4.1 HYPNOTICS AND ANXIOLYTICS

Benzodiazepine prescribing guidelines
- Benzodiazepines must not be prescribed routinely.
- Benzodiazepines must not be prescribed for more than 10 nights as a hypnotic or as an anxiolytic for more than 4 weeks.
- Apart from chronic users, patients should generally not be discharged from hospital taking a benzodiazepine. An example of where it may be appropriate includes patients receiving palliative care.
- Can be difficult to withdraw benzodiazepines if they have been taken regularly for more than a few weeks.

4.1.1 HYPNOTICS

- **Temazepam**
  - 10mg tablets
  - 10mg/5mL elixir

  Temazepam for ward stock must be ordered using the Controlled Drug order book.

- **Zopiclone**
  - 3.75mg, 7.5mg tablets

Hypnotics should only be prescribed for short term use. Patients requiring hypnotics in hospital should have them prescribed on the PRN side of the prescription chart. Such patients will not have hypnotics prescribed to them on discharge.

It is recommended that, because of the lack of compelling evidence to distinguish between zopiclone or the shorter acting benzodiazepine hypnotics, the drug with the lowest purchase cost (taking into account daily required dose and product price per dose) should be prescribed. ([NICE Technology Appraisal No 77](https://www.nice.org.uk/page/advice-technology-appraisals)).

Temazepam is therefore the preferred option for all patients on the basis of cost. However, in the Trust, zopiclone may be considered for first line use as it is not subject to internal controlled drug restrictions.

4.1.2 ANXIOLYTICS

- **Diazepam**
  - 2mg, 5mg tablets
  - 2mg/5mL elixir
  - 5mg/2.5mL, 10mg/2.5mL rectal solution
  - 10mg/2mL injection (emulsion)

- **Lorazepam**
  - 1mg, 2.5mg tablets
  - 4mg/mL injection
4.2 DRUGS USED IN PSYCHOSES AND RELATED DISORDERS

4.2.1 ANTIPSYCHOTIC DRUGS

- **Haloperidol**
  - 500microgram capsules
  - 1.5mg, 5mg tablets
  - 2mg/mL liquid
  - 5mg/mL injection

Care: high risk of extrapyramidal reactions when given by the parenteral route especially in young people.

Other antipsychotic medication should only be initiated on the advice of a psychiatrist.

4.3 ANTIDEPRESSANT DRUGS

4.3.1 TRICYCLIC AND RELATED ANTIDEPRESSANT DRUGS

- **Lofepramine**
  - 70mg tablets
  - 70mg/5mL liquid

4.3.3 SELECTIVE SEROTONIN RE-uptake INHIBITORS

- **Fluoxetine**
  - 20mg capsules
  - 20mg/5mL liquid

- **Citalopram**
  - 10mg, 20mg, 40mg tablets
  - 40mg/mL oral drops (SF)
  - NB 8mg (4 drops) equivalent to 10mg tablet

- **Sertraline**
  - 50mg, 100mg tablets
  - Consider as first line for patients post MI and epilepsy

- **Paroxetine**
  - 20mg, 30mg tablets
  - 10mg/5ml liquid
  - Drug of choice in liver impairment due to short half life
4.3.4 OTHER ANTIDEPRESSANT DRUGS

- **Duloxetine** 30mg, 60mg capsules

- **Mirtazepine** 15mg, 30mg, 45mg tablets
  15mg, 30mg, 45mg orodispersible tab
  15mg/mL oral solution

- **Venlafaxine** 37.5mg, 75mg tablets
  75mg, 150mg modified release caps

4.6 DRUGS USED IN NAUSEA AND VERTIGO

See local guidelines for advice on the choice of anti-emetic in palliative care

See Trust policy for the Protocol for Prevention and Treatment of Chemotherapy Induced Nausea and Vomiting
Guidelines for the management of post-operative nausea and vomiting are under development

**Antihistamines**

- **Cyclizine** 50mg tablets
  50mg/mL injection

- **Cinnarizine** 15mg tablets

- **Promethazine** 10mg, 25mg tablets
  5mg in 5mL elixir

  May be used for short term treatment of SEVERE nausea and vomiting in pregnancy

**Phenothiazines and related drugs**

- **Prochlorperazine** 5mg tablets
3mg buccal tablets (1-2 tablets twice daily)
5mg/5mL syrup
5mg, 25mg suppositories
12.5mg/mL injection

Prochlorperazine is NOT licensed for intravenous use since it may cause hypotension and is irritant to veins.

- **Levomepromazine**
  (methotrimeprazine)
  25mg tablets
  6mg tablets *(unlicensed)*
  25mg/mL injection

- **Haloperidol**
  500microgram capsules
  1.5mg tablets
  5mg/mL injection

**Domperidone and metoclopramide**

- **Domperidone**
  10mg tablets
  5mg/5mL suspension
  30mg suppositories

- **Metoclopramide**
  10mg tablets
  5mg/5mL elixir
  10mg/2mL injection

**5HT₃ antagonists**

- **Ondansetron**
  8mg tablets
  4mg/5mL syrup **SF**
  4mg/2mL, 8mg/4mL injection
  4mg oral lyophilisates (Zofran Melt®)

**Steroids**

- **Dexamethasone**
  2mg tablets
  2mg/5mL oral solution
- **Dexamethasone sodium phosphate** 10mg/2mL injection

**Neurokinin receptor agonist**

- **Aprepitant** 80mg, 125mg capsules

  Restricted for use with highly emetogenic chemotherapy as per Trust Protocol

**Drugs for Meniere’s disease**

- **Betahistine** 8mg, 16mg tablets

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### 4.7 ANALGESICS

This chapter also includes guidance on:

