazepam** 2mg, orally, three times daily (can be increased to 15 to 30mg daily).
For advice on how to discontinue benzodiazepine, see Benzodiazepine withdrawal advice.

2. **Longer-term treatment**

First choice
**Sertraline** 50mg, orally, daily
**NOTE:** The risk of adverse effects or of a worsening of symptoms during the first few days of treatment should be specifically discussed and monitored

Alternatives in the elderly
**Haloperidol** 0.5 to 1.5mg, orally, twice daily (short-term use only)
*Or*
**Quetiapine** 25mg, orally, at night (unlicensed indication)
**NOTE:** Consider and discuss cardiovascular risk factors

Alternative in patients with symptoms such as palpitations, sweating, tremor
**Propranolol** 40mg, orally, daily, increased to 40mg three times daily if required.

3. **Behavioural emergencies (rapid tranquillisation)**

De-escalation (talking patients down) should always be tried first before pharmacological treatment is used. Patients need to be at significant risk to themselves or others before rapid tranquillisation is administered, and prescribers must be aware that there are risks of mortality during rapid tranquillisation.
Oral treatment should be considered first.

For more information on which is the most appropriate treatment, see Rapid Tranquillisation in the General Hospital.

First choice — for most patients

**Lorazepam** For dose information, see Rapid Tranquillisation guideline

*Or*

**Midazolam** For dose information, see Rapid Tranquillisation guideline

**NOTE:** Flumazenil injection MUST be available when using benzodiazepines

Second choice

For information on how and when to use alternative treatments (eg, antipsychotics), see Rapid Tranquillisation in the General Hospital.

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## 4. Depression

Antidepressants should not be used in mild depression unless symptoms have persisted for more than 2 years or unless previous interventions have not been successful.

Following a first episode of moderate-to-severe depression, treatment should be continued for at least six months after symptoms have resolved (2 years in the elderly). Treatment should persist if residual symptoms or other factors increase the risk of relapse. It may take up to 6 weeks to establish improvement with an antidepressant.

First line

**Fluoxetine** 20mg, orally, once daily

*Or*

**Citalopram** 20mg, orally, once daily

*Or*

**Sertraline** 50mg, orally, once daily (especially for patients who have had a previous myocardial infarction)

**NOTE:** Previously successful drugs should also be considered first

Second line (use if first line is ineffective after 3 to 4 weeks or not tolerated)

**Swap to another SSRI**

*Or*

**Mirtazapine** 15 to 30mg, orally, daily. Can be increased to 45mg daily if necessary

**NOTE:** Can be sedating, cause weight gain or worsen confusion

*Or*

**Lofepramine** 70mg, orally, once daily for one week then increased to 140 mg daily

Third line

Refer to a mental health specialist

**Switching antidepressants**

Cross-tapering is preferred (ie, reduce dose of old antidepressant while the dose of the new antidepressant is slowly increased).
Further information on switching antidepressants can be found on the National Electronic Library for medicine website (www.nelm.nhs.uk) or by contacting Pharmacy Medicines Information (ext 5126).

5. Obesity management
First line  
**Orlistat** 120mg, orally, three times a day; take before, during or up to 1 hour after each main meal

For a treatment algorithm, and information on other treatments, see *Obesity — Treatment Interventions*.

6. Nausea and vomiting

Treatment is separated into:

i) Prophylaxis of postoperative nausea and vomiting
ii) Treating established postoperative nausea and vomiting
iii) If motility stimulation is required
iv) Nausea and vomiting in palliative care

**i) Prophylaxis of postoperative nausea and vomiting (PONV)**

Patients should have their risk of PONV assessed before prophylactic treatment is prescribed. Details on how to complete a risk assessment can be found in *Postoperative nausea and vomiting (adults) — clinical guideline*.

Options for prophylaxis include:

- **Cyclizine** 50mg, by slow IV bolus
- **Dexamethasone** 4mg, by slow IV bolus

**ii) Treating established postoperative nausea and vomiting (PONV)**

For details on how to treat established PONV in theatre recovery, see *Postoperative nausea and vomiting (adults) — clinical guideline*.

Treatment of established PONV on wards depends on whether or not the patient has been given a PCA (since, at present, these contain cyclizine):

If patient has been given a PCA
First line  
**Ondansetron** 4mg, dilute in 50mL sodium chloride 0.9% and infuse over 20 mins or give by slow IV bolus (over 2–5 mins), every 6 hours when required
**NOTE:** Allow 1 hour before trying the next antiemetic
If ondansetron is ineffective
**Prochlorperazine** 12.5mg, by IM injection, every 6 hours when required

If patient has **NOT** been given a PCA
First line
**Ondansetron** 4mg, dilute in 50mL sodium chloride 0.9% and infuse over 20 mins or give by slow IV bolus (over 2–5 mins), every 6 hours when required
**NOTE:** Allow 1 hour before trying the next antiemetic

If ondansetron is ineffective
**Cyclizine** 50mg, by IM injection, every 8 hours when required

If cyclizine is ineffective
**Prochlorperazine** 12.5mg, by IM injection, every 6 hours when required

**NOTE:** If an episode of nausea/vomiting develops after a patient starts eating post-op, this could be caused by a surgical condition (eg, ileus, bowel obstruction, acute gastric dilatation). For such patients, placement of a nasogastric tube might be more appropriate than antiemetic medicines.

