Trimipramine (Surmontil®): Guidance on withdrawal

Indication: Trimipramine is a tricyclic antidepressant (TCA) indicated in the treatment of depressive illness, especially where sleep disturbance, anxiety or agitation are presenting symptoms.[i]

Formulary status: On formulary.
Note: When an antidepressant is to be prescribed, TCAs are no longer considered first line treatment for depression due to their side effect profile. SSRIs are equally effective as other antidepressants and have a favourable risk-benefit ratio. [ii]

Dose: In the treatment of depression, the usual starting dose is 50 to 75 mg daily in divided doses *or* as a single dose at bedtime, increased if necessary to 150 to 300mg daily. The recommended initial dose for the elderly in the UK is 10-25 mg daily three times daily which should be increased with caution under close supervision. Half the normal maintenance dose may be sufficient to produce a satisfactory clinical response[.i]

Unlicensed uses: Neuropathic pain/chronic pain, insomnia, anxiety. NB: If prescribed for any other indication, pl

Mode of action: Serotonin and noradrenaline reuptake inhibitor.

- **Anticholinergic activity** may cause dry mouth, constipation and blurred vision.
- **H1 blockade** may cause sedation.
- **Adrenergic alpha 1 receptor blockade** may cause dizziness, sedation and hypotension.
- **Ion channel blockade** may cause cardiac arrhythmias and seizures especially in overdose**.**[iii]

Reasons for caution: Reports of cardiac arrhythmias, QTc prolongation, sinus tachycardia, orthostatic hypotension. Drug interactions. High rate of fatality in overdose.

Side effects:

- As listed above

Guidance and recommendations:

- No new patients should be prescribed trimipramine.
- Patients currently prescribed trimipramine should be identified and have their treatment history reviewed. Where possible trimipramine should be gradually withdrawn and stopped if no longer clinically indicated.
- Suitable alternatives may include an SSRI such as sertraline, mirtazapine (if a sedative antidepressant is required), imipramine or lofepramine if an alternative TCA is required. Individual product literature for each of these medicines is available from www.medicines.org.uk
- TCAs should not be terminated abruptly (unless a serious adverse event has occurred e.g. cardiac arrhythmia), instead gradually taper down the daily dose in weekly/two weekly decrements[iv] over **at least** 4 **weeks** to avoid withdrawal effects. [v]
- For patients who have been taking trimipramine for long term maintenance treatment (>1 year), more gradual tapering may be appropriate, in the region of at least 6 months[v]
- Even with a gradual dose reduction some withdrawal symptoms may appear within the first 5 days.[v] As with all swaps in medication tailor the withdrawal process to the individual patient, monitoring patient tolerability.

- In patients taking a split daily dose, the morning dose should ideally be completely reduced first before withdrawing the night time dose to minimise the change in effects on night-time sedation.

Few studies have specifically examined the best strategy for and outcomes of switching between antidepressants. The following advice is based on available information, theoretical concerns and clinical experience. It is intended for general guidance only. Whichever strategy is used, patients should be closely monitored for adverse effects. [iii]

Suggested withdrawal and crossover to mirtazapine schedule[iv]
(e.g. where sedative action required)

Drug	Current dose	Week 1	Week 3	Week 5	Week 7	Week 9
Trimipramine	75mg/day	50mg/day	25mg/day	20mg/day	10mg/day	STOP
Mirtazapine	Nil	Nil	15mg at night	15mg at night	30mg at night	Further dose ↑ based on response

Suggested withdrawal and crossover to imipramine/lofepramine schedule[iv]
(e.g. where anxiolytic action required)

Drug	Current dose	Week 1	Week 3	Week 5	Week 7	Week 9
Trimipramine	75mg/day	50mg/day	25mg/day	20mg/day	10mg/day	STOP
Imipramine* *Recommended [v] elderly doses	Nil	Nil	10mg at night	10mg at night	20mg at night	Further dose ↑ based on response.
Lofepramine	Nil	Nil	70mg twice daily	70mg twice daily	70mg twice daily	Further dose ↑ based on response.

Practical considerations:

- Issue 7 day scripts for safety reasons and to reduce waste
- Trimipramine is available as 10mg and 25mg tablets and 50mg capsules. Limit the prescribing of 2 different strengths for safety reasons and to make regimes simpler whilst reducing doses.
- Tailor the withdrawal and cross over process to the individual patient based on efficacy and tolerability.
- If the patient experiences any withdrawal effects then return to the previous dose of trimipramine and continue with the cross over at a slower pace using smaller decrements.
- Information on good sleep hygiene and non-pharmacological techniques may be found at www.nhs.uk/conditions/insomnia. Consider short term use of zopiclone but note risk of tolerance, addiction and falls risk.

Suggested monitoring:
BP, pulse, weight, BMI, U&E, eGFR, LFTS, full annual health check. (ECG as required)

References:

[i] Trimipramine 10mg Tablets. Concordia International- formerly Focus Pharmaceuticals. www.medicines.org.uk Last Updated on eMC 13-November-2017 .
[ii] CG90. Published date: October 2009. Last updated: April 2016. https://www.nice.org.uk/guidance/cg90
[iii] Maudsley Prescribing Guidelines Antidepressants. 12th Edition.
[iv] https://www.sps.nhs.uk/articles/how-do-you-switch-between-tricyclic-ssri-and-related-antidepressants/ [Accessed: 26/11/2017]
v Joint Formulary Committee. British National Formulary [Online] London: BMJ Group and Pharmaceutical Press Available: http://www.medicinescomplete.com [Accessed: 26/11/2017]