- Neuropathic pain
- Pain management (acute and chronic)
- Post-operative pain
- Pain relief in chronic opioid users
- Management of migraine

### 4.7.1 NON-OPIOID ANALGESICS

- **Paracetamol** 500mg tablets
  - 500mg soluble tablets
  - 120mg/5mL, 250mg/5mL suspension
  - 120mg, 240mg, 500mg suppositories
  - 1g/100mL infusion (hospital only)

  **Paracetamol infusion is indicated for post-operative pain relief, for patients NBM and nil PR or who refuse PR medication. It should be stopped as soon as the patient begins to take orally.**

**Compound analgesic preparations**

- **Co-codamol 8/500** tablets
• Co-codamol 30/500
dispersible tablets
effervescent tablets

Combinations with low doses of opioid e.g. co-codamol 8/500 have not been proven to provide more effective analgesia than paracetamol alone, yet still have opioid side effects. It is extremely important that when prescribing co-codamol that the strength is specified. **Nurses will refuse to administer orders for co-codamol if the strength is not stated.**

### 4.7.2 OPIOID ANALGESICS

**NPSA Guidance on reducing dosing errors with opioid medicines**

When opioid medicines are prescribed, dispensed or administered, in anything other than acute emergencies, the healthcare practitioner concerned, or their clinical supervisor, should:

• Confirm any recent opioid dose, formulation, frequency of administration and any other analgesic medicines prescribed for the patient. This may be done for example through discussion with the patient or their representative (although not in the case of treatment for addiction), the prescriber or through medication records.

• Ensure where a dose increase is intended, that the calculated dose is safe for the patient (e.g. for oral morphine or oxycodone in adult patients, not **normally** more than 50% higher than the previous dose).

• Ensure they are familiar with the following characteristics of that medicine and formulation: usual starting dose, frequency of administration, standard dosing increments, symptoms of overdose, common side effects.

While dose increments should be in line with this guidance, it is recognised that in palliative care higher than normal doses may be required (see palliative care chapter). These recommendations are not designed to restrict clinical use of opioid medicines, but to ensure they are used in a way that is as safe as possible for patients.

### Preparations

**Controlled Drug Prescribing Regulations apply to products marked “CD”. See guidelines**

• **Codeine**
  - 15mg/5mL linctus
  - 15mg, 30mg tablets
  - 60mg/mL injection CD

• **Diamorphine**
  - 5mg, 10mg, 30mg, 100mg, 500mg injection CD

• **Dihydrocodeine**
  - 30mg tablets
  - 10mg/5mL elixir
- **Morphine**
  5mg *m/r tablets* (MST®) CD
  10mg, 30mg, 60mg, 100mg, 200mg *m/r capsules* (Zomorph®) CD
  10mg/5mL oral solution
  (This strength of morphine solution is NOT legally a CD but in the hospital and hospice setting must be ordered as such, kept in the CD cupboard and the full CD register records kept.)

  100mg/5mL concentrated oral solution CD
  (Oramorph concentrated solution)
  10mg/mL injection CD

  Morphine has a bioavailability of about 35% when given orally. Depending on the route administered the following doses may be considered roughly equianalgesic
  10mg oral morphine ≈ 3 to 5mg IV/IM morphine

- **Fentanyl**
  12.5, 25, 50, 75, 100micrograms per hour transdermal patches CD.
  Specify brand when prescribing.

- **Oxycodone**
  5mg, 10mg, 20mg capsules (normal release, Oxynorm®) CD
  5mg/5mL oral solution SF CD
  10mg/mL concentrated oral solution SF CD
  5mg, 20mg, 40mg, 80mg *MR tablets* (Oxycontin®) CD
  10mg/mL injection (1mL amp and 2mL amp) CD

  NB Oxycodone has only been approved by Chester LMMC as second line treatment for use when morphine is not tolerated

- **Pethidine**
  50mg, 100mg injection

- **Tramadol**
  50mg capsules
  50mg soluble tablets
  100mg/2mL injection

  A number of modified release tramadol preparations are available but should not be considered first line especially for the management of acute pain. They are considerably more expensive than the normal release preparations and no modified release preparation has yet been approved for use by Western Cheshire LMMC.
4.7.3 NEUROPATHIC PAIN

First line

Amitriptyline

10 mg at night, increased slowly as necessary to a maximum of 75mg at night. Higher doses are rarely needed.

Second line

Gabapentin

300mg on day 1, 300mg twice daily on day 2 then 300mg three times daily on day 3, then increased according to response in steps of 300mg daily in three divided doses. (Table 1)

To reduce the incidence of side effects or in the elderly, very sick or renally impaired, a slower titration regime may be more appropriate (Table 2)

<table>
<thead>
<tr>
<th>Table 1 - standard titration regime</th>
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<tbody>
<tr>
<td>Day</td>
</tr>
<tr>
<td>-----</td>
</tr>
<tr>
<td>1</td>
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<tr>
<td>2</td>
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<tr>
<td>3</td>
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Dose may be further increased by 300mg/day every three days as needed to a maximum of 1200mg tds

<table>
<thead>
<tr>
<th>Table 2 - Slow titration regime</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day</td>
</tr>
<tr>
<td>-------</td>
</tr>
<tr>
<td>1+2</td>
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<tr>
<td>3 to 5</td>
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<tr>
<td>6 to 9</td>
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<tr>
<td>10 to 16</td>
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<tr>
<td>17 to 23</td>
</tr>
</tbody>
</table>

Doses may be further increased by 300mg/day every 3-7 days as needed to a maximum of 1200mg tds

For each regime, the titration should be stopped at the lowest dose which achieves pain control.