**iii) If motility stimulants are required**

Pro-kinetic drugs such as domperidone and metoclopramide stimulate gastric emptying and small intestinal transit. They reduce vomiting by strengthening oesophageal sphincter contraction. They are **NOT** useful in situations where smooth muscle contraction is either not possible or not advised.

First choice
**Domperidone** 10 to 20mg orally three times daily, or rectally 30mg three times daily.

Second choice
**Metoclopramide** (do not use in patients <20 years) 10mg orally three times daily

Domperidone is the preferred treatment choice as it is less likely to cause the sedation and acute dystonic reactions that are often experienced by young and very old patients who are treated with metoclopramide. It is licensed for a maximum duration of treatment of twelve weeks.

**iv) Nausea and vomiting in palliative care**

One of the main causes of nausea in palliative care patients is constipation — often due to opioid use. Haloperidol can prevent opiate-induced nausea. Other causes include pain, gastric stasis, hepatic metastases, anxiety, infection and uraemia. Also, concomitant drugs, such as aspirin, NSAIDs, corticosteroids and SSRIs, can contribute to nausea and vomiting.

Treatment should be dependent on the cause of nausea and vomiting. Seek specialist advice.
Haloperidol 1.5mg, orally, at night for 3 to 4 days (for opioid-induced nausea and vomiting)

7. Vertigo and other vestibular disorders

Many types of vertigo can be treated without medication, usually by vertigo rehabilitation exercises. For cases of benign positional vertigo, the Epley manoeuvre can be used.

First choice for preventing episodic vertigo of the "Meniere's" type
Betahistine 16mg, orally, three times daily

First choice for acute vertigo with nausea
Prochlorperazine 5mg, orally, three times daily; can be increased to 10mg three times daily. Maintenance: 5 to 10mg daily.
NOTE: This is a vestibular sedative and should only be taken for a short period. Prolonged use is thought to interrupt natural recovery.

8. Pain management

For further information on how to manage pain in various patient groups, the analgesic ladder, use of syringe drivers and treating opioid toxicity, refer to the Pain management clinical guideline.

For comprehensive information on the acute pain service, the use of patient-controlled analgesia (PCAs), nurse-controlled analgesia, epidurals or nitrous oxide, see the Acute Pain Guideline

For information on managing pain for patients who are in the terminal stage of their illness, refer to one of the following clinical guidelines:
- Care of the Dying
- Care of the Dying (Management in severe renal failure)

Guidance depends on the type of pain experienced. Types include:

i) Mild acute
ii) Moderate acute
iii) Severe acute
iv) More prolonged

i) Mild acute pain
First choice
Paracetamol 500mg to 1g, orally or rectally, every 4 to 6 hours. Max 4g daily.

Intravenous paracetamol can be used in patients who are unable to swallow, or unable to use or refuse suppositories. Liquid or suppositories should be considered first.
Under 50 kg: 15 mg/kg by IV infusion over 15 minutes every 4 to 6 hours. Max. 3g daily.
Over 50 kg: 1 g by IV infusion over 15 minutes every 4 to 6 hours. Max. 4g daily.
NOTE: For patients with hepatocellular insufficiency, chronic alcoholism or chronic malnutrition, the maximum daily dose is 3g

**ii) Moderate acute pain**
Add a weak opioid to regular paracetamol
- **Codeine** 30mg, orally, every 4 to 6 hours (regularly)
  - Or
- **Tramadol** 50 to 100mg orally every 6 hours (regularly)
  - Or
- **Dihydrocodeine** 30mg, orally, every 4 to 6 hours (regularly)

Combination products include:
- **Co-codamol 30mg/500mg** Two tablets, orally, every four to six hours. Maximum: 8 tablets in 24 hours.

For patients taking regular tramadol:
- **Tramadol MR** 100 to 200mg, orally, twice a day

A non-steroidal anti-inflammatory drug (NSAID) can be considered. The following NSAIDs are included in the Wirral formulary:
- First line
  - **Ibuprofen** 400mg, orally, every 6 to 8 hours — for general use
- Second line
  - **Diclofenac** 50mg, orally, every 8 hours — for SHORT-TERM USE ONLY following general or gynaecology surgery, and post-natal obstetrics.
  - Or
  - **Naproxen** 250mg, orally, every 6 hours — for patients with rheumatoid arthritis and osteoarthritis

If oral route is not appropriate
- **Ketoprofen** 100mg, IM or PR, every 12 hours — for use following general or gynaecology surgery

If an NSAID is unsuitable
- **Celecoxib** 100mg, orally, every 12 hours — for use when it is unsafe to use a regular NSAID

For information on when it is safe to prescribe an NSAID, see [Non-steroidal anti-inflammatory drugs — Prescribing in Rheumatoid Arthritis and Osteoarthritis](#)

**iii) Severe acute pain**
Patients with severe acute pain that is not easily controlled should be referred to the Acute Pain Team (Bleep 4396, 4397 or Ext 2473).

