Cheshire and Wirral Partnership NHS
NHS Foundation Trust

Dosulepin review advice

Dosulepin, a tricyclic antidepressant, is licensed for the treatment of depression, particularly where sedation is required. In December 2007 the MHRA advised that as dosulepin has a narrow safety margin its use in new patients should be avoided; the BNF marks it as a drug considered to be "less suitable for prescribing". NICE and CWP NHS Foundation Trust recommend that it is **not** used. Although often prescribed to aid sleep (unlicensed), it disrupts REM sleep and there is no evidence that it has sleep promoting effects. Nevertheless, dosulepin continues to be prescribed. Every year, up to 200 people in England and Wales fatally overdose with dosulepin. Of these about 20% are accidental.

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: 75-225mg / day (elderly 50mg / day initially)

Toxicity in overdose is rated as HIGH – less than 1 weeks' supply likely to cause serious toxicity or death. **Never** prescribe if a risk of Suicide is identified

Interacting medicines:
Anti-arrhythmics, atomoxetine – increased risk of ventricular arrhythmias;
Antipsychotics and SSRIs – plasma concentration of dosulepin increased, possible increased risk of ventricular arrhythmias
Medicines with a potential to cause electrolyte imbalance, e.g. diuretics – may indirectly affect cardiac conduction

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: http://www.choiceandmedication.org/cheshire-and-wirral/pdf/handychartdepression.pdf

Stopping dosulepin

Dosulepin should not be stopped abruptly unless serious side effects have occurred. Slowly tapering the dose over 3 to 4 weeks can help prevent discontinuation symptoms. These symptoms may include anxiety, flu-like symptoms and insomnia. Some people may require a more gradual tapering of the dose if withdrawal symptoms occur. The doses selected and the speed at which they are reduced will need to be individualised for each patient.

CWP Medicines management Team July 2015 (acknowledgements to TEWV pharmacy team)

A suggested withdrawal regimen for dosulepin is:

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

Switching to another antidepressant

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

- Depressive symptoms
- Relative side effects
- Physical illness
- 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 (most data supports fluoxetine)
Epilepsy	SSRIs
Hepatic impairment	Citalopram* (maximum dose 20mg/day)
Renal impairment	Citalopram* or sertraline
Parkinson's disease	SSRIs
Stroke	SSRIs (citalopram* if taking warfarin + consider Proton Pump Inhibitor (PPI) for gastric for gastric protection or mirtazapine (has a small effect on INR)

***Note:** Citalopram use is contraindicated in conjunction with antipsychotics.

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. Gradual cross tapering is usually recommended but in some cases a washout period between drugs is required.

Very general guidance on switching from dosulepin to another antidepressant is below:

- Dosulepin to an SSRI: gradually reduce the dose to 25 to 50mg / day then add the 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 37.5mg daily

References

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