NB. Gabapentin should be prescribed and supplied as CAPSULES as this is the most cost-effective preparation. i.e. doses of 600mg and above should be prescribed in multiples of 300mg capsules NOT as 600mg tablets.

Basic NHS cost: Gabapentin 300mg capsules - £8.73 for 100
(Drug tariff March 09) Gabapentin 600mg tablets - £106.00 for 100
Pregabalin

Only to be used if intolerable side effects with gabapentin or if gabapentin ineffective at maximum tolerated doses.

150mg per day, increased if necessary after 3 to 7 days to 300mg per day, further increased if necessary after 7 days to a maximum of 600mg per day.

Pregabalin should always be prescribed as a **twice daily dose** as this is the most cost-effective regime.

Basic NHS cost: Pregabalin all strengths (56 caps) - £64.40

(Drug tariff March 09)

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**Third line/adjuncts to oral treatment**

- **Capsaicin cream**
- **Lidocaine 5% medicated plaster** For management of established **post-herpetic neuralgia**, unresponsive to first line (amitriptyline), second line (gabapentin) and topical treatment including capsaicin

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**PAIN MANAGEMENT**

**Introduction**

Pain Management should be based on the World Health Organisation’s Analgesic Ladder with patients initiating therapy at the step most appropriate for their level of pain.

- When mild analgesics fail change to a stronger analgesic further up the pain ladder. Do not change to a drug of similar potency as this will not achieve better pain control
- Combinations of analgesics with different modes of action are more effective than single agents
- There is wide variation between individuals in the amount of pain that they will experience. It is impossible to predict someone’s requirement for analgesia with any degree of accuracy
- It is important to pre-empt and stay ahead of the pain
- Continuous pain warrants continuous analgesia so when required prescriptions should be avoided, similarly intermittent pain warrants intermittent analgesia
When prescribing opioids it is important to consider the use of anti-emetics and laxatives

ACUTE PAIN MANAGEMENT

MILD PAIN

**Paracetamol**: 500mg-1g orally or rectally every 4 to 6 hours. Max 4g daily.

There is a Trust wide protocol for the short term administration of oral and rectal paracetamol by nursing staff without the need for a prescription.

**Paracetamol 1g IV** as a 15 minute infusion is available for the management of mild to moderate pain in patients who are NBM and nil PR or who refuse PR medication.

MODERATE PAIN

Continue on regular paracetamol

**ADD**

Codeine 30-60mg every 4-6 hours (max 240mg in 24 hours) (May be given as cocodamol – see below)

or

Tramadol 50-100mg every 6 hours (max 400mg in 24 hours, max 600mg in 24 hours for max 7 days on advice of Consultant Pain Specialist)

**Co-codamol 30/500**

- Contains codeine phosphate 30mg and paracetamol 500mg per tablet. Dose 2 tablets with a minimum 4 hour interval but maximum of 8 tablets in 24 hours.

- It is considered easier for patients to take and easier for nursing staff to administer than using the separate ingredients. It has however the disadvantage of lack of flexibility with regards to the dose of opiate received, which may result in unacceptable levels of opiate side effects.

- It may be appropriate to prescribe the paracetamol and codeine separately for patients susceptible to opiate effects and also when stepping down analgesic requirements.

**NB**: If prescribing/administering compound analgesics be aware of other paracetamol preparations that the patient may be taking. Total dose of paracetamol should not exceed 1g in any 4 hour period and no more than 4g in 24 hours.

**Tramadol**

- 10% patients will experience side effects such as headaches, nausea, vertigo, drowsiness and hallucinations. Tramadol can also cause convulsions. The CSM advise that tramadol not be give to patients with a history of or susceptibility to seizures unless absolutely necessary. Use tramadol with caution in patients taking
drugs that lower the seizure threshold e.g. tricyclic antidepressants, serotonin re-uptake inhibitors.

**Prescribing notes**
- The use of two weak opioids together at maximum doses eg codeine and tramadol may not result in any additional pain relief but will increase the instance of opioid related side effects such as nausea and constipation.
- The analgesic efficacy of tramadol may be reduced by ondansetron. This could result in increased tramadol dose requirements and also an increase in tramadol side effects (including nausea and vomiting)

### Nonsteroidal anti-inflammatory drugs (NSAIDs)

See chapter on MUSCULOSKELETAL AND JOINT DISEASES for preparations

These are an important and effective group of analgesics. However they should be used with care in the surgical population and in the very ill

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
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<tbody>
<tr>
<td><strong>Ibuprofen</strong>:</td>
<td>200-400mg every 6 hours (lower dose in the elderly)</td>
</tr>
<tr>
<td><strong>Naproxen</strong>:</td>
<td>250-500mg BD</td>
</tr>
<tr>
<td></td>
<td>For acute musculoskeletal disorders: 500mg initially then 250mg every 6-8 hours prn. Maximum dose after the first day 1.25g daily</td>
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</table>

If no contraindication exists an NSAID may be prescribed, preferably on a regular rather than PRN basis, even if other analgesics are being used. They have a synergistic analgesic effect with opioids without increased opioid side effects.

**Absolute contraindications:**
- known sensitivity to NSAIDs
- active peptic ulcer disease
- renal impairment with a serum creatinine > 120 micromol/L
- hypotension, abdominal catastrophe and presumed sepsis
- severe cardiac failure

**Relative contraindications:**
- history of peptic ulcer disease, especially with bleeding,
- NSAIDs affect on platelets may lead to an increased risk of bleeding: caution if patient taking warfarin; monitor closely.
- liver impairment,
- mild renal impairment,
dehydration

cardiac failure.

