

# Trimipramine (Surmontil®): Guidance on withdrawal.

**Indication:** Trimipramine is a tricyclic antidepressant (TCA) indicated for depressive illness, particularly where sedation is required (1).

**Formulary status:** Trimipramine has been removed from the SW London formulary. TCAs are no longer considered first line treatment for depression due to their side effect profile (2).

**Dose:** In the treatment of depression, the usual initial dose is 50 to 75 mg daily, increased if necessary, to 150 to 300mg daily. The recommended initial dose for the elderly in the UK is 30 to 75 mg daily.

**Unlicensed uses:** Neuropathic pain/chronic pain, insomnia, anxiety.

**Mode of action:** Serotonin and noradrenaline reuptake inhibitor.

**Reasons for caution:** Reports of arrhythmias, QTc prolongation, orthostatic hypotension, sinus tachycardia, myocardial infarction, stroke.

## Side effects:

- Sedation
- Blurred vision, dry mouth, urinary retention, constipation.
- Nausea, diarrhoea, heartburn, unusual taste in mouth, weight gain.
- Fatigue, weakness, dizziness, headache, anxiety, nervousness, restlessness
- Sexual dysfunction (impotence)
- Sweating, rash, itching.
- Orthostatic hypotension, cardiac arrhythmias, tachycardia, seizures.

## 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 Where possible trimipramine should be gradually withdrawn.
- Suitable alternatives may include an SSRI such as sertraline or fluoxetine, mirtazapine if a sedative antidepressant is required, imipramine or lofepramine if an alternative TCA is required. Individual product literature for each of these medicines available from [www.medicines.org.uk](http://www.medicines.org.uk)

## Stopping

- TCAs should not be terminated abruptly, instead gradually taper down the daily dose in weekly/two weekly decrements over **at least** 4-8 weeks to avoid discontinuation symptoms.
- For patients who have been taking trimipramine for a long duration (>1 year) of time more gradual tapering may be appropriate, in the region of at least 6 months (3). For patient specific guidance, GPs should contact their local specialist Mental Health MI department.
- Even with a gradual dose reduction some discontinuation symptoms e.g. flu-like symptoms (headache, nausea, chills, excess sweating), Insomnia and irritability may appear within the first 2 weeks. Symptoms can vary in duration and intensity and are usually mild and self-limiting (4) but can occasionally be severe. Discontinuation symptoms will improve quickly (usually within days) if trimipramine is restarted at the previous dose before symptoms became troublesome. As with all swaps in medication tailor the withdrawal process to the individual patient.
- 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.
- For further information and advice please contact your practice pharmacist or Medicines Information (MI) at Springfield University Hospital on 020 3513 6829 or [medinfo@swlstg.nhs.uk](mailto:medinfo@swlstg.nhs.uk). GPs can also obtain additional support on withdrawal from local Primary Care Liaison services
- Practice pharmacists can refer to [caroline.mollison@swlstg.nhs.uk](mailto:caroline.mollison@swlstg.nhs.uk) for patient specific advice.

Few studies have specifically examined the best strategy for switching between antidepressants. The following advice is based on available information, theoretical concerns and clinical experience. It is intended for general guidance only. For patients with complex medical or prescription histories, specialist advice should be sought via Medicines Information as above. Whichever strategy is used, patients should be closely monitored for adverse effects (4). Please note that SSRIs should be the 1<sup>st</sup> line pharmacological choice for anxiety associated with depression. Contact your specialist MI department for specific switching advice. (5)

#### Suggested withdrawal and crossover to sertraline schedule (5)

Medicine	Current dose	Week 1	Week 3	Week 5	Week 7	Week 9
Trimipramine	75mg/day	50mg/day	25mg/day	20mg/day	10mg/day	STOP
Sertraline	Nil	Nil	50mg	50mg	Dose ↑ based on response.	

