Trimipramine Review Advice

Background

Trimipramine is a tricyclic antidepressant (TCA) indicated for the treatment of depressive illness, particularly where sedation is required.

- Tricyclic antidepressants are not recommended as a first line treatment option in adults with depression by NICE.
- Where a TCA is indicated, as set out by NICE, trimipramine does not represent a cost-effective choice as it has been subjected to excessive price inflation and more cost-effective products are available.
- Due to the significant cost associated with trimipramine and the availability of alternative treatments NHSE have included trimipramine in their guidance " Items which should not routinely be prescribed in primary care: Guidance for CCGs2 published in November 2017

Suggested Action

- Do not start or switch to trimipramine.
- TCAs should not be used first line for the treatment of depression. Selective serotonin reuptake inhibitors (SSRIs) are recommended by NICE as they are equally effective and have a more favourable risk-benefit ration.
- **Complex/ higher risk cases may warrant a secondary care review and if currently under secondary care then it would be advisable for GP to seek view of the treating Psychiatrist before implementing a change which may precipitate relapse.**
- Document outcome of discussions
- Document treatment plan if switching
- Clearly identify reason if continuing trimipramine

Withdrawal of trimipramine.

A trial discontinuation of trimipramine should be considered if long-term maintenance is no longer considered necessary. Discontinuation should be done slowly with gradual dose reductions. The doses selected and the speed at which they are reduced will need to be individualised for each patient.

Example:

Starting dose of Trimipramine	Week 1	Week 2	Week 3	Week 4
150mg/day	100mg /day	50mg/day	25mg/day	stop
100mg/day	75mg/day	50mg/day	25mg/day	stop
75mg/day	50mg/day	25mg/day	10mg/day	stop

Switching to an SSRI

The dose of trimipramine must be reduced to 50% slowly before cross tapering to an SSRI. Cross-taper over four or more weeks. The speed of cross tapering should be judged by monitoring patient's tolerability. No clear guidelines are available so caution is required. If patients are not tolerating, cross taper more slowly. See flow chart.

Serotonin syndrome

This generally occurs if high doses are used or the use of two agents that both increase levels of serotonin. Symptoms can occur on a spectrum and the effects seen and severity is usually dose related. Symptoms include – Psychiatric effects – agitation, excitement, confusion, restlessness, lack of coordination Neuromuscular activity –tremor, clonus, myoclonus, hyper-reflexia and pyramidal rigidity, shivering Autonomic activity – diaphoresis, fever, mydriasis, tachycardia, tachypnoea, diarrhoea, vomiting, hypertension Onset of symptoms is usually rapid within a few doses of the second drug being introduced. Severe symptoms will need urgent management in an acute care setting such as Emergency Departments. The causative agents should be stopped and the switch re-assessed.

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.

Switching to imipramine

The dose of trimipramine must be halved before cross tapering to another tricyclic. Cross-taper over four or more weeks. The speed of cross tapering should be judged by monitoring patient's tolerability. No clear guidelines are available so caution is required. If patients are not tolerating, cross taper more slowly. See flow chart.

Patient Information:

An adaptable template for dose reduction or cross tapering from trimipramine to sertraline or imipramine will be available in emis shortly.

References

https://www.england.nhs.uk/wp-content/uploads/2017/11/items-which-should-not-be-routinely-precscribed-in-pc-ccg-guidance.pdf

