Dosulepin – stopping & switching guidance

Summary

- Dosulepin is a tricyclic antidepressant (TCA) which is no longer recommended for use by NICE, NHSE Hertfordshire Partnership Foundation Trust (HPFT), Essex Partnership University Trust (EPUT) or Herts and West Essex Integrated Care Board (HWE ICB).
- Patients should NOT be initiated on, or switched to dosulepin.
- There are significant safety concerns with dosulepin as it carries increased cardiac risks (especially QT interval prolongation causing arrythmias). It is highly toxic in overdose.
- For existing patients, it may be appropriate to stop dosulepin or switch to another antidepressant.
- In **exceptional** cases there may be a clinical need to continue dosulepin. In these cases, the decision should be made in conjunction with a consultant or other specialist healthcare professional.

Background and rationale

- NICE guidance (NG 222) on treating and managing depression in adults recommends selective serotonin reuptake inhibitor (SSRI) are first line if antidepressants are indicated as they have a more favourable risk-to-benefit ratio compared to TCAs.
- Evidence supporting the tolerability of dosulepin relative to other antidepressants is outweighed by the increased cardiac risk and toxicity in overdose.
- TCAs and monoamine oxidase inhibitors (MAOIs) have the highest toxicity in overdose compared to other antidepressants.

Recommended actions

- Do not initiate or switch to dosulepin in any patients.
- 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.
- Existing patients should be reviewed (and specialist input requested where required) in line with current NICE clinical guidance to assess their ongoing need and suitability for dosulepin. Consideration should be given as to whether dosulepin should be switched to an alternative or treatment stopped entirely.
- Document the outcome of discussions and clearly identify the reason(s) if continuing dosulepin.

Suggested review process

- Patients taking dosulepin should be prioritised for review.
- Dosulepin should not be prescribed for any unlicensed indication, including anxiety, neuropathic pain, fibromyalgia or insomnia.
- This guidance document focusses on deprescribing or switching dosulepin when it has been initiated as an antidepressant. There are many alternative, safe, cost effective antidepressants available and review of dosulepin for this indication should be considered a practice priority.

- Patients who are on dual antidepressant therapy with dosulepin should be referred to a secondary care specialist for advice and support to deprescribe/switch.
- Patients who are taking dosulepin for an indication other than depression may need to be referred back to their initial prescribing team for advice and support to deprescribe.
- Please note dosulepin is **non-formulary** across HWE ICB.

Stopping dosulepin

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).

Dosulepin should not routinely be stopped abruptly (unless serious side effects have occurred) because abrupt withdrawal may cause withdrawal related side effects. Discontinuation of therapy should be with gradual dose reductions. Withdrawal effects usually occur within five days of stopping treatment.

Reduce dose gradually over at least 4 weeks; longer if withdrawal symptoms emerge. **For patients who have taken dosulepin for several years, consideration should be given to a slower withdrawal.** This advice is in line with NICE guidance who advocate individual patient involvement in the speed of the reduction of dose.

A suggested withdrawal regimen for dosulepin is shown below, with a minimum frequency of dose reduction of weekly intervals, although longer intervals may be needed depending on the response to each dose reduction. Please note, doses below are represented as *total daily doses* and do not reflect frequency. The lowest possible dose using tablets or capsules is 25mg.

	Current total daily dose	**Reduction one**	**Reduction two**	**Reduction three**	**Reduction four**
Reducing from dosulepin 150mg daily dose	150 mg daily	100 mg daily	50 mg daily	25 mg daily	STOP

Where a decision is taken to switch from dosulepin the alternative treatment options should be discussed with each patient. Considerations will include relative side effects, current diagnoses, past treatment history (including tolerability and effect of previous antidepressant medications) and drug interactions with other medication.

Switching from dosulepin to an alternative antidepressant (see Appendix 1 for further suggested guidance on switching from dosulepin)

Seek specialist advice if needed.

Where a decision is taken to switch from dosulepin the alternative treatment options should be discussed with the patient. Considerations will include the duration and severity of past depressive episodes, co-morbidities (see table below), relative side effects, current diagnoses, past treatment history (including tolerability and effects of previous antidepressant medications) and drug interactions with other medication. Whilst moving to another antidepressant option, it would be prudent to *only* provide small supplies of dosulepin and of the new drug, to agree a plan and review this with the patient, as required.

Patient profile	Suggested options*
In need of sedation	Mirtazapine (lower doses are more sedating)
In need of activation	SSRI or venlafaxine
Cardiac disease	Mirtazapine or sertraline
Diabetes	SSRIs (most data supports fluoxetine)
Epilepsy	SSRIs
Hepatic impairment	Citalopram[Δ] (maximum dose 20mg/day)
Renal impairment	Citalopram[Δ] or sertraline
Parkinson's disease	SSRIs
Anticoagulated e.g. Stroke	SSRIs (citalopram[Δ]) if taking warfarin consider Proton Pump Inhibitor for gastric protection or mirtazapine (has a small effect on INR). Choice based on individual patient risk factors; close monitoring is required.

* For further information refer to the manufacturer's SmPC for the individual drug. These can be accessed via: www.medicines.org.uk

Δ NOTE: Citalopram use is contraindicated in conjunction with medications that are known to prolong the QT interval or those patients with known QT prolongation. The maximum dose for adults is now 40mg daily (20mg daily for over 65s) due to risks of QT interval prolongation.