Asthmatics have a 5% chance of bronchospasm with NSAID and a history of previous exposure should be sought.

Epidural haematoma formation may be increased, due to anti-platelet activity. For this reason it is best not to administer NSAIDs with epidural analgesia. Seek advice from a Consultant Anaesthetist.

NSAIDs should be used with greater caution in the elderly and at lower doses with U&E monitoring.

The continued need for a NSAID must be reviewed daily and reconsidered after 3 days treatment, to minimise side effects. GPs should not normally be asked to continue NSAIDs for the management of acute or post-operative pain once the patient is discharged from hospital. If longer treatment is deemed necessary then its continuing need MUST be reviewed regularly.

Consider gastro protection in at risk patients but remember all prescriptions for gastro protective agents should be STOPPED when treatment with the NSAID stops

Only one NSAID should be administered, to reduce the risk of complications, especially GI side effects. Patients may be admitted on NSAIDs prescribed by their GP. The risk of GI side effects is also increased in patients taking low dose aspirin.

SEVERE PAIN

Continue on regular paracetamol, weak opioid +/- NSAID and add

Morphine Sulphate Oral Solution 10mg/5ml: 10mg 4hrly prn (start at 5mg in the elderly)

If oral route is not possible: 10mg IM every 4 hours or 2.5mg IV hourly when required

N.B. Prescribing of opiates should be done on an individual basis with ONE route specified for the dose of administration i.e. NOT IV/IM/PO

If requirements for oral morphine sulphate are high (e.g. more than 4 doses daily) contact pain team for further advice on pain management

Remember even with high levels of pain, paracetamol is a good co-analgesic and should be given regularly every 4 to 6 hours.

CHRONIC PAIN MANAGEMENT

Manage as for acute pain then:

Morphine Sulphate modified release capsules (Zomorph) bd
Initial dose is determined by calculating the total daily requirement of oral morphine solution and any other weak opioids such as codeine and giving this total in two divided doses of Zomorph

e.g. Patient is taking 240mg of codeine and 40mg of morphine sulphate oral solution
  100mg codeine is approx. equivalent to 10mg morphine
  240mg of codeine is equivalent to 24mg of morphine
  patient is therefore taking a total daily dose equivalent to 64mg of morphine
  Suitable Zomorph dose would be 30mg bd

**Breakthrough Pain**
Continue on morphine sulphate oral solution for breakthrough (give one sixth of the total daily dose every 4 hours when required)
For further information on the management of chronic pain including oral opioid dose equivalents and the use of adjuvants see Palliative care guidelines
Consider specialist referral.

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### 4.7.4 ANTIMIGRAINE DRUGS

**Migraine with or without aura**

Migraine headaches characterised by episodic severe headaches with associated symptoms such as photophobia, phonophobia and nausea and vomiting respond to simple analgesics or NSAIDs in combination with triptans and anti-emetics if considered appropriate.

When migraines are chronic, (i.e., 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.

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.

Treatment is divided into categories based on NICE CG150:

i) Acute migraine—for infrequent episodic migraines

ii) Prophylaxis of migraine –for frequent/chronic migraine

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**4.7.4.1 Treatment of acute migraine**

Consider patients preference, comorbidities and risk of adverse effects
First line

Offer combination therapy (NICE CG150) i.e., analgesic in combination with triptan of lowest acquisition cost

Preparations should be taken at, or soon after, the onset of the headache phase of a migraine attack.

Analgesic:

Paracetamol: 1g orally every 4 to 6 hours: maximum 4g daily.
Or
Ibuprofen: 200-400mg orally three times a day. Take with or after food, maximum 2.4g daily.
Or
Naproxen: 250-500mg orally twice a day. Take with or after food, maximum 1g daily.

Triptan (listed in order of increasing cost)

1. Sumatriptan: 50mg orally (some patients require 100mg), dose can be repeated after 2 hours if migraine recurs (max 300mg in 24 hours). The 100mg dose is only marginally more effective than 50mg but has more adverse effects. 
   
   Note - intranasal sumatriptan should be used for 12-17 years (tablets not licensed) - sumatriptan 10mg into one nostril repeat dose once after at least 2 hours if migraine recurs, max 20mg in 24 hours.

   Or, if nausea is a problem or sumatriptan ineffective or not tolerated:

2. Zolmitriptan orodispersible: 2.5mg orally, dose can be repeated after not less than 2 hours if migraine recurs (increase to 5mg for subsequent attacks in patients not achieving satisfactory relief with 2.5mg dose), max 10mg in 24 hours (not licensed under 18 years of age).

   Or, if sumatriptan or zolmitriptan ineffective or not tolerated

3. 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) maximum 25mg in 24 hours.(not licensed under 18 years of age)

Antiemetic

Consider an antiemetic even in the absence of nausea and vomiting (NICE CG150). A prokinetic will increase GI motility and rate of absorption of the analgesic, these measures should be initiated as early as possible during an attack.

Metoclopramide - prokinetic orally 10mg (5mg in young adults 15-19 years, body weight under 60kg) three times daily (caution extrapyramidal side effects in children, young adults and elderly).

or

Prochlorperazine – orally 5mg three times daily (unlicensed).  


NOTE: gastric stasis is a feature of migraine. Avoid codeine and other opioids or combinations thereof as they can reduce gastric motility, have an emetic effect and increase the risk of medication overuse headache. Avoid ergot derivatives.

