Trimipramine Deprescribing Guidance

Trimipramine, a tricyclic antidepressant (TCA), is licensed for the treatment of depression, particularly where sedation is required. Trimipramine is also used off-licence as a painkiller. It has a clinical efficacy and side-effect profile comparable to other TCA’s; however the acquisition cost is significantly higher for trimipramine than other TCA’s at approximately £380 for 28 days’ supply. In light of this, NHS England recently highlighted trimipramine as a medicine which should not routinely be prescribed in primary care1. TEWV FT therefore recommends that it is **not** initiated in any new patients. Nevertheless, £17.9 million is still spent on Trimipramine every year in the UK1.

Reducing risks with trimipramine

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

**Licensed dose:**
50-300 mg daily in divided doses  
**Elderly:** 10-25 mg daily initially

**MODERATLY toxic in overdose**  
Less than 3 weeks’ supply likely to cause serious toxicity or death.

**Interacting medicines:**
- ACE inhibitors, alcohol, alpha blockers, angiotensin II blockers, atypical antipsychotics, beta-blockers, calcium channel blockers, L-dopa, nitrates – **Hypotension**
- Carbamazepine, NSAIDs, SSRI’s – **Hyponatraemia**
- Typical Antipsychotics – **Hypotension & antimuscarinic effects**
- Diuretics – **Hyponatraemia & hypotension**
- Lithium – **Neurotoxicity**
- MAOIs, tranylcypromine – **Increased toxicity**
- TCAs – **Hyponatraemia, hypotension & antimuscarinic effects**

**Trimipramine should be avoided in patients with:**
- cardiac disease, diabetes, chronic constipation, urinary retention, epilepsy, glaucoma, prostatic hypertrophy, psychosis, bipolar disorder and phaeochromocytoma.

**Trimipramine 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 antidepressants. It is toxic in overdose – warn about accidental overdose

**Handy chart comparing antidepressant treatments:**

**Stopping Trimipramine** (and not replacing with an alternative antidepressant)

Trimipramine should not be stopped abruptly unless serious side effects have occurred. Slowly tapering the dose in 25 – 50 mg increments over 3 to 4 weeks, or longer if necessary, can help prevent discontinuation symptoms such as anxiety, flu-like symptoms and insomnia. The rate at which the dose is reduced will need to be individualised for each patient, according to the starting dose, how long they have been taking trimipramine and the occurrence of withdrawal symptoms during the reduction. Some people may require a more gradual tapering of the dose over a long period of time to withdraw successfully.
Switching to another antidepressant

There should be very close monitoring of patients being switched from trimipramine to another antidepressant, 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 depression is and which drug is being switched to. It is ideal to completely withdraw trimipramine before starting the new drug; however, cross-tapering is usually necessary to maintain symptom control. The dose of trimipramine should be at least halved before starting the new drug. Further reductions in trimipramine dose should occur once the new treatment is established. There is a risk of enhanced side-effects and serotonin syndrome during the overlap phase.

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

- Depressive (target) symptoms
- Relative side effects of antidepressants (see handy chart, link above)
- Physical co-morbidities
- Interactions with other prescribed medication

<table>
<thead>
<tr>
<th>Patient profile</th>
<th>Suggested options</th>
</tr>
</thead>
<tbody>
<tr>
<td>In need of sedation</td>
<td>Mirtazapine (lower doses more sedating)</td>
</tr>
<tr>
<td>In need of activation</td>
<td>SSRI or venlafaxine</td>
</tr>
<tr>
<td>Cardiac disease</td>
<td>Mirtazapine or sertraline</td>
</tr>
<tr>
<td>Diabetes</td>
<td>SSRIs (fluoxetine or sertraline) or venlafaxine</td>
</tr>
<tr>
<td>Epilepsy</td>
<td>SSRIs</td>
</tr>
<tr>
<td>Hepatic impairment</td>
<td>Citalopram (maximum dose 20 mg/day) – see Trust guidance</td>
</tr>
<tr>
<td>Renal impairment</td>
<td>Citalopram</td>
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<tr>
<td>Parkinson’s disease</td>
<td>SSRIs</td>
</tr>
<tr>
<td>Stroke</td>
<td>SSRIs (citalopram if taking warfarin + consider PPI for gastric protection) or mirtazapine</td>
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</tbody>
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Very general guidance on switching from trimipramine to other antidepressants is below:

- Trimipramine to an **SSRI**: gradually reduce the dose to 25-50 mg / day, then add SSRI at usual starting dose. Then slowly withdraw the remaining trimipramine over 5-7 days.
- Trimipramine to **mirtazapine**: cross taper cautiously
- Trimipramine to **venlafaxine**: cross taper cautiously starting with venlafaxine 37.5 mg daily

Patient Information Leaflet

Available online at:


References

1. NHS England. *Items which should not routinely be prescribed in primary care: Guidance for CCGs*, November 2017