*Add to regular paracetamol and consider NSAIDs*
- **Morphine sulphate 10mg/5mL oral solution** 5 to 10mg every 4 hours when required (If oral route not available, give 10mg IM every 4 hours or 2.5mg IV hourly when required)
NOTE: IV morphine is potentially dangerous. It should only be administered by nurses on trauma, ITU or HDU, otherwise by a doctor.

iv) Prolonged pain
First choice
Treat as for acute pain then add

**Morphine sulphate MR capsules (Zomorph®)** Initial dose: determine total daily requirements of morphine sulphate oral solution. This dose should be given in two divided doses of Zomorph.

*(eg, if 6 doses of 10mg morphine oral solution have been given in 24 hours, prescribe Zomorph 30mg, orally, twice a day)*

And *(for breakthrough pain)*
Continue **morphine sulphate oral solution** Give one sixth of the total daily morphine dose every 4 hours when required.

*For patients unable to tolerate morphine refer to Acute Pain Team (or palliative care if appropriate)*

Second choice
Consider simple measures such as:
- Appropriate re-hydration
- Treating opioid-related nausea with anti-emetics (see section 6. Nausea and vomiting)
- If patient is confused, investigate other causes of confusion

Third choice
Consider changing morphine to oxycodone if the patient has:
- Confusion thought to be caused by morphine
- Renal impairment (ie, CKD 4 or 5)
- Nausea and vomiting with morphine that is not alleviated by anti-emetics

**Oxycodone MR tablets (OxyContin®)** Oxycodone is twice as potent as morphine. To change from morphine MR to oxycodone MR, half the dose first — ie, if patient was taking morphine MR 40mg twice daily, to change to oxycodone MR 20mg twice daily.

And *(for breakthrough pain)*

**Oxycodone 5mg/5mL liquid (OxyNorm®)** Give one sixth of the total daily oxycodone dose every 4 hours when required.

**Further guidance**
For information on pain management for specific patient groups, and on using syringe drivers, see *Pain management clinical guideline*. 
9. Neuropathic pain or painful diabetic neuropathy

The International Association for the Study of Pain defines neuropathic pain as “pain caused a lesion or disease of the somatosensory system”. Painful diabetic neuropathy and other neuropathic pain can be difficult to treat. The treatment for both is broadly similar. More information can be found in the Neuropathic pain clinical guideline.

First choice

**Amitriptyline** 10mg orally, at night, increased to 50mg at night if necessary. Higher doses (up to 75mg) are rarely required, offer limited additional analgesia and markedly increase the incidence of side effects. Treatment should be trialled for at least six weeks.

If adequate pain control is achieved with amitriptyline but side effects are not tolerated **Nortriptyline** 10mg orally, at night, increasing by 10 to 25mg daily (depending upon starting dose) every week, as tolerated to 50mg at night. Higher doses (up to 75mg) are rarely required, offer limited additional analgesia and markedly increase the incidence of side effects. Treatment should be trialled for at least six weeks.

**Second choice — replace or add to initial treatment**

**Gabapentin** 300mg, orally, three times daily, then increase according to response in steps of 100 to 300mg daily in three divided doses. Maximum: 3.6g daily. Treatment should be trialled for at least six weeks.

*NOTE: Some patients require a slower titration — see the clinical guideline*

*Or if gabapentin is not effective, or side effects not tolerated*

**Pregabalin** 75mg, orally, twice daily; increased if necessary after two weeks to 150mg twice daily. Treatment should be trialled for at least four weeks.

*NOTE: In secondary care, pregabalin should only be initiated by a consultant*

**Third choice — replace or add (for painful diabetic neuropathy only)**

**Duloxetine** 60mg, orally, daily. Assess after two months and increase to 60mg twice daily if necessary.

*NOTE: Duloxetine should only be initiated in secondary care by a consultant*

*If the above treatment fails*

If patients do not achieve adequate pain control with the treatment above, they should be referred to a neuropathic pain specialist. While waiting for an appointment, add to or replace second choice treatment with **Tramadol** 50mg, orally, four times daily. Increase by 50mg every 3 days up to a maximum of 400mg per day. Treatment should be trialled for four weeks.

*In secondary care, consider adding*

**Capsaicin cream 0.075%** Apply, regularly, three or four times a day. Assess response after six weeks.

*NOTE: Only licensed for post herpetic neuralgia and diabetic polyneuropathy*
Or

**Lidocaine patches 5%** Apply daily to intact, dry, non-hairy, non-irritated skin once daily for up to 12 hours, then remove for at least 12 hours. Assess response at 2 weeks and discontinue treatment after 4 weeks if response is poor.

**NOTE: Only licensed for post herpetic neuralgia**

Or, if the above options fail, consider

**Capsaicin 8% patch** Apply up to 4 patches to the affected area of skin. If applied to the feet, remove after 30 minutes. If applied to any other areas, remove after 60 minutes. Treatment can be repeated after 90 days.