**Second line**

**Alternative Routes** (if vomiting restricts oral treatment, consider parenteral triptans or intranasal triptans and IV/IM metoclopramide or prochlorperazine (unlicensed) or NSAID rectally.

**Intranasal zolmitriptan:** 5mg (1 spray) into one nostril as soon as possible after onset, repeated after not less than 2 hours if headache recurs (max 10mg in 24 hours). Provides 30% drug absorption through the nasal mucosa (unlicensed under 18 years of age).

**Subcutaneous sumatriptan:** 6mg using an auto-injector, dose may be repeated once after at least 1 hour if headache recurs, (max 12mg in 24 hours).

NOTE: this is the most expensive triptan option (unlicensed under 18 years of age).

NOTE: All 5HT1 agonists (i.e., triptans) are contraindicated for patients with ischaemic heart disease, previous myocardial infarction, coronary vasospasm (including Prinzmetal's angina), uncontrolled severe hypertension, TIA/stroke and peripheral vascular disease. They should be used with caution in the elderly (unlicensed) and in conditions which predispose to coronary artery disease (pre-existing cardiac disease).

**4.7.4.2 Prophylaxis of migraine**

Firstly patients should be advised on lifestyle factors such as the avoidance of common triggers, sleep hygiene and reducing stress. Rest in a quiet darkened room is also recommended. Advise patients that riboflavin 400mg once daily (unlicensed) may reduce migraine frequency and intensity (NICE CG 150)

**From patients’ preference, comorbidities and risk of adverse effects either:**

**Propranolol** initially 40mg, orally, two to three times daily

Then

**Propranolol modified release** 80-160 mg, orally, once daily

Or

**Topiramate** 25mg orally at night increasing at weekly intervals in steps of 25mg to 50mg orally twice daily, maximum 200mg daily, specialist supervision required (unlicensed under 18 years of age).

NOTE: Advise women of child bearing potential that topiramate is associated with a risk of foetal malformations and can impair the effectiveness of hormonal contraceptives. Ensure they are offered suitable contraception.

Review the need for continuing prophylaxis after 6 months from first taking. For patients who are already having another form of prophylaxis e.g., amitriptyline (unlicensed) and whose migraine is well controlled, continue the current treatment as required.
If either unsuitable or ineffective consider a course of up to 10 sessions of acupuncture over 5-8 weeks, or gabapentin max 1200mg daily (unlicensed). [NICE CG150]

Prevention of headaches in adults with chronic migraine as defined by NICE TA260

Botulinum toxin type A - for use in line with NICE TA260.

4.8 ANTIEPILEPTIC DRUGS

Drugs used in Epilepsy
Intravenous phenytoin
Therapeutic drug monitoring of phenytoin
Management of prolonged seizures (Adults)
Management of status epilepticus (Adults)

4.8.1 CONTROL OF EPILEPSY

GENERAL INFORMATION

- One seizure does not mean a diagnosis of epilepsy - seek specialist advice if considering long term drug therapy.
- Consider seizure type, patient type and preferences, and tailor therapy accordingly.
- Start at a low dose and increase gradually until seizures are controlled to minimise side effects.
- Encourage patient compliance by keeping dosing frequency as low as possible.
- There are many significant drug interactions involving antiepileptic drugs. Consider concomitant drug therapy when initiating antiepileptic drugs and also check if adding any other medication to already established antiepileptic therapy. There are significant interactions between antiepileptic drugs themselves which are unpredictable and highly variable. Please consult the BNF, product SPC on www.medicines.org.uk or Medicines Information (x 5680) for advice.
- Avoid abrupt withdrawal: seek specialist advice on withdrawing therapy or changing from one antiepileptic to another.
- Routine therapeutic drug level monitoring of antiepileptics is not necessary, except for phenytoin.

FIRST CHOICE AGENTS

Carbamazepine or lamotrigine would be considered first choice agents for partial-onset epilepsy. They are both equally effective but lamotrigine is better tolerated.

For generalised-onset epilepsy sodium valproate is the most effective, but lamotrigine would be an alternative, particularly in women.
• **Carbamazepine**
  100mg, 200mg, 400mg tablets
  200mg, 400mg m/r tablets
  100mg/5mL liquid
  125mg, 250mg suppositories

Carbamazepine modified release tablets are more expensive than the conventional carbamazepine preparations. The modified release preparations should only be used when patients suffer from side effects due to the peak plasma concentrations of carbamazepine experienced with the conventional preparations. When switching from oral preparations of carbamazepine to suppositories, increase the normal oral dose by 25% to a daily maximum of 1000mg ie.250mg 6 hourly.

• **Lamotrigine**
  25mg, 50mg, 100mg tablets
  5mg, 25mg, 100mg dispersible tablets

• **Sodium valproate**
  100mg crushable tablets
  200mg, 500mg e/c tablets
  200mg/5mL liquid SF
  400mg injection

Patients who need intravenous sodium valproate should be given the same dose as they would take orally.

**SECOND CHOICE AGENTS**

These agents may be used either as monotherapy or adjunct therapy, depending on the type of epilepsy and the current licensed indications. Please refer to **NICE Guideline CG137**, October 2004 for the use of antiepileptic drugs according to the seizure type.

Not all agents or all strengths are routinely stocked in Pharmacy and would only normally be ordered on request following initiation by a consultant neurologist or for an individual patient admitted on that treatment.

