Tees, Esk and Wear Valleys NHS
NHS Foundation Trust

Dosulepin De-prescribing Guidance

Dosulepin, a tricyclic antidepressant, is licensed for the treatment of depression, particularly where sedation is required. Although often prescribed to aid sleep, it disrupts REM sleep and there is no evidence that it has sleep-promoting effects. In December 2007 the MHRA advised that, as dosulepin has a narrow safety margin, it should be avoided[1] - it is marked in the BNF as "less suitable for prescribing". NHS England has issued guidance that dosulepin should not routinely be prescribed in primary care[2]. NICE[3] and TEWV FT recommend that it is **not** used. Nevertheless, over £2.6 million is still spent on dosulepin every year in the UK[1].

Dosulepin overdose is associated with a high mortality rate, even with hospital treatment, with cases of ten x 75 mg tablets (750 mg) having fatal consequences.

Reducing risks with dosulepin

Review

- Check:
  - Dose - is it a therapeutic dose?
  - Indication - is it being used to treat depression?
  - Effectiveness of treatment
  - Suicide risk
  - Co-prescribing of interacting drugs known to increase cardio-toxicity
  - Comorbidity

Discuss

- Risks/benefits of dosulepin
- NICE does not recommend use of dosulepin
- Alternative options e.g. stopping, switching (see handy comparison chart via link below)

Document

- Document outcome of discussions
- Clearly identify reason if continuing dosulepin
- Document treatment plan if stopping or switching

Licensed dose:
75 - 225 mg daily in divided doses or at bedtime
Elderly: 50 mg daily initially

HIGHLY toxic in overdose
Less than 1 weeks' supply likely to cause serious toxicity or death.
Never prescribe if a risk of suicide identified

Interacting medicines:

- ACE inhibitors, alcohol, alpha blockers, angiotensin II blockers, atypical antipsychotics, beta-blockers, calcium channel blockers, L-dopa, nitrates – *Hypotension*
- Carbamazepine, NSAIDs, SSRIs – *Hyponatraemia*
- Typical antipsychotics – *Hypotension & antimuscarinic effects*
- Diuretics – *Hyponatraemia & hypotension*
- Lithium – *Neurotoxicity*
- MAOIs, tranylcypromine – *Increased toxicity*
- TCAs – *Hyponatraemia, hypotension & antimuscarinic effects*

Dosulepin **should be avoided in patients with** cardiac disease, diabetes, epilepsy, hepatic impairment, renal impairment, Parkinson's disease and Alzheimer's disease

Dosulepin has an established link with a number of **adverse cardiovascular effects** (hypotension, tachycardia/arrhythmia and QTc prolongation)
Relative incidence and severity of side effects is higher than other antidepressants
It is extremely toxic in overdose – warn about accidental overdose

Handy chart comparing antidepressant treatments:
https://www.choiceandmedication.org/generate.php?sid=55&fname=handychartdepression.pdf

Stopping dosulepin (and not replacing with an alternative antidepressant)

Dosulepin should not be stopped abruptly unless serious side effects have occurred. Slowly tapering the dose in 25 – 50 mg increments over 3 to 4 weeks, or longer if necessary, can help prevent discontinuation symptoms such as anxiety, flu-like symptoms and insomnia. The rate at which the dose is reduced will need to be individualised for each patient, according to the starting dose, how long they have been taking dosulepin and the occurrence of withdrawal symptoms during the reduction. Some people may require a more gradual tapering of the dose over a long period of time to withdraw successfully.

Switching to another antidepressant [4,5]

There should be very close monitoring of patients being switched from dosulepin to another antidepressant, as there are no published guidelines to determine exactly how the switch should take place. The switch will need to be tailored to each individual and carried out cautiously. The regimen should depend upon the reason for the switch, how severe the depression is and which drug is being switched to. It is ideal to completely withdraw dosulepin before starting the new drug; however, cross-tapering is usually necessary to maintain symptom control. The dose of dosulepin should be at least halved before starting the new drug. Further reductions in dosulepin dose should occur once the new treatment is established. There is a risk of enhanced side-effects and serotonin syndrome during the overlap phase.

The choice of new antidepressant should be discussed with the patient. Considerations include:

- Depressive (target) symptoms
- Relative side effects of antidepressants (see handy chart, link above)
- Physical co-morbidities
- Interactions with other prescribed medication

Patient profile	**Suggested options**
In need of sedation	Mirtazapine (lower doses more sedating)
In need of activation	SSRI or venlafaxine
Cardiac disease	Mirtazapine or sertraline
Diabetes	SSRIs (fluoxetine or sertraline) or venlafaxine
Epilepsy	SSRIs
Hepatic impairment	Citalopram (maximum dose 20 mg/day) – see Trust guidance
Renal impairment	Citalopram
Parkinson's disease	SSRIs
Stroke	SSRIs (citalopram if taking warfarin + consider PPI for gastric protection) or mirtazapine

Very general guidance on switching from dosulepin to other antidepressants is below:

- Dosulepin to an **SSRI**: gradually reduce the dose to 25-50 mg / day, then add SSRI at usual starting dose. Then slowly withdraw the remaining dosulepin over 5-7 days.
- Dosulepin to **mirtazapine**: cross taper cautiously
- Dosulepin to **venlafaxine**: cross taper cautiously starting with venlafaxine 37.5 mg daily

Patient Information Leaflets

Available online at:

- https://www.prescqipp.info/resources/category/414-items-which-should-not-routinely-be-prescribed-in-primary-care-patient-leaflets
- https://www.choiceandmedication.org/generate.php?sid=55&fname=pilldosulepin.pdf

References

1. Medicines and Healthcare products Regulatory Agency. Drug Safety Update: vol.1, issue 5. December 2007
2. NHS England. Items which should not routinely be prescribed in primary care: Guidance for CCGs. November 2017
3. NICE CG90. Depression in adults: recognition and management. October 2009
4. Bazire S. Psychotropic Drug Directory. 2016
5. Taylor D et al. Maudsley Prescribing Guidelines in Psychiatry, 12th Edition