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

Medicine	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 nocte	15mg nocte	30mg nocte	Dose ↑ based on response

#### Suggested withdrawal and crossover to imipramine schedule (5) (6) (e.g. where anxiolytic action required)

Medicine	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*	Nil	Nil	10mg nocte	10mg nocte	20mg nocte	Dose ↑ based on response

\*Recommended elderly doses (7)

#### Suggested withdrawal for someone on a long term dose of 175mg/day

Medicine	Month 1	Month 2	Month 3	Month 4	Month 5	Month 6
Trimipramine	150mg/day	125mg/day	100mg/day	75mg/day	50mg/day	25mg/day then STOP

#### Practical considerations:

- Issue 14 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.
- Smaller dose decrements than those suggested above can be employed using the 10mg strength tablets.
- **Tailor the withdrawal and cross over to the individual patient based on efficacy and tolerability.**
- If the patient experiences any discontinuation effects, then return to the previous dose of trimipramine and continue with the cross over at a slower pace using smaller decrements.
- For advice on withdrawal of doses of trimipramine greater than 75mg daily please contact Medicines Information at Springfield University Hospital as above.

**Suggested monitoring:** ECG, BP, pulse, weight, BMI, U&E, eGFR, LFTS, full annual health check.

#### References

1. Trimipramine 10mg Tablets. Concordia International- formerly Focus Pharmaceuticals. . [www.medicines.org.uk](http://www.medicines.org.uk). [Online] Last Updated on eMC 11-May-2016.
2. South West London and St George's NHS Trust Formulary. <http://www.swlstg-tr.nhs.uk/documents/related-documents/health-professionals/437-formulary/file>. [Online]
3. BNF online. [https://www.medicinescomplete.com/mc/bnf/current/PHP2386-trimipramine.htm?q=trimipramine&t=search&ss=text&tot=23&p=1#\\_hit](https://www.medicinescomplete.com/mc/bnf/current/PHP2386-trimipramine.htm?q=trimipramine&t=search&ss=text&tot=23&p=1#_hit), accessed 28-Mar-2018. [Online]
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6. Maudsley Prescribing Guidelines Antidepressants Swapping and Stopping. 12th Edition. .
7. Stahl's Essential Pharmacology Prescriber Guide 5th edition Imipramine Monograph.
8. Imipramine Tablets 10mg (Posology and method of administration) Accord-UK Ltd Last Updated on eMC 19-Jun-2017. [www.medicines.org.uk](http://www.medicines.org.uk). [Online]

## Guidance for patients

### Trimipramine for depression and associated sleep disturbance

#### Why should I stop Trimipramine?

Trimipramine is an older tricyclic antidepressant that is unsafe when taken in large doses. National guidelines for the treatment of depression recommend that tricyclic antidepressants should not be used first line as there are alternative antidepressants which have less side effects and are safer in overdose. The price of trimipramine has also increased significantly in recent years and it does not represent good value for money for the NHS. The NHS now recommends that trimipramine should not be initiated for any new patients. Trimipramine should be slowly reduced to prevent any adverse effects.

#### Will I get any effects on stopping trimipramine?

Trimipramine is an antidepressant, which can be used to treat depression and associated anxiety and insomnia. On stopping antidepressants 'discontinuation' symptoms can occur. These symptoms are usually mild and are lessened by slowly lowering the dose in small steps. These symptoms include flu-like symptoms (headache, nausea, chills, excess sweating), insomnia and irritability.

#### Is trimipramine addictive?

Trimipramine is not addictive, it does not cause tolerance (meaning a higher dose is needed to get the same effect) or craving (a feeling of the need or urge to take it).

#### What if I've been taking trimipramine to manage low mood/depression?

The first thing you and your GP need to consider is if you still need to take an antidepressant. As a guide the following is the recommended time to take anti-depressants for:

- For a first episode of major depression or anxiety, your chances of becoming unwell again are much lower if you keep taking the antidepressant for six months after you have recovered. This will be longer if you have risk factors for becoming depressed again such as remaining symptoms or if you have experienced stressful or traumatic life events.
- For a second episode of depression, your chances of becoming depressed again are lower if you keep taking the antidepressant for one or two years after you get better.
- For depression that keeps coming back, continuing to take an antidepressant longer term has been shown to have a protective effect for at least five years.