• **Levetiracetam**
  250mg, 500mg, 750mg, 1g tablets
  100mg/mL oral solution (SF)
  100mg/mL IV infusion (dilute before use)

• **Topiramate**
  25mg, 50mg, 100mg tablets

• **Clobazam**
  10mg tablets
- Ethosuximide 250mg capsules
  250mg/5mL syrup

- Gabapentin 100mg, 300mg, 400mg capsules

- Oxcarbazepine 150mg, 300mg, 600mg tablets

- Pregabalin 25mg, 50mg, 75mg, 150mg, 300mg capsules
  For epilepsy use only – prescribing pregabalin BD is the most cost effective use of this agent.

- Zonisamide 25mg, 50mg, 100mg capsules

- Retigabine in line with NICE guidance TA 232

Phenytoin and phenobarbital are rarely used in modern practice but are included here for the purposes of continuation of therapy.

- Phenobarbital (phenobarbitone) 30mg tablets

- Phenytoin sodium 25mg, 50mg, 100mg, 300mg capsules

- Phenytoin base 30mg/5mL suspension

Phenytoin sodium 100mg is therapeutically equivalent to 90mg of phenytoin base i.e. one 100mg capsule/tablet is equivalent to 15mL of the 30mg/5mL suspension.

Some unlicensed phenytoin suspensions exist e.g. 100mg/5mL – take care with patients being admitted on phenytoin suspension.

Absorption of phenytoin suspension is reduced when administered at the same time as enteral feeds. The problem can be avoided as follows:

1. Give enteral feeds for 18 to 20 hours per day.
2. Flush the tube with water.
3. Wait for 2 hours.
4. Administer phenytoin suspension.
5. Flush the tube with water.
6. Wait for two hours and restart feed.
Monitoring of oral phenytoin treatment
Phenytoin levels should be taken at least one week after initiating therapy or changing a dose. The elimination half-life of phenytoin is long; the actual sampling time is unimportant. Contact ward pharmacist or Medicines Information for advice on monitoring and interpreting levels and on any dose adjustments.

4.8.2 DRUGS USED IN STATUS EPILEPTICUS

- **Diazepam**  
  10mg/2mL emulsion (Diazemuls)  
  10mg/2ml injection  
  5mg/2.5mL, 10mg/2.5mL rectal tubes

- **Lorazepam**  
  4mg/mL injection

- **Midazolam**  
  10mg/mL buccal solution

Buccal midazolam is an unlicensed route of administration. It is administered using an unlicensed preparation. However, it may be more acceptable to patients than rectal diazepam.

- **Phenytoin**  
  250mg/5mL ampoules

MANAGEMENT OF PROLONGED OR REPEATED SEIZURES IN ADULTS

**Definitions:**  
Convulsive seizures lasting 5 minutes or longer  
Three or more seizures in an hour

**Initial treatment:**  
DIAZEPAM IV (as emulsion) or PR if there is no intravenous access. PR is the route most likely to be used in the community

**IV dose:**  
adults and children over 10kg - 500 micrograms/kg  
elderly - 250 micrograms/kg

**PR dose:**  
10-20 mg, repeated once 15 minutes later if status continues to threaten

**Alternatively:**  
Buccal midazolam 10mg
If no response after 10 minutes a second dose of 10mg can be given. This may be a more acceptable drug and route for patients, especially for use in the community. It is currently unlicensed and should be initiated by specialists along with appropriate patient information and education.

Failure of above treatment: If one of the above fails to control the seizure(s) follow the guidelines below for the management of status epilepticus

MANAGEMENT OF STATUS EPILEPTICUS IN ADULTS

| General measures | ABC, bloods (U&Es, FBCs, glucose, anti-epileptic drug levels), establish IV access. |
| | Administer IV glucose 50% in 50mL and/or IV thiamine 250mg (as 1 pair of Pabrinex IV amps) if alcohol abuse or malnutrition suspected. |
| | Emergency antiepileptic drug (AED) therapy |

| Early status (0-30mins) | Lorazepam IV (0.1mg/kg) usually as 4mg bolus (rate not critical) |
| | Repeat once after 10-20mins |
| | Give usual AED therapy if already on treatment |
| | Status controlled in approx 80% of patients at this stage |

| Established status (30-60mins) | If seizures continue for 30 minutes in spite of the above treatment then alert anaesthetist and ITU. |
| | Administer phenytoin loading dose 20mg/kg by slow IV injection (maximum rate of 50mg/min or 1mL/minute) directly into a large vein through a large-gauge needle or intravenous catheter. **DO NOT DILUTE** |
| | If patient is already receiving phenytoin reduce dose to 150-250mg. Follow loading dose with 100mg 3-4 times daily, orally or IV. The intramuscular route is unreliable and should be avoided. |
| | Follow each phenytoin injection or infusion with sodium chloride 0.9% flush to avoid local venous irritation |
| | Continuous ECG and blood pressure monitoring is essential during administration of the loading dose. (see above for further guidelines on the administration and monitoring of intravenous phenytoin) |

| Refractory status (>60mins) | General anaesthesia required (propofol, thiopentone, midazolam) |
INTRODUCTION

General management guidelines

People with suspected Parkinson’s disease should be referred quickly and untreated to a specialist.

Diagnosis should be reviewed regularly and reconsidered if atypical clinical features develop.

Delay in prescribing medication on admission is likely to worsen symptom control.

When admitted to hospital, medication MUST be prescribed and administered at the exact times the patient takes them at home.

Please see NICE clinical guideline CG35 Parkinson’s disease: diagnosis and management in primary and secondary care for further information including pharmacological management.

4.9.1 DOPAMINERGIC DRUGS USED IN PARKINSONISM

There is no universal first choice drug therapy for patients with Parkinson’s disease. A holistic approach is important especially in the older patients, where non-Parkinson’s disease related problems may be more evident.