**NOTE: Treatment should be applied under the supervision of Dr Peter Williams**

Or

**Morphine** Dose as per product information

Or

**Oxycodone** Use if morphine is causing intolerable side effects, if the patient does not respond to morphine, or if they have severe renal dysfunction (chronic kidney disease stage 4 or 5)

For further information on the use of opiates refer to the [Pain management clinical guideline](#).

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### 10. Migraine

Most episodic migraine headaches respond to simple analgesics or NSAIDs. Metoclopramide, given a few minutes before the analgesic, enhances absorption (gastric motility is reduced during a migraine attack). Use of regular opiates in migraine is to be strongly discouraged.

Prophylaxis against migraine should be considered if attacks are frequent (two or more a month), cause significant disability or if other acute treatments are contraindicated. It may take up to three months for the full effects of the preventative drug to be seen.

When migraines are chronic (ie, more than 15 days of headaches per month for 3 months) regular analgesic use (defined as more than two doses of any analgesic in a week) should be avoided as it will not have any sustained benefit and will result in medication-induced headaches.

Propranolol is the preferred beta-blocker for migraine prophylaxis, since it is not cardioselective (although, occasionally, metoprolol and atenolol are used). Pizotifen, though licensed, is no longer considered as a first- or second-line agent due to poor efficacy and a high incidence of adverse effects.

Treatment is divided into:

i) **Acute migraine** — for infrequent episodic migraines

ii) **Prophylaxis of migraine** — for frequent/ chronic migraine
i) Acute migraine

First choice
**Paracetamol** 1g, orally, every 4 to 6 hours. Maximum 4g daily.
*Or*
**Aspirin** 600 to 900mg, orally, every 4 to 6 hours. Maximum 4g daily.
*Or*
**Ibuprofen** 200 to 400mg, orally, three times a day. Take with or after food; max: 2.4g daily
*Or*
**Naproxen** 250 to 500mg, orally, twice a day. Take with or after food; max: 1g daily

**Also, if antiemetic is required**
First choice
**Metoclopramide** 10mg, orally, three times a day
Second choice
**Cyclizine** 50mg, orally, three times a day
*Or*
**Prochlorperazine** 5mg, orally, three times a day
Third choice
**Ondansetron** 4-8mg, orally, three times a day

**Second choice**
**Sumatriptan** 50mg (some patients require 100mg), orally; dose can be repeated after 2 hours if migraine recurs; max: 300mg in 24 hours

**Third choice**
**Almotriptan** 12.5mg, orally, as soon as possible after onset of migraine, repeated after 2 hours if migraine recurs (patients not responding should not take a second dose for the same attack); max: 25mg in 24 hours

**NOTE:** All 5-HT1 agonists (ie, triptans) are contraindicated for patients with ischaemic heart disease, moderate and severe hypertension, TIA or stroke, and peripheral vascular disease

ii) Prophylaxis of migraine

First choice
**Propranolol** Initially 40mg, orally, two to three times daily
Then
**Propranolol modified release** 80 to 160 mg, orally, once daily

*Or*
**Amitriptyline** 10mg, orally, at night, increased as required to 25 or 50 mg at night (unlicensed use)
*Or*
**Nortriptyline** 10 to 20mg, orally, at night (unlicensed use)

**Second choice**
**Sodium valproate** 300mg, orally, twice daily, increased to 1.2g daily in divided doses (unlicensed use)

Or

**Topiramate** 25mg, orally, at night; increase by 25mg per day every 2 weeks until on 100 to 200mg daily (in two divided doses)

**NOTE:** Women of childbearing potential must be using effective methods of contraception when taking sodium valproate or topiramate.

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### 11. Epilepsy

Epilepsy should only be diagnosed by a neurologist or other epilepsy specialist (due to the high rate of mis-diagnosis, as recommended by NICE).

Treatment with antiepileptic drugs is usually recommended after a second epileptic seizure. Anti-epileptic therapy should be considered after a first unprovoked seizure in patients that:

- Have a previous neurological deficit (CNS involvement)
- Have structural abnormality in brain imaging
- Have an EEG that shows unequivocal epileptic activity
- Consider the risk of seizure recurrence to be unacceptable

For epilepsy resistant to monotherapy, the diagnosis should be reviewed and the patient’s compliance with medication assessed.

Consider combination therapy if treatment with two first-line antiepileptics has failed, or seizure control is not achieved on the maximum dose of the first antiepileptic.

**i) Partial and secondary generalised seizures**

First line

**Carbamazepine.** 100 to 200mg, orally, once or twice daily, increased by 100 to 200mg every 2 weeks according to response. Usual maintenance dose: 800mg to 1200mg daily in divided doses (maximum 2g daily).

Or

**Lamotrigine** — dose depends on whether used as monotherapy or as an adjunct

- **Monotherapy** 25mg, orally, daily for 14 days, then 50mg daily for 14 days, then increase by 50 to 100mg/day every 7 to 14 days according to response. Usual maintenance dose: 100 to 200mg daily in 1 or 2 divided doses.