#### If needed is there another medicine I can take to treat my low mood/depression?

There are a number of different antidepressants available which your GP can discuss with you. When choosing the right antidepressant for you the GP will consider your depressive (target) symptoms, side-effects of the antidepressant, interaction(s) with other prescribed medicines and any physical conditions you may have.

A handy chart which can help you compare the different medicines used to treat depression is available at: <https://www.choiceandmedication.org/swlstg-tr/generate/handychartdepression.pdf>

#### How will my GP stop trimipramine completely or switch to another antidepressant?

If you and your GP decide it is appropriate for you to stop trimipramine, then this will be done gradually and cautiously to prevent discontinuation symptoms such as anxiety, flu-like symptoms and insomnia. The rate at which the dose of trimipramine is reduced will depend on your current dose, how long you have been taking trimipramine and if you experience any discontinuation symptoms. The dose is usually reduced weekly over a period of at least 4 weeks or in some cases much longer. You will be reviewed regularly by your GP during this time.

If switching antidepressants is thought to be the most appropriate option for you; your GP will tailor, the switch specifically to your needs. How your GP carries out the switch will depend on which antidepressant you are switching to and the nature of your depression. It is ideal to completely withdraw trimipramine before starting a new antidepressant; however, a cross-over period is often necessary to ensure that your symptoms of depression continue to be treated. During the cross-over period the dose of trimipramine is reduced and the new antidepressant is started at a low dose. As the dose of the new antidepressant is increased the trimipramine is gradually stopped.

### **Is there anything I can do to improve my sleep?**

Sleep hygiene aims to make you more aware of the different factors that may affect sleep. Your GP may advise you to:

- Establish fixed times for going to bed and waking up (and avoid sleeping in after a poor night's sleep).
- Try to relax before going to bed.
- Maintain a comfortable sleeping environment (not too hot, cold, noisy or bright).
- Avoid napping during the day.
- Avoid caffeine, nicotine and alcohol within six hours of going to bed.
- Avoid exercise within four hours of bedtime (although exercise earlier in the day is beneficial).
- Avoid eating a heavy meal late at night.
- Avoid watching or checking the clock throughout the night.
- Avoid using the bedroom for anything other than sleep and sex.
- Keep a sleep diary to monitor the progress of treatment, noting duration of sleep, diet and exercise.

Further information on good sleep hygiene and non-pharmacological techniques may be found at [www.nhs.uk/conditions/insomnia](http://www.nhs.uk/conditions/insomnia)

### **Is there another medicine I can take to help my sleep?**

Sleeping tablets (hypnotics) are medications that encourage sleep. They may be considered if your symptoms are particularly severe, to ease short-term insomnia or if the sleep hygiene methods have not helped. However, it is not normally recommended to prescribe this type of medication as although they can provide short-term relief of symptoms, they do not treat the underlying cause of your insomnia, they can also be addictive. If you have long term insomnia, sleeping tablets are unlikely to help. Your GP may consider referring you to a clinical psychologist to discuss other approaches to treatment.

### **What if I decide to stay on trimipramine?**

Your doctor will need to record your decision in your patient notes. You must ensure that you keep to the prescribed dose. You should immediately seek advice and help from a doctor if you take more than the dose prescribed by your doctor. Your medicines must be kept away from children and others to help prevent someone accidentally taking them. Your GP may also reduce the quantity you get on each prescription. Your GP will continue to review your medicines with you over time.

#### **References:**

- Electronic Medicines Compendium: <https://www.medicines.org.uk/emc/product/7187/smpc>
- National Institute for Health and Care Excellence, Depression in adults: recognition and management, Clinical Guideline [CG90], published date 28<sup>th</sup> October 2009
- Items which should not routinely be prescribed in primary care: Guidance for CCGs, version 2, June 2019, NHS England and NHS Improvement
- Taylor DM et al. The Maudsley Prescribing Guidelines in Psychiatry 13<sup>th</sup> Edition