

DOSULEPIN DEPRESCRIBING

Summary

- Prescribers in primary care should not initiate dosulepin for any new patient.
- CCGs to support prescribers in de-prescribing dosulepin in all patients and, where appropriate, ensure the availability of relevant services to facilitate this change.
- IF, in exceptional circumstances, there is a clinical need for dosulepin to be prescribed in primary care, this should be undertaken in a cooperation arrangement with a multi-disciplinary team and/or other healthcare professional

Background

Dosulepin is a tricyclic antidepressant. The following NICE recommendation has been in place since the publication of NICE CG90 in 2009;

“Do not switch to, or start, dosulepin because evidence supporting its tolerability relative to other antidepressants is outweighed by the increased cardiac risk and toxicity in overdose.”

The medication features on the [Presc-QIPP drop list](#). Further to this, in 2016 PrescQIPP released recommendations and resources regarding the medication in Bulletin 126, among which was the statement; *“Review all patients prescribed dosulepin for suitability for switching to a safer antidepressant or suitable agent. For patients under the care of a relevant specialist, involve them in the decision to discontinue or switch treatment”*.

In December 2017, in the NHS document “Items which should not be routinely prescribed in primary care”, dosulepin was categorised as one of the *“Products of low clinical effectiveness, where there is a lack of robust evidence of clinical effectiveness or there are significant safety concerns.”*

National spending is cited as £2,652,544 in 2016, and local figures show that in the Greater Nottingham area there was £41,686.59 spent on the medication over a 1 year period.

NHS England recommends, and this document will work towards implementing;

- Advise CCGs that **prescribers in primary care should not initiate dosulepin** for any new patient.
- Advise CCGs to **support prescribers in de-prescribing dosulepin in all patients** and, where appropriate, ensure the availability of relevant services to facilitate this change.
- Advise CCGs that if, in exceptional circumstances, there is a clinical need for dosulepin to be prescribed in primary care, this should be undertaken in a cooperation arrangement with a multi-disciplinary team and/or other healthcare professional.

Stopping or switching

When reviewing these patients, consideration should be given as to whether the medication should be switched to an alternative, or treatment stopped entirely.

Antidepressant treatment should be continued for at least six months after remission of an episode of depression, increased for those at risk of relapse to at least two years. Patients are at particular risk of relapse if;

- they have had two or more episodes of depression in the recent past, during which they experienced significant functional impairment
- they have other risk factors for relapse such as residual symptoms, multiple previous episodes, or a history of severe or prolonged episodes or of inadequate response

Prior to discontinuation there should be a full discussion of the potential consequences of relapse, taking into account previous history (including suicide attempts, loss of functioning, severe life disruption, inability to work or manage childcare). The timing of discontinuation should include a consideration of social context.

Where a decision is taken to switch from Dosulepin to another antidepressant medication, be aware that there is no direct antidepressant replacement for Dosulepin. Possible alternatives, include less toxic tricyclic antidepressants (such as Lofepramine **but not Amitriptyline**), SSRI medications (such as Sertraline), SNRI

medications (such as [Venlafaxine](#)), or other antidepressants (including [Mirtazapine](#) or [Vortioxetine](#)). The decision of which to use as an alternative should be taken in collaboration with the patient, based on an informed discussion including past treatment history (including tolerability and effect of previous antidepressant medications).

Patient choice is important when switching medications. They should be aware of common side effects of the medications where relevant.

The patient should be made aware of information available that may answer questions they have on their medication. A good resource is;

<http://www.choiceandmedication.org/nottinghamshirehealthcare/condition/depression/>

In light of the increased cardiac risk and toxicity in overdose, dosulepin should not be prescribed. Dosulepin is licensed for the treatment of depressive illness in adults so should not be prescribed for any unlicensed indication including anxiety, neuropathic pain or insomnia. The Nottinghamshire APC has published guidance on treating [Neuropathic Pain in Primary Care](#).

The following tables explain the stopping/switching process. Due to the risk of discontinuation syndrome with sudden cessation of therapy with antidepressants, discontinuation and switching must be managed carefully. 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. 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. However, the speed of cross-tapering is best judged by individual patient tolerability. If patients are not tolerating the change, cross-taper more slowly (a patient that has been using trazodone for many years may require cross tapering over several months). It should be noted that there are no clear guidelines on switching antidepressants, so caution is required. The following advice has been interpreted from Maudsley, MIMS and BNF guidance.

It should be noted due to the side effect profile of the medication that dosulepin is contraindicated in patients who have had a recent myocardial infarction, patients with a heart block or any other cardiac arrhythmia. The medication is also contraindicated in mania and liver disease.