- **Adjunctive therapy with valproate** 25mg, orally, on alternate days for 14 days, then 25mg daily for 14 days, then increase by 25 to 50mg/day every 7 to 14 days; usual maintenance dose: 100 to 200mg daily in 1 or 2 divided doses

**NOTE:** The initiation schedule for lamotrigine must be adhered to. Higher initial doses or more rapid dose escalation are associated with severe skin reactions

Second line

**Sodium valproate** 300mg, orally, twice daily, increased by 200mg/day every 3 days according to response to maximum 2.5g daily in divided doses.

Or

**Levetiracetem** — dose depends on whether used as monotherapy or as an adjunct
• **Monotherapy** 250mg, orally, twice daily, then increase to 500mg twice daily after two weeks. The dose can be further increased by 250mg twice daily every two weeks depending on clinical response. Max: 1500mg twice daily

• **Adjunctive therapy** 500mg, orally, twice daily. The dose can be increased by 500mg twice daily every two to four weeks according to response and tolerability. Max: 1,500mg twice daily.

**NOTE:** Only to be initiated by an epilepsy specialist

**Or**

**Oxcarbazepine** 300mg, orally, twice daily. The dose can be increased by 600mg/day at weekly intervals to achieve a clinical response. (In hospital, dose increases up to 2,400mg/day have been achieved over 48 hours.) Therapeutic range: 300 to 1,200mg twice daily.

**NOTE:** Only to be initiated by an epilepsy specialist

**NOTE:** In trials, most patients receiving oxcarbazepine as adjunctive therapy were unable to tolerate 2400mg/day dose without the dose of their other antiepileptic medicines being reduced (due to CNS-related adverse events)

**ii) Primary generalized seizures and uncertain seizure types**

First choice

**Sodium valproate** (dose as above)

Alternative

**Lamotrigine** (dose as above for monotherapy)

**Withdrawal of antiepileptic therapy**

Antiepileptic therapy can be considered for withdrawal if a patient has been seizure-free for at least 2 years. However, discontinuation is not always appropriate, particularly for conditions where the risk of recurrence is high. These include patients with juvenile myoclonic epilepsy, other types of primary generalized epilepsy and most cases of symptomatic epilepsy (ie, structural lesions, such as tumours or vascular malformations, etc).

Due to the risk of rebound seizures, abrupt withdrawal should be avoided. Dose reduction should be carried out over a number of months. If the patient is taking several antiepileptic medicines, only one should be withdrawn at a time.

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**12. Status epilepticus**

Status epilepticus is a continuous seizure lasting for at least 30 minutes or at least two discrete seizures between which the patient does not regain consciousness. It should be treated as a medical emergency since mortality can be high in this group of patients.

For serial or prolonged seizures

**Rectal diazepam** 10 to 20mg stat

Alternative
**Buccal midazolam** 10mg stat

**NOTE:** Midazolam solution is available in two concentrations: 10mg/2mL and 10mg/mL. The correct dose, volume and concentration of midazolam must be prescribed and administered. Wirral Drug & Therapeutics Panel advises the use of licensed buccal midazolam solutions where possible. Buccolam® (10mg/2mL) is licensed to treat prolonged, acute, convulsive seizures in infants, toddlers, children and adolescents (from 3 months to <18 years). Its use in adults is off label.

If generalised status epilepticus develops

Secure airway, give oxygen, assess cardiac and respiratory function, secure IV access, check blood gases, glucose, U+Es, full blood count, liver function tests, calcium, clotting, antiepileptic drug concentrations

**Lorazepam** 4mg, IV, stat

*Or, if lorazepam unavailable*

**Diazepam** 10mg, IV, stat (use emulsion for injection)

*Or, if IV access is delayed*

**Diazepam** 10mg, rectally, stat

If the patient is hypoglycaemic

**Glucose 10%** Give 150 to 160mL, by IV infusion, over 10–15 minutes

*Or*

**Glucose 20%** Give 75 to 80mL, by IV infusion, over 10–15 minutes

*Or*

**Glucagon** 1mg, by IM injection, stat

After 10–15 minutes, repeat blood glucose measurement. If patient is still hypoglycaemic (blood glucose <4mmol/L), repeat above treatment.

*Plus give a long-acting carbohydrate — see section 2 (“Hypoglycaemia”).*

If the patient has impaired nutritional status or is known to abuse alcohol

**Pabrinex** give 2 pairs of ampoules by IV infusion in 100mL sodium chloride 0.9% over 30 minutes

**NOTE:** If the patient usually takes antiepileptic medicines, continue these (use IV or nasogastric routes if the oral route is unavailable — contact pharmacy for advice).

If status epilepticus persists

**Phenytoin** 20mg/kg (calculate dose using ideal body weight), by slow IV injection or infusion, at a rate no greater than 50mg per minute (dilute in sodium chloride 0.9%, max concentration 10mg/ml). Maximum: 1.8g

**NOTE:** Give phenytoin via an in-line filter; ECG and blood pressure monitoring is required

Followed by

**Phenytoin** 100mg, by slow IV injection or infusion, every 6 to 8 hours (dilute in sodium chloride 0.9%, max concentration 10mg/ml)

**NOTE:** Contact pharmacy for advice on blood levels

If status epilepticus persists, discuss further management with critical care
13. Parkinson’s disease

Treatment of Parkinson’s disease is often a compromise between symptom control and side effects. All antiparkinsonian drugs should be started at low doses and increased slowly to reduce adverse effects. Slow withdrawal after long-term treatment is advised to avoid marked worsening of parkinsonism or neuroleptic malignant-like syndrome. All patients with a likely diagnosis of Parkinson’s disease should be referred to a Parkinson’s disease specialist for advice on its initial treatment.

