NHS
Tees, Esk and Wear Valleys
NHS Foundation Trust

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[1,2]; however the acquisition cost is significantly higher for trimipramine then other TCA's at approximately £600-£1200 for 28 days' supply. In light of this, NHS England highlighted trimipramine as a medicine which should not routinely be prescribed in primary care[3]. TEWV FT therefore recommends that it is **not** initiated in any new patients. Nevertheless, £12.7 million is still spent on Trimipramine every year in the UK[3].

Reducing risks with trimipramine

Review

- 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

Discuss

- Risks/benefits of trimipramine
- NICE does not recommend use of trimipramine
- Alternative options e.g. stopping, switching (see handy comparison chart via link below)

Document

- Document outcome of discussions
- Clearly identify reason if continuing trimipramine
- Document treatment plan if stopping or swtiching

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, SSRIs – *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:
https://www.choiceandmedication.org/generate.php?sid=55&fname=handychartdepression.pdf

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 [4,5]

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

Patient profile	Suggested options
In need of sedation	Mirtazapine (lower doses more sedating)
In need of activation	SSRI or venlafaxine
Cardiac disease	Mirtazapine or sertraline
Diabetes	SSRIs (fluoxetine or sertraline) or venlafaxine
Epilepsy	SSRIs
Hepatic impairment	Citalopram (maximum dose 20 mg/day) – see Trust guidance
Renal impairment	Citalopram
Parkinson's disease	SSRIs
Stroke	SSRIs (citalopram if taking warfarin + consider PPI for gastric protection) or mirtazapine

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:

- https://www.prescqipp.info/resources/category/414-items-which-should-not-routinely-be-prescribed-in-primary-care-patient-leaflets
- https://www.choiceandmedication.org/generate.php?sid=55&fname=pilltrimipramine.pdf

References

1. Datapharm Communications Limited. Trimipramine 25mg Tablets Zentiva. Available via [https://www.medicines.org.uk/emc/product/2962/smpc] (updated 03 Feb 2021)
2. BMA Group, Royal Pharmaceutical Society. British National Formulary online edition. Pharmaceutical Press, London. Available via [https://www.medicinescomplete.com]

3. NHS England. Items which should not routinely be prescribed in primary care: Guidance for CCGs, Version 2. June 2019
4. Bazire S. Psychotropic Drug Directory 2020/21. Lloyd-Reinhold Publications, Norwich.
5. Taylor D et al. Maudsley Prescribing Guidelines in Psychiatry, 13th Edition

Dosulepin has a number of adverse cardiovascul effects (hypotension, tachycardia and QTc prolongation).
It is extremely toxic in overdose – ward about accidental overdose