Levodopa preparations

- Co-careldopa (carbidopa/levodopa)
  - Sinemet 62.5 (12.5/50)
  - Sinemet-Plus (25/100)
  - Sinemet-275 (25/250)
  - Half Sinemet CR (25/100 MR)
Sinemet CR (50/200 MR)

Dose (expressed as levodopa):
Initially 50mg (Sinemet 62.5) or 100mg (Sinemet-plus) three times a day with food.
Increase as required up to 800mg daily in divided doses.
Alternatively, initially 125mg (as ½ tablet of Sinemet-275) once to twice daily up to 750mg daily in divided doses.

**NB** Sinemet -110 tablets are not included in this formulary as they are not recommended because they contain insufficient proportion of dopa-decarboxylase inhibitor.

- **Co-beneldopa**
  (benserazide/levodopa)
  Madopar 62.5 (12.5/50) capsules and dispersible tablets
  Madopar 125 (25/100) capsules and dispersible tablets
  Madopar 250 (50/200)
  Madopar CR (25/100) – not as effective as Sinemet CR therefore not recommended

Dose (expressed as levodopa):
Initially 50-100mg twice daily.
Increase according to response: usual maintenance dose 400-800mg daily in divided doses with food.

**General prescribing considerations:**
- Levodopa dose should be kept as low as possible to reduce development of motor complications.
- A combination of dispersible, standard and controlled release preparations may be needed to control symptoms.
- Although there may be an earlier response, it may take up to 3 months to see a response following initiation of levodopa therapy.

**Precautions and side effects:**
- Contraindications: narrow-angle glaucoma, pregnancy and breast feeding.
- Caution: pulmonary and cardiovascular disease, diabetes, peptic ulceration, open-angle glaucoma and psychiatric illness.
- Side-effects: nausea and vomiting, postural hypotension, insomnia, agitation, dizziness, reddish discoloration of urine, anorexia, neuropsychiatric symptoms. Sudden onset of sleep – warn drivers.

**Dopamine receptor agonists**
In most cases non-ergot derived dopamine agonists (ropinirole) should be preferred over ergot-derived dopamine agonists (bromocriptine).

*The CSM advise that ergot derivatives have been associated with pulmonary, retroperitoneal and pericardial fibrotic reactions*

- **Ropinirole**
  1mg, 2mg, 5mg tablets
Starter pack - 250microgram, 500microgram, 1mg tablets
Follow-on pack - 500microgram, 1mg, 2mg tablets
Initially 750micrograms daily in 3 divided doses, increase by 750microgram at weekly intervals to usual dose of 3-9mg. Max dose 24mg daily.
Levodopa dose may need to be reduced by approx 20% if used in combination

- **Bromocriptine**
  - 2.5mg tablets
  - 5mg, 10mg capsules
Initially 1-1.25mg at night, increase after 1 week to 2-2.5mg at night
Increase daily dose by 2.5mg at weekly intervals until optimum dose is achieved. Usual range 10-40mg daily, max 80mg daily. Take with food.

- **Rotigotine**
  - A dopamine agonist patch available in 2mg, 4mg, 6mg and 8mg strengths. Only to be initiated under consultant specialist's advice.
**Precautions and side effects:**
- **Caution:** severe cardiac disease and major psychiatric disorders.
- **Side-effects:** Nausea and vomiting, postural hypotension, ankle oedema, hallucinations. Sudden onset of sleep – warn drivers.
- **Rotigotine:** the backing layer contains aluminium. Therefore, to avoid skin burns, the patch should be removed before the patient undergoes magnetic resonance imaging or cardioversion

**Apomorphine:**

- **Apomorphine**
  - 10mg/mL, 2mL and 5mL ampoule
  - 10mg/mL, 3mL pen injector (for outpatient use)

**By continuous subcutaneous infusion:**
Initially 1mg/hour by subcutaneous infusion increased according to response by 500mcg (no more than every 4 hours) to usual rate of 1-4mg/hour. Infusion site should be changed every 12 hours to prevent nodule formation. Given during waking hours only, unless severe night-time symptoms.

**By subcutaneous injection:**
Usual range (after initiation) 3-30mg daily in divided doses. Maximum single dose 10mg.
- For specialist initiation only: specialist supervision is advisable throughout treatment.
- Used to reduce “off” episodes in patients with severe motor complications.
- Highly emetogenic. Need at least 2 days pre-treatment with domperidone 20mg TDS to prevent/reduce nausea and vomiting.
Infusion may be preferable in patients requiring more than 10 subcutaneous injections daily.

Also refer to shared care guidelines issued by Walton Centre for Neurology.

Precautions and side effects:
- Contraindications: respiratory depression, hypersensitivity to opioids, neuropsychiatric problems or dementia.
- Caution: pulmonary or cardiovascular disease and history of postural hypotension.
- If using with levodopa test initially and every 6 months for haemolytic anaemia.
- Side effects: nausea and vomiting, drowsiness, confusion, hallucinations, injection site reactions (nodule formation and ulceration).

**Catechol-O-methyltransferase (COMT) inhibitors**

- **Entacapone**
  - 200mg tablet
  - 200mg with each dose of levodopa to a max dose of 2g daily.
  - Levodopa dose may need to reduce by approx 10-30%.

**Precautions and side effects:**
- Should not be given in conjunction with non-selective monoamine oxidase inhibitors. Selective MAO-B inhibitors should not be used at higher than recommended doses when co-administered with entacapone.
- Enhances anticoagulant effect of warfarin.
- May increase levodopa associated side effects (reduce levodopa dose).
- Urine may be coloured reddish-brown.