Parkinson’s symptoms are often controlled by a number of different agents taken at precise times throughout the day.

NOTE: A DELAY in prescribing antiparkinsonian medication on admission is likely to WORSEN symptom control and cause anxiety. Furthermore, medication MUST be prescribed and administered at the EXACT TIMES the patient takes them at home.

For information on how to diagnose Parkinson’s disease, useful contact numbers and suggestions for treating other conditions that can affect Parkinson’s disease, see Wirral Parkinson’s Disease Guidelines.

Selecting an appropriate treatment depends on the patient’s age at the onset of disease, and the main symptoms that they are experiencing.

i) If tremor IS the main symptom

For patients under 65 years of age

Trihexyphenidyl 1mg, orally, daily, increasing gradually to 5-15mg daily in 3 to 4 divided doses; usual dose: 2mg three times a day

Or

Orphenadrine 50mg, orally, daily, increasing gradually to 150-300mg daily in divided doses

NOTE: These can be used in patients over 65 years if there is no evidence of cognitive impairment; however they are generally best avoided in the elderly.

For patient over 65 years of age — for postural/action tremor (ie, not resting tremor) Propranolol 40mg, orally, twice or three times a day. Maintenance dose 80 to 160 mg may be required.

ii) If tremor IS NOT the main symptom and there is no sign of cognitive impairment

First line — for patients OVER 70 years

Levodopa (Co-beneldopa or Co-careldopa) 12.5/50mg, orally, once or twice daily; adjust dose by 12.5/50mg daily every 4 to 7 days; usual maintenance dose: 75/300 to 150/600mg daily in divided doses. For more information on using levodopa, see Levodopa prescribing advice.

First line — for patients UNDER 70 years of age
**Ropinirole** 250 micrograms, orally, three times a day, increased weekly over 4 weeks to initial maintenance dose of 1 mg three times a day (as per starter pack). Usual maintenance dose: 3 to 9 mg daily; maximum: 24 mg daily.

**NOTE:** Prolonged release preparations are available for when compliance or motor fluctuations become a problem. However, these are considerably more expensive so should not be used for initial therapy

*Or*

**Pramipexole** 264 micrograms, orally, daily in 3 divided doses; increase every 5 to 7 days; max: 3.3 mg daily in 3 divided doses (dose expressed as pramipexole base)

**NOTE:** Prolonged release preparations are also available but are considerably more expensive than immediate release tablets

*Or*

**Selegiline** 5 mg, orally, each morning; increase to 10 mg each morning (or 5 mg at breakfast and 5 mg at midday). Can be used as monotherapy or adjuvant therapy if patient has motor complications

*If selegiline is contraindicated/not tolerated or if once-daily medication would aid compliance*

**Rasagiline** 1 mg, orally, once daily

*Shared care guidelines for rasagiline* are available.

Second line — for patients **OVER 70 years**

**Ropinirole** or **pramipexole** or **selegiline** or **rasagiline** can be used as adjuvant therapy or when patients experience adverse effects with levodopa. For doses, see above.

Second line — for patients **UNDER 70 years**

**Levodopa** can be added to or replace first line treatment symptom control is inadequate, or there are problems with side effects or cognitive impairment

If “end-of-dose wearing off” symptoms develop with levodopa — add

**Entacapone** 200 mg, orally, with each dose of levodopa (max: 2 g daily)

**NOTE:** MUST be taken at the same times as levodopa, available as combination product with levodopa (ie, Stalevo®), which may improve compliance

*Or*

**Tolcapone** 100 mg, orally, three times daily (must be at least 6 hours between each dose)

Maximum 200 mg, orally, three times daily in exceptional circumstances.

**NOTE:** ONLY to be prescribed by Dr O’Neill, Consultant in Elderly Medicine

Third line

**Apomorphine** Dose determined by Parkinson’s disease team following apomorphine challenge. For more information on the use of apomorphine, including pre-treatment with domperidone, see [Apomorphine prescribing advice](#)

**NOTE:** Useful for patients experiencing unpredictable ‘off’ periods or unacceptable dyskinesias with dopaminergic drugs, or those unable to swallow other medicines; may allow dose reduction of levodopa

*Or*

**Rotigotine** 4 mg/24 hour patch (replace every 24 hours) increase in steps of 2 mg/24 hours at weekly intervals if required. Max: 16 mg/24 hours
iii) For controlling symptoms of moderate dyskinesia

Amantadine 100mg, orally, daily; increase after one week to 100mg twice daily. Maximum: 400mg daily

iv) Nausea in patients with Parkinson’s disease

Nausea and vomiting is common with anti-parkinsonian medicines, although tolerance to this side effect can develop. Suitable anti-emetics include domperidone or ondansetron. Metoclopramide and prochlorperazine may worsen parkinsonian symptoms and must be avoided. Cyclizine can cause tremor.

v) Parkinson’s disease-induced hallucinations

Hallucinations can be caused by many anti-parkinsonian medicines (eg, anticholinergics, dopamine agonists, amantadine, selegiline, entacapone) and might respond to dose reduction. If needed, low-dose quetiapine can be tried.