There is a small difference in cost between dosulepin and the alternatives (28 tablets of dosulepin 75mg costs £1.20 while 28 tablets of sertraline costs £0.91). This switch is based on concerns over the medication's safety profile.

How to stop

To stop dosulepin, the following could be used as a general guide (as per PrescQIPP Bulletin 126);

Current dose	Week 1	Week 2	Week 3	Week 4
150mg/day	100mg/day	50mg/day	25mg/day	STOP

This would be generally classified as a "slow withdrawal".

However, for patients who have taken this drug for several years, a more graduated withdrawal over several months, rather than several weeks, should be considered. In either case, the patient should be made aware of potential discontinuation symptoms and monitored during the period of discontinuation.

What to switch to

There is no direct antidepressant replacement for Dosulepin. Possible alternatives, include less toxic tricyclic antidepressants (such as [Lofepramine](#) **but not Amitriptyline**), SSRI medications (such as [Sertraline](#)) and SNRI medications (such as [Venlafaxine](#)), or other antidepressants (including [Mirtazapine](#) or [Vortioxetine](#)). The decision of which to use as an alternative should be taken in collaboration with the patient, based on an informed discussion including past treatment history (including tolerability and effect of previous antidepressant medications).

How to cross-taper

The Maudsley prescribing guidelines in psychiatry recommend "cautious cross-tapering". The speed of the

cross-tapering should be judged by monitoring the tolerability of the switch by the individual patient. The following tables are interpretations of the advice given in Maudsley and the BNF.

	Medication	Current dose	Week one	Week two	Week three	Week four
Cautious switch from dosulepin to SERTRALINE	Dosulepin	150mg	75mg	50mg	25mg	Stop
	Sertraline	0mg	0mg	25mg	50mg	50mg

Gradually reduce the dose of dosulepin to 25-50mg/day as per the above withdrawal regimen, and then add in the SSRI. Continue cross tapering and review the sertraline following the switch.

	Medication	Current dose	Week one	Week two	Week three	Week four
Cautious switch from dosulepin to LOFEPRAMINE	Dosulepin	150mg	75mg	50mg	25mg	Stop
	Lofepramine	0mg	35mg	35mg	70mg	70mg

Gradually reduce the dose of dosulepin to 25-50mg/day as per the above withdrawal regimen, and then add in lofepramine cautiously (tablets are scored).

	Medication	Current dose	Week one	Week two	Week three	Week four
Cautious switch from dosulepin to VENLAFAXINE	Dosulepin	150mg	75mg	50mg	25mg	Stop
	Venlafaxine	0mg	0mg	75mg	75mg	75mg

Gradually reduce the dose of dosulepin to 25-50mg/day as per the above withdrawal regimen, then start a low dose of venlafaxine. Following introduction, venlafaxine can be increased if necessary up to 300mg/day (doses over 300mg/day are classified as AMBER 2, and will require specialist intitation).

	Medication	Current dose	Week one	Week two	Week three	Week four
Cautious switch from dosulepin to MIRTAZAPINE	Dosulepin	150mg	75mg	50mg	25mg	Stop
	Mirtazapine	0mg	0mg	15mg	15mg	15mg

Gradually reduce the dose of dosulepin to 25-50mg/day as per the above withdrawal regimen, and then add in the mirtazapine at the usual starting dose. Review whether to increase the mirtazapine dose after this.

Further support

Pharmacy Contacts - Nottinghamshire Healthcare NHS Foundation Trust

Wells Road Centre Pharmacy - 01159 555 357
 Highbury Hospital Pharmacy - 0115 854 2247
 Millbrook Mental Health Unit Pharmacy - 01159 560 883 x14604
 Email - MI@nottshc.nhs.uk

Information for patients

Information for patients has been written by PrescQIPP;



Patient information -
Changes to dosulepin

Withdrawal

Following therapy with Dosulepin, particularly for a prolonged period, an incremental dosage reduction to withdrawal is recommended to minimise the occurrence of withdrawal symptoms.

Onset of symptoms is seen usually within 5 days of stopping treatment, or occasionally during tapering. 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
- Anxiety

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. Remember by discontinuing/cross-tapering slowly and by educating the patient on what to expect during a switch, the symptoms (and a patient's perception of their severity) will be lessened or avoided entirely.

Cognitive Behavioural Therapy ("Talking Therapy")

Treating issues around depression is a process that might not be that might not be addressed by the use of medications alone. There are several "talking therapy" services across Nottinghamshire that patients can refer themselves to, or with consent healthcare providers can refer them to.



Tel: 0115 956 0888



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References

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PrescQIPP bulletin 126 – Dosulepin (drop list)- <https://www.prescqipp.info/resources/send/313-dosulepin-drop-list/2857-bulletin-126-dosulepin-drop-list>

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