Prescribing of trimipramine is not supported

Thurrock CCG, and Basildon and Brentwood CCG do not support the prescribing of trimipramine as it is not a cost effective option and lacks evidence of superior efficacy and safety, and this position is supported by NHS England.

Trimipramine is a tricyclic antidepressant (TCA) indicated for the treatment of depressive illness, particularly where sedation is required. However, TCAs are not recommended as a first line treatment option in adults with depression by NICE and they are not recommended at all for children and adolescents (aged under 18 years). Selective Serotonin Reuptake Inhibitors (SSRIs) are preferred as they have less side effects, are safer in overdose, require less dosage titration and only need once daily dosing which may mean better patient adherence.

Where a TCA is indicated, as set out by NICE, trimipramine does not represent a cost-effective choice of TCA as it has been subjected to excessive price inflation. More cost effective products are available.

Recommendations

- TCAs should not be used first line for the treatment of depression.
- SSRIs are recommended by NICE as they are equally effective and have a more favourable risk-benefit ratio.
- Where a TCA is indicated in accordance with NICE, trimipramine should not be prescribed as it is not considered to be cost effective for prescribing on the NHS.
- Patients already being prescribed trimipramine should be reviewed in line with the current NICE clinical guidance.
- Ongoing prescribing of antidepressants should be reviewed after six months or two years depending on the person's risk of relapse.
- If trimipramine is being prescribed for an unlicenced indication (e.g. anxiety, neuropathic pain, fibromyalgia or insomnia) consider discontinuation or switching treatment to a more appropriate alternative in collaboration with an appropriate specialist.

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. Antidepressant treatment should be continued for at least six months after remission of a dose of depression, increased to at least two years for those at risk of relapse.

Due to the risk of discontinuation syndrome with sudden cessation of therapy with antidepressants, discontinuation and switching must be managed carefully. Dosage adjustments should be made carefully on an individual patient basis, to maintain the patient at the lowest effective dose. Dosage during long term therapy should be kept at the lowest effective level, with subsequent adjustment depending on therapeutic response. Any discontinuation of therapy should be done slowly, with gradual dose reductions, for patients who have been taking an antidepressant regularly for six weeks or more. A suggested withdrawal regimen for trimipramine is:

	Current daily dose	Week 1	Week 2	Week 3	Week 4
Reducing from 150mg daily dose	150mg daily	100mg daily	50mg daily	25mg daily	Stop
Reducing from 100mg daily dose	100mg daily	75mg daily	50mg daily	25mg daily	Stop
Reducing from 75mg daily dose	75mg daily	50mg daily	25mg daily	10mg daily	Stop

Please note, doses 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.

Switching trimipramine

Where antidepressant treatment is still indicated, SSRIs are usually preferred due to their more favourable risk/benefit profile. Choice of treatment should take into account the duration of the episode of depression and the trajectory of symptoms, previous course of depression and response to treatment, likelihood of adherence to treatment and any potential adverse effects and the person's treatment preferences and priorities.

If an SSRI represents a clinically appropriate alternative for the individual patient, then a managed switch from trimipramine to sertraline should be tried. SSRIs are associated with an increased risk of bleeding (gastrointestinal, uterine, cerebral and peri-operative), especially in older people or in people taking other drugs that have the potential to damage the gastrointestinal mucosa or interfere with clotting. In particular, consider prescribing a gastroprotective drug in older people who are also taking nonsteroidal anti-inflammatory drugs (NSAIDs) or aspirin.

If an SSRI isn't appropriate and an alternative TCA would be a more suitable alternative, a managed switch to imipramine is recommended as it is less sedative, cost effective and less cardiotoxic in overdose. Bear in mind that TCAs are associated with the greatest risk in overdose of all antidepressant classes and an increased likelihood of the person stopping treatment because of side effects.

When changing from one antidepressant to another, abrupt withdrawal should usually be avoided. Any switching should be carried out with the appropriate cross-tapering regimen and patients should be very carefully monitored.

Switching from trimipramine to sertraline:

	Medication	Current daily dose	Week 1	Week 2	Week 3	Week 4
Switching from trimipramine 150mg daily dose to sertraline	Trimipramine	150mg daily	75mg daily	50mg daily	25mg daily	Stop
	Sertraline	None	25mg daily	50mg daily	50mg daily	*
Switching from trimipramine 100mg daily dose to sertraline	Trimipramine	100mg daily	50mg daily	25mg daily	10mg daily	Stop
	Sertraline	None	25mg daily	50mg daily	50mg daily	*
Switching from trimipramine 75mg daily dose to sertraline	Trimipramine	75mg daily	35mg daily	20mg daily	10mg daily	Stop
	Sertraline	None	25mg daily	50mg daily	50mg daily	*

*****_If necessary, start to titrate sertraline up by 50mg at intervals of 1 week until minimum effective dose reached. Maximum daily dose 200mg._

Switching from trimipramine to imipramine:

	Medication	Current daily dose	Week 1	Week 2	Week 3	Week 4	Week 5
Switching from trimipramine 150mg daily dose to imipramine	Trimipramine	150mg daily	100mg daily	75mg daily	50mg daily	25mg daily	Stop
	Imipramine	None	50mg daily	75mg daily	100mg daily	125mg daily	*
Switching from trimipramine 100mg daily dose to imipramine	Trimipramine	100mg daily	75mg daily	50mg daily	25mg daily	Stop	
	Imipramine	None	25mg daily	50mg daily	75mg daily	100mg daily	*
Switching from trimipramine 75mg daily dose to imipramine	Trimipramine	75mg daily	50mg daily	25mg daily	Stop		
	Imipramine	None	25mg daily	50mg daily	75mg 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_

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.

This position is supported by NHS England as part of the items which should not routinely be prescribed in primary care.

Providers commissioned to provide services on behalf of Thurrock CCG and Basildon and Brentwood CCG are reminded that they are required to follow the local joint formulary and prescribing guidance, or relevant Medicines Management agreement.

Position Statement No.	54
Title	Prescribing of trimipramine is not supported
References	PrescQIPP bulletin 204 Trimipramine: https://www.prescqipp.info/media/1711/b204-trimipramine-20.pdf
Acknowledgements	N/A
Version	1
Author	Medicines Management Team
Approved by	**Basildon and Brentwood CCG:** Prescribing Subgroup, Patient Quality and Safety Committee, Board **Thurrock CCG:** Medicines Management and Safety Group, Patient Quality and Safety Committee, Transformation and Sustainability Committee, Board
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