

### Trimipramine withdrawal guidance

#### Introduction

Trimipramine is a tricyclic antidepressant (TCA) licensed for depression. However it has been prescribed for unlicensed indications such as anxiety, neuropathic pain, fibromyalgia or insomnia.

SSRIs are recommended by NICE as the first line option for depression as they have less side effects, are safer in overdose, require less dosage titration and instead of, need only once daily dosing which may mean better patient adherence and better patient adherence.

Where a TCA is indicated, trimipramine does not represent a cost-effective choice of TCA as it has been subjected to excessive price inflation. Over the last year Ipswich and East Suffolk CCG has spent over £140,000 on trimipramine alone

NHS England have recently issued guidance stating that while trimipramine may be effective other more cost effective preparations may be used. This guidance aims to provide GPs with the necessary information to review the trimipramine usage and to consider stopping it or switching patients to a more cost effective alternative

#### Reviewing prescribing in depression

##### 1) Stopping trimipramine

A trial discontinuation of trimipramine should be considered if long-term maintenance is no longer considered necessary. Evaluation of this should take into account comorbid conditions, risk factors for relapse and severity and frequency of episodes of depression.

Please note, doses below are represented as total daily doses and do not reflect frequency.

Reduce dose gradually over at least four weeks or longer if withdrawal symptoms emerge.

	Current daily dose	Week 1	Week 2	Week 3	Week 4
Reducing from <b>trimipramine 150mg daily dose</b>	150mg daily	100mg daily	50mg daily	25mg daily	Stop
Reducing from <b>trimipramine 100mg daily dose</b>	100mg daily	75mg daily	50mg daily	25mg daily	Stop
Reducing from <b>trimipramine 75mg daily dose</b>	75mg daily	50mg daily	25mg daily	10mg daily	Stop

2) Switching from trimipramine to sertraline

Start by halving the dose of trimipramine then add sertraline and cross-taper over four weeks. Doses below are represented as total daily doses and do not reflect frequency. The lowest effective dose of the replacement antidepressant should be used and adjusted individually according to the patient's response.

	Medication	Current daily dose	Week 1	Week 2	Week 3	Week 4
Switching from <b>trimipramine 150mg daily</b> dose to sertraline (minimum effective dose)	Trimipramine	150mg daily	75mg daily	50mg daily	25mg daily	Stop
	Sertraline	0mg daily	25mg daily	50mg daily	50mg daily	If necessary, start to titrate sertraline up by 50mg at intervals of one week until minimum effective dose reached. Maximum daily dose 200mg
Switching from <b>trimipramine 100mg daily</b> dose to sertraline (minimum effective dose)	Trimipramine	100mg daily	50mg daily	25mg daily	10mg daily	Stop
	Sertraline	0mg daily	25mg daily	50mg daily	50mg daily	If necessary, start to titrate sertraline up by 50mg at intervals of one week until minimum effective dose reached. Maximum daily dose 200mg
Switching from <b>trimipramine 75mg daily</b> dose to sertraline (minimum effective dose)	Trimipramine	75mg daily	35mg daily	40mg daily	10mg daily	Stop
	Sertraline	0mg daily	25mg daily	50mg daily	50mg daily	If necessary, start to titrate sertraline up by 50mg at intervals of one week until minimum effective dose reached. Maximum daily dose 200mg

3) Switching from trimipramine to imipramine

Cross tapering between two different tricyclic antidepressants should be done cautiously. Please note, doses below are represented as total daily doses and do not reflect frequency. The lowest effective dose of the replacement antidepressant should be used and adjusted individually according to the patient's response. The usual maintenance dose of imipramine is 50-100mg daily.

	Medication	Current daily dose	Week 1	Week 2	Week 3	Week 4	Week 5
Switching from <b>trimipramine 150mg daily</b> dose to imipramine (minimum effective dose)	Trimipramine	150mg daily	100mg daily	75mg daily	50mg daily	25mg daily	Stop
	Imipramine	0mg daily	50mg daily	75mg daily	100mg daily	125mg daily	If needed dose can be taken to 150mg-200mg. Maintain this dose until improvement is seen then gradually reduce to a maintenance dose of 50mg to 100mg
Switching from <b>trimipramine 100mg daily</b> dose to imipramine (minimum effective dose)	Trimipramine	100mg daily	75mg daily	50mg daily	25mg daily	Stop	
	Imipramine	0mg daily	25mg daily	50mg daily	75mg daily	100mg daily	If needed dose can be taken to 150mg-200mg. Maintain this dose until improvement is seen then gradually reduce to a maintenance dose of 50mg to 100mg

	Medication	Current daily dose	Week 1	Week 2	Week 3
Switching from <b>trimipramine 75mg daily</b> dose to imipramine (minimum effective dose)	Trimipramine	75mg daily	50mg daily	25mg daily	Stop
	Imipramine	0mg daily	25mg daily	50mg daily	75mg If needed dose can be taken to 150mg- 200mg. Maintain this dose until improvement is seen then gradually reduce to a maintenance dose of 50mg to 100mg

### **Reviewing prescribing for other indications**

If trimipramine is being prescribed for an unlicensed indication (e.g. anxiety, neuropathic pain, fibromyalgia or insomnia) consider discontinuation as above or switching treatment to a more appropriate alternative in collaboration with an appropriate specialist.

### **Withdrawal effects**

Withdrawal effects may occur within five days of stopping treatment with antidepressant drugs. They are usually mild and self-limiting but in some cases can be severe. The risk of withdrawal symptoms is increased if an antidepressant is stopped suddenly after regular administration for eight weeks or more.

Common symptoms:

- Flu-like symptoms (chills, myalgia, excessive sweating, headache, nausea)
- Insomnia
- Excessive dreaming.

Occasionally:

- Movement disorders
- Mania
- Cardiac arrhythmias.

Treatment of discontinuation symptoms is pragmatic. If symptoms are mild, it may be enough to simply reassure the patient that such symptoms are not uncommon and that they normally pass in a few days.

If symptoms are more severe, the original antidepressant should be re-introduced (or another from the same class but with a longer half-life), and then tapered off much more gradually while closely monitoring for further symptoms

### **References**

1. PrescQIPP bulletin- Trimipramine December 2017