Promazine De-prescribing Guidance

Promazine is a phenothiazine-type, first generation (typical) antipsychotic with relatively weak antipsychotic activity but pronounced sedative effects. It is licensed firstly for short-term adjunctive management of psychomotor agitation, and secondly for agitation and restlessness in the elderly. Promazine is subject to considerable first-pass metabolism, resulting in significant plasma concentration variations between patients and the BNF marks it as a drug considered to be “less suitable for prescribing”. It is highly toxic in overdose and can result in grand mal seizures, QRS prolongation and coma. TEWV Foundation Trust recommend that it is not used. Promazine is associated with withdrawal symptoms following abrupt cessation, therefore a gradual withdrawal is recommended.

Reducing risks with promazine

- **Check:**
  - Dose - is it a therapeutic dose?
  - Indication - is it being used to treat agitation?
  - Effectiveness of treatment
  - Suicide risk
  - Co-prescribing of interacting drugs known to increase CNS depression
  - Comorbidity

- **Licensed dose:**
  - 100-200mg FOUR times a day
  - **Elderly:** 25-50mg FOUR times a day

- **HIGHLY toxic in overdose**
  - Less than 1 weeks’ supply likely to cause serious toxicity or death.
  - **Never** prescribe if a risk of suicide identified

- **Interacting medicines:**
  - Alcohol – Hypotension & CNS depression
  - ACE inhibitors, alpha blockers, beta blockers, calcium channel blockers, diuretics, nicoandil, nitrates & TCAs – Hypotension
  - Antipsychotics, benzodiazepines, gabapentin, mirtazapine, opioids, pregabaline, trazodone, venlafaxine & Z-drugs – CNS depression
  - Lithium – Neurotoxicity
  - MAOIs – Neuroleptic malignant syndrome

- **Promazine should be avoided in patients with**
  - cardiac disease, epilepsy, diabetes, hepatic impairment, Parkinson’s disease, prostatic hypertrophy, phaeochromocytoma and glaucoma

- **Promazine has an established link with a number of adverse cardiovascular effects** (hypotension, tachycardia/arrhythmia and QTc prolongation)
  - Relative incidence and severity of side effects is higher than other antipsychotics
  - It is extremely toxic in overdose – warn about accidental overdose

- **Handy chart** comparing antipsychotic treatments:

**Stopping promazine**

Promazine should not be stopped abruptly unless serious side effects have occurred. Slowly tapering the dose over 3 to 4 weeks can help prevent discontinuation symptoms. These symptoms may include nausea, vomiting, sweating and insomnia. Recurrence of psychotic symptoms may also occur, and the emergence of involuntary movement disorders (such as akathisia, dystonia and dyskinesia) has been reported. Some people

<table>
<thead>
<tr>
<th>Title</th>
<th>Promazine De-prescribing Guidance</th>
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<tbody>
<tr>
<td>Approved by</td>
<td>Drug &amp; Therapeutics Committee</td>
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<tr>
<td>Protocol Number</td>
<td>PHARM/0089/V1.0</td>
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<td>Date of Approval</td>
<td>21st November 2017</td>
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<td>Date of Review</td>
<td>21st November 2020</td>
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may require a more gradual tapering of the dose if withdrawal symptoms occur. The doses selected and the speed at which they are reduced will need to be individualised for each patient. The smallest tablet strength is 25mg so reduction increments as small as 25mg can be used if necessary.

**A suggested withdrawal regimen for promazine is:**

<table>
<thead>
<tr>
<th>Current dose</th>
<th>Week 1</th>
<th>Week 2</th>
<th>Week 3</th>
<th>Week 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>800 mg / day</td>
<td>600 mg / day</td>
<td>400 mg / day</td>
<td>200 mg / day</td>
<td>nil</td>
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</table>

**Switching to another medication**

The choice of medication should be discussed with the patient. Considerations include:

- Agitation symptoms
- Relative side effects
- Physical illness
- Interactions with other prescribed medication

### Patient profile

<table>
<thead>
<tr>
<th>Patient profile</th>
<th>Suggested options</th>
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<tbody>
<tr>
<td>In need of sedation</td>
<td>Promethazine, Lorazepam</td>
</tr>
<tr>
<td>Psychotic features</td>
<td>Haloperidol or alternative antipsychotic</td>
</tr>
<tr>
<td>Cardiac disease</td>
<td>Aripiprazole, Risperidone, Flupentixol or Promethazine, Lorazepam</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Haloperidol, Amisulpride, Aripiprazole or Promethazine, Lorazepam</td>
</tr>
<tr>
<td>Epilepsy</td>
<td>Haloperidol, Amisulpride or Lorazepam or Diazepam</td>
</tr>
<tr>
<td>Hepatic impairment</td>
<td>Haloperidol, Amisulpride or Lorazepam</td>
</tr>
<tr>
<td>Renal impairment</td>
<td>Haloperidol, Olanzapine or Lorazepam</td>
</tr>
<tr>
<td>Parkinson’s disease</td>
<td>Quetiapine or Promethazine, Lorazepam</td>
</tr>
</tbody>
</table>

There should be very close monitoring of patients being switched from promazine to another antipsychotic, as there are no published guidelines to determine exactly how the switch should take place. The switch will need to be tailored to each individual and carried out cautiously. The regimen should depend upon the reason for the switch, how severe the agitation is and which drug is being switched to. Gradual cross tapering is usually recommended but in some cases a washout period between drugs is required.

**References**

Datapharm Communications Limited. Promazine Hydrochloride 50mg/5ml Oral Syrup Rosemont Pharmaceuticals Limited [www.medicines.org.uk/emc/medicine/10771] (updated 10/10/13)