See Appendix 1 of the HPFT depression guideline for useful comparison table of relative side effects. *(link)*

There should be close monitoring of patients being switched from dosulepin to another antidepressant, particularly in the elderly. The regimen will depend upon how severe the depression has been, the dose of dosulepin prescribed, length of time it has been prescribed and which drug it is being switched to.

Resources

- A local patient information leaflet to support the changes is available at: https://www.hweclinicalguidance.nhs.uk/all-clinical-areas-documents/search-results/dosulepin-patient-information-leaflet/

References

1. Electronic Medicines Compendium. Summary of medicines characteristics. Individual product monographs www.medicines.org.uk
2. MHRA Drug Safety Update Volume 1, Issue 5, December 2007. Dosulepin: measures to reduce risk of fatal overdose. Available at: https://webarchive.nationalarchives.gov.uk/ukgwa/+/http:/www.mhra.gov.uk/Safetyinformation/DrugSafetyUpdate/CON084687
3. NHSE, October 2023. Items which should not be routinely prescribed in primary care: policy guidance: NHS England » Items which should not routinely be prescribed in primary care: policy guidance
4. NICE guideline (NG 222): Depression in adults: treatment and management (June 2022): Overview | Depression in adults: treatment and management | Guidance | NICE
5. Taylor D, Barnes T, Young A. The Maudsley Prescribing Guidelines 13th Edition. Wiley Blackwell.
6. SPS document April 2024: Tricyclics to other antidepressants: switching in adults

Appendix 1

The following tables are interpretations of the advice given in The Maudsley Prescribing Guidelines and the BNF and provide some additional guidance on how to manage switching, however, the speed of cross tapering is best judged by individual patient tolerability and response. If patients are not tolerating the change, cross-taper more slowly. The lowest effective dose of the replacement antidepressant should be used and adjusted individually according to the patient's response. **Please note doses below are represented as total daily dose and do not reflect frequency.**

Switching from dosulepin to an SSRI

	Medication	Current total daily dose	Week one	Week two	Week three	Week four	
Switch from dosulepin to an SSRI* (minimum effective dose)	Dosulepin	150mg daily	75mg daily	50mg daily	25mg daily	STOP	
	Sertraline	-	-	25mg daily	50mg daily	50mg daily	The dose can be increased gradually by 50mg at intervals of at least one week until the minimum effective dose is reached (maximum dose 200mg/day).
	OR						
	Citalopram	-	-	10mg daily	20mg daily	20mg daily	The dose can be increased gradually by 10mg at intervals of at least 2 weeks until the minimum effective dose is reached. Maximum daily dose 40mg (20mg in elderly).

For patients who have taken dosulepin for several years, a more cautious cross-taper may be considered.
Doses are represented as *total daily doses* and do not reflect frequency.
See the SmPC for citalopram drops section 4.2 for dose equivalence between tablets and liquid.
*Consider risk of serotonin syndrome especially in patients on other serotonergic medications.

Switching from dosulepin to an alternative TCA

	Medication	Current total daily dose	Week one	Week two	Week three	Week four	
Switch from dosulepin to alternative TCA (minimum effective dose)	Dosulepin	150mg daily	75mg daily	50mg daily	25mg daily	STOP	
	Lofepramine	-	-	70mg daily	70mg daily	140mg	Usual total daily dose 140mg (the elderly may respond to lower doses – refer to SmPC). Maximum total daily dose 210mg.
	OR						
	Imipramine	-	25mg daily	50mg daily	75mg daily	100mg daily	If needed dose can be taken to 150mg-200mg daily. Maintain this dose until improvement is seen then gradually reduce to a usual maintenance dose of 50mg to 100mg daily (the elderly may respond to lower doses – refer to SmPC).

For patients who have taken dosulepin for several years, a more cautious cross-taper may be considered. Doses are represented as *total daily doses* and do not reflect frequency.

Switching from dosulepin to mirtazapine

	Medication	urrent total daily dose	Week one	Week two	Week three	Week four	
Switch from dosulepin to mirtazapine (minimum effective dose)	Dosulepin	150mg daily	75mg daily	50mg daily	25mg daily	STOP	
	Mirtazapine	-	-	15mg daily	15mg daily	30mg daily	The dose can be increased gradually by 15mg at intervals of at least one week until the minimum effective dose is reached. Maximum total daily dose 45mg.

For patients who have taken dosulepin for several years, a more cautious cross-taper may be considered. Doses are represented as *total daily doses* and do not reflect frequency.

Switching from dosulepin to venlafaxine (SNRI)

	Medication	Current total daily dose	Week one	Week two	Week three	Week four	
Switch from dosulepin to venlafaxine (minimum effective dose)	Dosulepin	150mg daily	75mg daily	50mg daily	25mg daily	STOP	
	Venlafaxine*	-	-	37.5mg daily	75mg daily	75mg daily	The dose can be increased gradually by 37.5 -75mg at intervals of at least two weeks until the minimum effective dose is reached. Maximum total daily dose 375mg.**

For patients who have taken dosulepin for several years, a more cautious cross-taper may be considered. Doses are represented as *total daily doses* and do not reflect frequency.

*Doses over 300mg/day should only be prescribed under the supervision or advice of a specialist mental health practitioner.

*Consider risk of serotonin syndrome especially in patients on other serotonergic medications.

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