NHS
Nottingham and Nottinghamshire
Integrated Care Board

Dosulepin Review and Deprescribing
Advice for Primary Care Prescribers

Introduction

- Aim – To review all patients prescribed dosulepin for suitability of deprescribing antidepressant therapy, switching to an alternative antidepressant or reducing the dose.
- Dosulepin has a very small margin of safety between the (maximum) therapeutic dose and potentially fatal doses. Overdose is associated with a relatively **high rate of mortality.** Doses of 750 mg in adults and 15 mg/kg in children have been associated with fatalities as per a 2007 MHRA update.
- Dosulepin features on the PrescQIPP DROP-List as an item which is not recommended for prescribing in view of its unfavourable safety profile compared with other available antidepressant options.
- The BNF states that dosulepin is not recommended for the treatment of depression, due to the increased risk of fatality in overdose; and that when used, initiation should be by a specialist.
- Dosulepin has an unfavourable cardiac profile, even within BNF dose guidelines.
- Dosulepin should not be used as an anxiolytic, for neuropathic pain or for its sedative effects to aid sleep.
- Dosulepin should not be stopped abruptly unless serious side effects have occurred.
- Dosulepin is associated with a high anticholinergic burden.

Review process and principles

- Identify all patients with dosulepin on repeat prescription.
- Identify if the person is under a specialist (e.g. community mental health team) and involve them in decisions to discontinue or switch treatment.
- Invite the person for a face-to-face consultation.
- Explain to the person reasons for the review and provide reassurances; this may be an anxiety inducing change.
- Clarify the indication for dosulepin prescribing by gathering information from the person/family/carers and healthcare records.

Dosulepin for off-label indications

- Off label indications may include, but are not limited to, anxiety, insomnia, and neuropathic pain.
- Consider discontinuation of dosulepin in these cases and discuss alternative management strategies with the person.
- Amitriptyline is not recommended for insomnia or anxiety.
- See section below on how to stop dosulepin safely.
- Useful resources:
  - Improving Access to Psychological Therapies (IAPT) – Let's Talk Wellbeing, Insight Healthcare and Trent PTS
  - Sleep hygiene patient information leaflet and MIND patient information leaflet on sleep problems
  - Nottinghamshire APC neuropathic pain guideline

Dosulepin for depression or anxiety – stopping or switching to an alternative antidepressant?

- If the person is open to mental health services, seek specialist advice on stopping or switching dosulepin.
- Discuss with the person whether to continue a pharmacological treatment for depression based on their clinical needs and preferences.
- Continuation of antidepressant treatment after full or partial remission may reduce the risk of relapse.
- Treatment with an antidepressant should continue for at least 6 months following remission of symptoms.

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- For people who are assessed as being at higher risk of relapse, consider continuing antidepressant treatment for two years or longer following remission, with minimum 6 monthly review during maintenance.
- The risk of relapse may be increased by the following factors:
  1) History of recurrent episodes of depression, particularly if occurred frequently or within the last two years
  2) History of incomplete response to treatment, including residual symptoms
  3) Unhelpful coping strategies
  4) A history of severe depression (including significant functional impairment)
  5) Other chronic physical or mental health problems
  6) Personal, social, and environmental factors that contributed to their depression that are still present (e.g. unemployment, stress, financial problems, social isolation, poverty)
- If a shared decision is made to continue antidepressant treatment, switch to an alternative with a better safety profile.

How to stop dosulepin safely

- There may be concerns about stopping antidepressant medication (relapse or withdrawal symptoms) and most people will need support to stop successfully.
- Offer regular reviews (face to face or telephone) to check progress and monitor mental state.
- Dosulepin should not be stopped abruptly unless serious side effects have occurred.
- The speed and duration of the withdrawal should be agreed with the person on an individual basis.
- Reduce the dose gradually. Unless there are reasons for more rapid discontinuation (e.g. side-effect burden), then consider reducing over weeks, or months depending on duration of use (typically over weeks if previously taken for months; and over months if previously taken for years). Reduce at each stage by a maximum of 50% of the current dose and consider smaller percentage reductions as the total dose gets lower (e.g. 25% reductions; be guided by the advice ‘as you go lower go slower’, particularly if the patient is finding withdrawal difficult).
- Ensure that any withdrawal symptoms have resolved before making the next dose reduction.
- Discontinuation may take weeks or months to complete successfully.
- Advise the person to seek help as soon as possible if symptoms of depression return or residual symptoms worsen.
- Discuss with the person psychological therapy for relapse prevention. Refer to IAPT if appropriate.

