Doxepin (Sinepin®): Guidance on withdrawal

Indication: Doxepin is a tricyclic antidepressant (TCA) indicated in the treatment of depressive illness, especially where sedation is required.[i]

Formulary status: Non formulary (but some patients may have been initiated and maintained historically).
Note: When an antidepressant is to be prescribed, TCAs are no longer considered first line treatment for depression due to their side effect profile. SSRIs are equally effective as other antidepressants and have a favourable risk-benefit ratio.[ii]

Dose: For the majority of patients with moderate or severe symptoms, it is recommended that treatment commences with an initial dose of 75mg daily in divided doses *or* as a single dose at bedtime. . The dose required may vary from 25-300mg daily. Doses up to 100mg daily may be given on a divided or once daily schedule. Should doses over 100mg daily be required, they should be administered in three divided doses daily (no more than 100mg max at any one time).

Unlicensed uses: Neuropathic pain/chronic pain, insomnia, anxiety.

Mode of action: Serotonin and noradrenaline reuptake inhibitor.
Anticholinergic activity may cause dry mouth, constipation and blurred vision.

- **H1 blockade** may cause sedation.
- **Adrenergic αlpha 1 receptor blockade** may cause dizziness, sedation and hypotension.
- **Ion channel blockade** may cause cardiac arrhythmias and seizures especially in overdose**.**[iii]
- **Reasons for caution:** Reports of cardiac arrhythmias, QTc prolongation, sinus tachycardia, orthostatic hypotension. Drug interactions. High rate of fatality in overdose.

Side effects:

- As listed above

Guidance and recommendations:

- No new patients should be prescribed Doxepin.
- Patients currently prescribed doxepin should be identified and have their treatment history reviewed. Where possible doxepin should be gradually withdrawn and stopped if no longer clinically indicated.
- Suitable alternatives may include an SSRI such as sertraline, mirtazapine if a sedative antidepressant is required, imipramine or lofepramine if an alternative TCA is required. Individual product literature for each of these medicines is available from www.medicines.org.uk
- TCAs should not be terminated abruptly (unless a serious adverse event has occurred e.g. cardiac arrhythmia), instead gradually taper down the daily dose in weekly/two weekly decrements[iv] over **at least** 4 **weeks** to avoid withdrawal effects.[v]
- For patients who have been taking doxepin for long term maintenance treatment (>1 year), more gradual tapering may be appropriate, in the region of at least 6 months.[v]
- Even with a gradual dose reduction some withdrawal symptoms may appear within the first 5 days.[v] As with all swaps in medication tailor the withdrawal process to the individual patient, monitoring patient tolerability.
- In patients taking a split daily dose, the morning dose should ideally be completely reduced first before withdrawing the night time dose to minimise change on night-time sedation.

Few studies have specifically examined the best strategy for and outcomes of switching between antidepressants. The following advice is based on available information, theoretical concerns and clinical experience. It is intended for general guidance only. Whichever strategy is used, patients should be closely monitored for adverse effects.[iii]

Suggested withdrawal and crossover to mirtazapine schedule[iv]
(E.g. where sedative action required)

Drug	Current dose	Week 1	Week 3	Week 5	Week 7
Doxepin	75mg/day	50mg/day	25mg/day	25mg/ alternate days	STOP
Mirtazapine	Nil	Nil	15mg/day (at night)	30mg/day (at night)	Further dose ↑ based on response

Suggested withdrawal and crossover to imipramine/lofepramine schedule[iv]
(E.g. where anxiolytic action required)

Drug	Current dose	Week 1	Week 3	Week 5	Week 7
Doxepin	75mg/day	50mg/day	25mg/day	25mg/ alternate days	STOP
Imipramine* *Recommended elderly doses[v]	Nil	Nil	10mg/day (at night)	10mg/day (at night)	Further dose ↑ based on response
Lofepramine	Nil	Nil	70mg twice daily	70mg twice daily	Further dose ↑ based on response

Practical considerations:

- Issue 7 day scripts for safety reasons and to reduce waste.
- Doxepin is available as 25mg and 50mg capsules. Limit the prescribing for safety reasons and to make regimes simpler whilst reducing doses.
- Tailor the withdrawal and cross over process to the individual patient based on efficacy and tolerability.
- If the patient experiences any withdrawal effects then return to the previous dose of doxepin and continue with the cross over at a slower pace using smaller decrements.
- Information on good sleep hygiene and non-pharmacological techniques may be found at www.nhs.uk/conditions/insomnia. Consider short term use of zopiclone but note risk of tolerance, addiction and falls risk.

References:

[i] Doxepin SPC. MHRA.gov.uk [Accessed 26/11/2017]
[ii] CG90. Published date: October 2009. Last updated: April 2016. https://www.nice.org.uk/guidance/cg90
[iii] Maudsley Prescribing Guidelines Antidepressants. 12th Edition
[iv] https://www.sps.nhs.uk/articles/how-do-you-switch-between-tricyclic-ssri-and-related-antidepressants/ [Accessed: 26/11/2017]
[v] Joint Formulary Committee. British National Formulary [Online] London: BMJ Group and Pharmaceutical Press Available: http://www.medicinescomplete.com [Accessed: 26/11/2017]