Quetiapine 12.5mg, orally, twice a day for two doses. If successful response, continue and increase if necessary up to 50mg daily in 2 divided doses. Consult psychiatric liaison if unsuccessful

Traditional antipsychotics like haloperidol should be avoided as they can worsen Parkinsonian symptoms. If hallucinations persist and are associated with cognitive impairment, consider referral to a Parkinson’s disease specialist/Old Age Psychiatry.

vi) Drug-induced Parkinson’s disease

The symptoms of Parkinson’s disease can be induced by medicines that are dopamine antagonists (eg, antipsychotics, metoclopramide). These symptoms can be treated with anticholinergics (eg, procyclidine). However, if possible, the causative medicine should be withdrawn or have their dose reduced.

Procyclidine 2.5 to 5mg, orally, three times daily; increase dose gradually if necessary to a max: 30mg daily in 3 divided doses.

14. Restless legs syndrome

Most cases of restless legs syndrome (RLS) are primary with unknown origin. The three main reversible causes of RLS are related to depleted iron stores:
- Iron-deficiency anaemia
- End-stage renal disease
- Pregnancy (this usually resolves after birth and is possibly due to iron deficiency)

Other causes include B12 or folate deficiency, and peripheral neuropathy.

Treatment depends on the severity and frequency of symptoms. Mild RLS can be controlled by offering the patients reassurance and through non-pharmacological interventions such as:
- Good sleep hygiene
- Walking and stretching; taking a bath; relaxation exercises and massaging the affected limbs these may provide relief during an attack
- Avoidance of drugs that can aggravate symptoms of RLS (e.g. CNS stimulants, drugs that block dopamine transmission – e.g. prochlorperazine, metoclopramide, diuretics, tricyclic antidepressants, calcium antagonists and phenytoin
- Caffeine and alcohol should also be avoided.

Secondary causes should be identified and corrected. A serum ferritin level of <50mcg/L (normal range: 30–284mcg/L) has been associated with greater severity of RLS. Correction of the deficiency has been reported to improve or resolve symptoms.

Severe cases may require drug therapy. Patients must have an RLS rating score of greater than 20 before drug therapy is considered (for information on RLS rating, see Restless legs syndrome rating scale). Treatment can be long term although an attempt to gradually withdraw it could be made if symptoms are controlled. Intermittent therapy may be appropriate. Treatment should be reviewed after 3 months and stopped if little or no benefit is seen.

In RLS due to iron deficiency
Ferrous sulphate 200mg, orally, three times daily (in primary care, ferrous fumarate is the iron preparation of choice)

For initiation by a DME consultant only
Pramipexole 125micrograms (dose expressed as salt), orally, daily given 2 hours before retiring to bed. The dose can be doubled every 4 to 7 days as required to a maximum of 750micrograms daily.
Or
Ropinirole 250micrograms, orally, at night for 2 days, then increase (if tolerated) to 500micrograms at night for 5 days, then to 1mg at night for 7 days, the dose can be increased further at weekly intervals in steps of 500micrograms daily according to response; usual dose: 2mg at night; max: 4mg at night
NOTE: Repeat dose titration if treatment is restarted after a break of more than a few days

Alternative agents (unlicensed indications with limited evidence base)
Gabapentin 300mg, orally, at night; increased gradually to a max: 2.4g daily
Or
Clonazepam 0.5 to 2mg, orally, once daily in the evening
Severe unremitting RLS may require treatment with opioid analgesics. Weak opioids (e.g., codeine) should be tried first, stronger opioids (e.g., morphine) should only be used when other treatments have failed and symptoms are severe.

15. Opioid dependence/misuse

For patients being treated with methadone or misusing opiates, see Opioid dependence algorithm

If the patient is taking methadone as part of a drug substitution programme, contact the patient’s drug service to confirm their usual dose before prescribing methadone. If the patient’s drug service is closed or the patient is not a client at drug service, confirm that the patient is taking methadone or opiates via a urine sample.

16. Alcohol withdrawal

When patients present with symptoms of alcohol withdrawal, the severity of their withdrawal symptoms should be documented using the Alcohol Integrated Care Pathway. This pathway is also used to prescribe appropriate doses of chlordiazepoxide.

Vitamin supplementation

For patients with established, or at high risk of, Wernicke’s encephalopathy

Parenteral thiamine (Pabrinex®) Give 2 pairs of ampoules, by IV infusion, in 100mL sodium chloride 0.9% or glucose 5% over 15 to 30 minutes, three times a day for 3 days

Then, in established Wernicke’s encephalopathy ONLY if symptoms improve after initial treatment

Parenteral thiamine (Pabrinex®) Give 1 pair of ampoules, by IV infusion, in 100mL sodium chloride 0.9% or glucose 5% over 15 to 30 minutes, once a day for a further 3 to 5 days

(then continue with oral thiamine as below)

NOTE: In large doses, Pabrinex has been associated with anaphylactic reactions. Ensure treatment for anaphylaxis is available.