**Monoamine-oxidase-B inhibitors**

- **Selegiline**
  - 5mg, 10mg tablets

  Initially 5mg in the morning, increase to maintenance dose of 10mg daily.
  Levodopa dose may need to be reduced by approx 20-50%.
  Zelapar 1.25mg oral lyophilisate, is equivalent to 10mg selegiline, it is placed on the tongue and allowed to dissolve. Use restricted to specialist consultant only

**Precautions and side effects:**
- Side effects: nausea and vomiting, hypotension, confusion, agitation, sleep disorders (metabolised to amphetamine).
- Avoid concomitant use with pethidine.
- Seek advice before starting an antidepressant.

**Other drugs used**
• **Amantadine**  
  100mg capsules
  50mg/5mL syrup

  100mg daily increased after one week to 100mg twice daily, usually in conjunction with other treatment.  
  Max 400mg daily.

**Precautions and side effects:**
- Contraindicated in epilepsy.
- Side-effects: nausea, nervousness, insomnia, dizziness, ankle oedema, blurred vision, livedo reticularis.

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### 4.9.2 ANTIMUSCARINIC DRUGS USED IN PARKINSONISM

Avoid in the elderly as they may cause confusion

May also be used to reduce symptoms of drug-induced parkinsonism e.g. from antipsychotics but should not be prescribed routinely unless symptoms develop.

**NB:** They will not improve tardive dyskinesia and may make it worse.

- **Trihexyphenidyl hydrochloride**  
  (Benzhexol)  
  2mg, 5mg tablets
  5mg/5mL syrup

  1mg daily, increased gradually to maintenance dose of 5-15mg daily in 3-4 divided doses. Max. 20mg daily.

- **Procyclidine**  
  5mg tablets
  2.5mg/5mL, 5mg/5mL syrup
  10mg/2mL injection (for acute dystonias)

  2.5mg three times a day, increased gradually by 2.5-5mg daily every 2-3 days as necessary, up to max 30mg daily in 2-4 divided doses.

- **Orphenadrine**  
  50mg tablets
  25mg/5mL syrup

  Initially 50mg three times a day, increased gradually in steps of 50mg every 2-3 days according to response to usual maintenance dose of 150-300mg daily in divided doses. Max. 400mg daily.
Precautions and side effects of anticholinergics

- Contraindications: gastro-intestinal obstruction and myasthenia gravis
- Caution: cardiovascular disease, hypertension psychotic disorders, prostatic hypertrophy, pyrexia, closed-angle glaucoma.
- Side-effects: constipation, dry mouth, nausea, vomiting, tachycardia, confusion, falls, urinary retention, agitation and hallucinations.

DRUG INDUCED PARKINSONISM

- Offending drug should be withdrawn if possible.
- Can be treated with anticholinergics.
- Possible causative drugs e.g. neuroleptics, lithium, calcium channel blockers, pethidine, metoclopramide, methyldopa.

ANTI-EMETICS IN PARKINSON’S DISEASE

- Domperidone is the drug of choice for Parkinson’s disease as this is a peripherally acting dopamine antagonist i.e. does not cross the blood brain barrier.
- Domperidone is not available in a parenteral form therefore cyclizine is a suitable alternative.
- Metoclopramide and the phenothiazines may worsen parkinsonian symptoms and must be avoided.

NON MOTOR FEATURES OF PARKINSON’S DISEASE

- Refer to consultant specialist for advice

Depression

- Management should be tailored to the individual, in particular, to their co-existing therapy.

Psychotic symptoms

- Symptoms may improve with a reduction in Parkinson’s medication.
- Typical antipsychotics (e.g. phenothiazine and butyrophenones) should not be used as they exacerbate the motor symptoms of the condition.
- Quetiapine may be considered if neuropsychiatric symptoms are not well tolerated.

Management of excessive daytime sleepiness:

- Modafinil may be considered.
**Management of sialarrhoea/drooling**
- Refer to specialist
- Treatment includes:
  - Atropine 1% ophthalmic solution given sublingually twice a day (unlicensed use).
  - Botulinium toxin A

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**4.9.3 DRUGS USED IN ESSENTIAL TREMOR, CHOREA, TICS AND RELATED DISORDERS**
- **Riluzole**
  - 50mg tablets

Available for prescribing by visiting neurologists for motor neurone disease in line with [NICE TA20](#).

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**4.10 DRUGS USED IN SUBSTANCE DEPENDENCE**

**4.10.1 ALCOHOL DEPENDENCE**

- **Chlordiazepoxide**
  - Refer to urgent care pathway for prescribing guidelines

**4.10.2 NICOTINE DEPENDENCE**

In Primary Care, nicotine replacement products should be tailored to the patient’s preference, and smoking history and pattern.
The following products are stocked are COCH

- **Nicotinell**
  - 24 hour patches
- **Nicorette**
  - 16 hour patches, gum, inhalator
- **NiQuitin**
  - Lozenges

Refer to the Trust NRT Policy for prescribing guidelines

- **Verenicline**
  - For Primary Care initiation only
  - See [NICE guidance TA 123](#) - Varenicline for smoking cessation
### 4.11 DRUGS FOR DEMENTIA

- **Donepezil**
- **Galantamine**
- **Rivastigmine**
- **Memantine**

For specialist initiation only in line with [NICE guidance TA 217](https://www.nice.org.uk/guidance/ta217) - Donepezil, galantamine, rivastigmine and memantine for the treatment of Alzheimer's disease (review)