Managing withdrawal symptoms

- Advise the person that they may experience withdrawal symptoms (insomnia, headaches, nausea, anxiety, flu-like symptoms) but the risk is minimised with gradual dose reduction.
- Reassure the person that withdrawal symptoms are usually mild with gradual dose reductions and often self-resolve within 1-2 weeks.
- Explain to the person that experiencing withdrawal symptoms does not mean they are having a relapse of their depression. Withdrawal symptoms usually start soon after the medication is reduced whereas the return of depression or anxiety takes longer (typically weeks or months).
- If a person experiences mild withdrawal symptoms, initially monitor them and provide reassurance. Do not make another dose reduction until the symptoms have resolved.
- If withdrawal symptoms are more severe, consider increasing dosulepin to the previous dose and then attempt dose reduction in a smaller increment once symptoms have resolved.

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Switching dosulepin to an alternative antidepressant

- There is no direct antidepressant replacement for dosulepin.
- The decision of which antidepressant to switch to must be a shared decision with the person.
- Discuss with the person: past treatment history (efficacy and tolerability of previous antidepressants), potential side effects and potential interactions with other medicines or physical health conditions.
- When switching from one antidepressant to another, abrupt withdrawal should be avoided unless there has been a serious adverse event or serious side effects.
- The method of switching depends on several factors:
  1) How long the person has been taking dosulepin and the current dose.
  2) Which antidepressant is being switched to.
  3) The urgency of the switch (if less urgent then a more cautious switching approach can be used).
  4) The person's physical condition (more caution advised in older adults or those with co-morbidities).
  5) The risk of serotonin syndrome (higher risk if the person is taking other medication with serotinergic activity – see UKMi Q&A on serotonin syndrome.)
  6) The person's ability to understand a switching regimen (risk of medication errors). Provide written and verbal instructions on the agreed switching plan.
- NICE Clinical Knowledge Summary – Depression contains useful information on switching antidepressants. Note that dosulepin is a tricyclic antidepressant (TCA).
- **Do not switch to amitriptyline due to increased risk of fatality in overdose.**
- Options for switching may include SSRIs (e.g. sertraline, citalopram, escitalopram, fluoxetine), SNRIs (e.g. venlafaxine, duloxetine), mirtazapine (useful if sedative effect is required) or another TCA (e.g. lofepramine, this is the safest TCA option for depression).
- Cautious cross-tapering is the preferred method of switching from dosulepin to SSRIs, SNRIs and mirtazapine[4,5,6].
- The initial dosulepin reduction in these examples is 50% of the current dose; this redution may need to be done in smaller steps depending on the person's response and any withdrawal symptoms.

Example switch from DOSULEPIN to SERTRALINE	**Medication**	**Current dose**	**Week 1**	**Week 2**	**Week 3**	**Week 4**
	Dosulepin	150mg	75mg	50mg	25mg	STOP
	Sertraline	0mg	0mg	25mg	50mg	50mg Titrate according to response and tolerability

Example switch from DOSULEPIN to MIRTAZAPINE	**Medication**	**Current dose**	**Week 1**	**Week 2**	**Week 3**	**Week 4**
	Dosulepin	150mg	75mg	50mg	25mg	STOP
	Mirtazapine	0mg	0mg	15mg	15mg	15mg Titrate according to response and tolerability

Example switch from DOSULEPIN to VENLAFAXINE MR	**Medication**	**Current dose**	**Week 1**	**Week 2**	**Week 3**	**Week 4**
	Dosulepin	150mg	75mg	50mg	25mg	STOP
	Venlafaxine	0mg	0mg	37.5mg	75mg	75mg Titrate according to response and tolerability

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- Switching from dosulepin to another TCA (e.g. lofepramine) may be carried out via a cautious cross taper or direct switch if there is more urgency[5,6]. An example of each type of switch is provided below.

Cautious cross-taper

Example switch from DOSULEPIN to LOFEPRAMINE	Medication	Current dose	Week 1	Week 2	Week 3	Week 4
	Dosulepin	150mg	75mg	50mg	25mg	STOP
	Lofepramine	0mg	0mg	35mg* (half a tablet)	70mg	140mg Titrate according to response and tolerability

*Lofepramine 70mg tablets are scored.

Direct switch

Example switch from DOSULEPIN to LOFEPRAMINE	Medication	Current dose	Week 1	Week 2
	Dosulepin	150mg	75mg	STOP
	Lofepramine	0mg	0mg	140mg Titrate according to response and tolerability

The dosulepin should first be gradually reduced to the usual starting dose (50-75mg daily). Once reduced to the usual starting dose, dosulepin can be stopped and the new TCA started the next day with the usual starting dose as per the BNF.

Patient information

- Patient information on psychotropic medicines, including easy read and translated leafets , are available at Choice and Medication.
- Patient information leaflet on stopping antidepressants – Royal College of Psychiatrists.

References and further information

1) NICE. Clinical Guideline 222. June 2022. Depression in adults: treatment and management - https://www.nice.org.uk/guidance/ng222
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