For all patients

Multivitamins one tablet/capsule, orally, once daily

And

Thiamine 100mg, orally, three times daily. Delay thiamine until after course of Pabrinex® has completed.

NOTE: Review on discharge whether there is a need to continue vitamin supplements
17. Smoking cessation (“Stop Smoking” pharmacotherapies)

All patients smoking status should be documented on admission. Smokers should be informed that the hospital has a smoke free policy and have their motivation to quit assessed.

Wirral Stop Smoking Service information should be made available to all smokers, regardless of whether they are motivated to quit or not.

Wirral’s Stop Smoking Service is available to anyone in need of help and advice.
Telephone for free advice: 0151 630 8383
Locations and opening times for drop-in clinics can be found at: http://www.wirralct.nhs.uk/ourservices/stopsmoking/

Other useful websites include: www.ash.org.uk and www.smokefree.nhs.uk

Therapies should be chosen with the following taken into account:
- Contraindications and potential for adverse affects
- Clients’ personal preference
- Availability of appropriate counselling and support
- Likelihood of completing course of treatment
- Previous experience of stop smoking aids

1. For patients in secondary care

First line
Nicotine replacement therapy For information on product selection, and when NRT should or should not be prescribed, see Nicotine replacement therapy for hospital inpatients
Or Varenicline 500micrograms, orally, once daily for 3 days, increase to 500micrograms twice daily for 4 days then 1mg twice daily for 11 weeks; start 1 to 2 weeks before quit date. NOTE: Only to be prescribed on the advice of a respiratory consultant or Wirral Stop Smoking advisor. DO NOT commence course without organising ongoing support with Wirral Stop Smoking Service.

Second choice
Bupropion 150mg, orally, daily for 6 days, then 150mg twice daily; continue for 7 to 9 weeks; start 1 to 2 weeks before quit date. NOTE: Only to be prescribed on the advice of a respiratory consultant or Wirral Stop Smoking advisor. DO NOT commence course without organising ongoing support with Wirral Stop Smoking Service.

2. For patients in primary care

Prescribing information for patients treated in primary care can be found in NHS Wirral’s Smoking Cessation Pharmacotherapy Guidelines.
18. Dementia

Pharmacological interventions for patients with dementia include:

i) Those to treat behavioural problems
   - Medicines prescribed by the Memory Clinic

i) Treating behavioural problems

For more information on how to manage and treat patients with dementia, see Dementia Care — clinical guideline.

For patients with Alzheimer’s dementia

1. To treat psychosis, aggression or severe anxiety/agitation
   - First line
     Risperidone 0.25mg, orally, twice a day. Increase dose according to response every other day by 0.25mg twice a day; usual dose: 0.5mg twice a day. Max: 1mg twice a day.
     - Second line
       Refer to liaison psychiatry

2. To treat depression, apathy or moderate anxiety/agitation
   - First line
     Citalopram 20mg, orally, daily
     Or
     Sertraline 50mg, orally, daily
     - Second line
       Mirtazapine 15mg, orally, daily at night. Increase dose if necessary after two to four weeks to 30mg daily at night. Max: 45mg daily at night. Use high doses cautiously in elderly patients.
     - Third line
       Refer to liaison psychiatry

For patients with Parkinson’s dementia or dementia with Lewy bodies

1. To treat psychosis, aggression or severe anxiety/agitation
   - First line
     Quetiapine 25mg, orally, daily. Increase dose according to response every other day by 25mg per day; max: 100mg twice a day.
     NOTE: This indication is unlicensed
     - Second line
       Refer to liaison psychiatry
2. To treat depression, apathy or moderate anxiety/agitation
First line
**Citalopram** 20mg, orally, daily

Second line
Refer to liaison psychiatry

**ii) Medicines prescribed by the Wirral Memory Assessment Service (WMAS) or Chester Memory Clinic**

The acetylcholinesterase inhibitors, donepezil, rivastigmine and galantamine, and the glutamate receptor antagonist, memantine, are available to treat dementia in Alzheimer’s disease.

**Initiation of these drugs on the NHS must be made by a consultant psychiatrist working in WMAS or the Memory Clinic in Chester.**

Patients receive their supply of acetylcholinesterase inhibitors via an FP10 (HNC) prescription which is dispensed by a community pharmacy

Patients living in Wirral attend the Wirral Memory Assessment Service — for enquiries, please telephone 0151 488 7758.
Patients living in Neston, Ellesmere Port or around Chester attend the Memory Clinic in Chester — for enquiries, please telephone 01244 364560.

**In primary care: acetylcholinesterase inhibitors and memantine should not be initiated by GPs.**

**In secondary care: Patients’ own drugs should be used wherever possible; if further supplies are required please contact the appropriate service above.**

**NOTE: Some patients are treated privately and obtain these medicines on private prescription.**