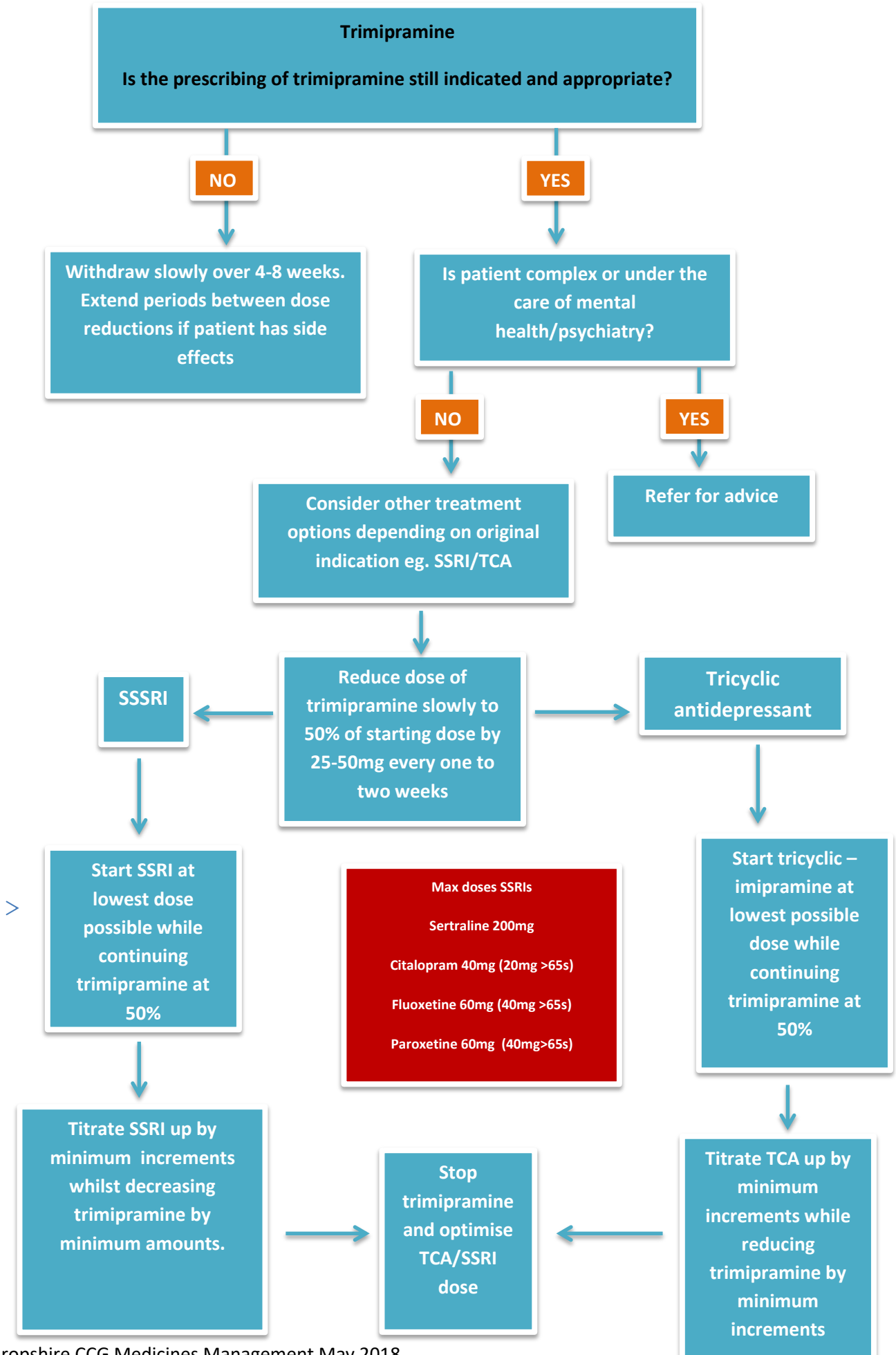
Bazire, S. Psychotropic Drug Dictionary 2016

PrescQIPP DROP-List Bulletin available at www.presqipp.info

Joint Formulary Committee. British National Formulary (online) London:BMJ Group and Pharmaceutical Press www.medicinescomplete.com http://dx.doi.org/10.18578/BNF.253045598 accessed 17/5/2018

Electronic medicines compendium www.emc.org accessed 17/5/2018

Taylor D, Paton C, Kapur S, The South London and Maudsley NHS Foundation Trust. Oxleas NHS Foundation Trust. The Maudsley Prescribing Guidelines. 12th Edition. June 2015


Trimipramine
Is the prescribing of trimipramine still indicated and appropriate?
NO
YES
Withdraw slowly over 4-8 weeks. Extend periods between dose reductions if patient has side effects
Is patient complex or under the care of mental health/psychiatry?
NO
YES
Refer for advice
Consider other treatment options depending on original indication eg. SSRI/TCA
Reduce dose of trimipramine slowly to 50% of starting dose by 25-50mg every one to two weeks
SSSRI
Tricyclic antidepressant
Start SSRI at lowest dose possible while continuing trimipramine at 50%
Max doses SSRIs
Sertraline 200mg
Citalopram 40mg (20mg >65s)
Fluoxetine 60mg (40mg >65s)
Paroxetine 60mg (40mg>65s)
Start tricyclic – imipramine at lowest possible dose while continuing trimipramine at 50%
Titrate SSRI up by minimum increments whilst decreasing trimipramine by minimum amounts.
Stop trimipramine and optimise TCA/SSRI dose
Titrate TCA up by minimum increments while reducing trimipramine by minimum increments