DEPRESCRIBING GUIDE FOR TRICYCLIC ANTIDEPRESSANTS (TCAs)

(including secondary amines [e.g. nortriptyline] and tertiary amines [e.g. amitriptyline, clomipramine, doxepin, dosulepin (dothiepin), imipramine])

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This guide provides deprescribing information that can be applied to written and/or verbal communication (in the form of "preferred language") between clinicians, patients and/or carers. Adapt appropriately for individual patients.

CONSIDER TWO STEPS WHEN DEPRESCRIBING:

1 Should I deprescribe?

2 How do I deprescribe?

STEP 1

STEP 1: SHOULD I DEPRESCRIBE? (PATIENT ASSESSMENT)

Deprescribing triggers:

- Inappropriate indication, no current indication, presence or risk of adverse events, drug interaction, drug-disease interaction, high drug burden index (DBI),[1] poor adherence, or patient preference.

1a) Is there a documented indication or symptoms supporting continued use?

Inappropriate indication for continued use:

- Use of tertiary amines in older people.
- No current depression >6 months. Consult or review with treating psychiatrist.
- Sedation or insomnia, urinary incontinence, or other off-label use.

Do not deprescribe if:

- Recurrent or severe depression, or neuropathic pain. Discuss with the treating psychiatrist.

1b) Are there adverse effects?

Consider potential adverse effects:

- Falls, sedation, dry mouth, blurred vision, dry eyes, constipation, weight gain, orthostatic hypotension, tachycardia, QT prolongation, urinary retention, reduced gastrointestinal motility, delirium (particularly in older adults and in Parkinson's disease), impotence, loss of libido, tremor, dizziness, sweating, agitation, insomnia, anxiety, confusion.[2]

1c) Is this medication likely to cause more harm than benefit?

See Evidence-based advice for additional information on risks of harm and benefits of continued use.

1d) Does the patient/carer agree with the recommendation to deprescribe?

Following provision of information, discussion and shared-decision making, the patient or carer has communicated that they would like to proceed with or decline the deprescribing recommendation.

PREFERRED LANGUAGE:

(Adapt for each patient and medicine as appropriate)

_____ is currently taking _____
(patient name) (drug name: e.g. amitriptyline 10mg daily)

for _____ , and is currently experiencing/at risk of _____.
(indication: e.g. insomnia) (patient issue: e.g. adverse effects)

The _____ outweighs the _____ for continued use of _____.
(risk/benefit + rationale) (risk/benefit + rationale) (drug name: e.g. amitriptyline)

Discussed with _____ and _____ deprescribing recommendation.
(patient /carer name) (agreed/willing to trial/considering/declined)

STEP 2: HOW DO I DEPRESCRIBE? (RECOMMENDATION AND MANAGEMENT)

2a) How to wean

Key Points

- Establish a supportive and trusting relationship with the patient to engage in complex/sensitive discussions.
- Accompany weaning with commencement of relevant non-pharmacological therapy. See Alternative management recommendations.
- In general, wean gradually by 25% of the daily dose every 1-4 weeks.
- If reason for deprescribing is due to serious adverse effects, consider weaning faster.
- Substitution with other sedative medicines is not recommended as the same adverse effects and outcomes may occur.
- Provide advice to patient/carer on self-monitoring and what to do if symptoms re-occur.
- Organise appropriate follow up appointments with general practitioner (GP) (frequency determined by rate of weaning).

Initiation

Reduce dose slowly by 25-50% of the daily dose each week to month.

Adjustments depend on response

Adjust according to response (see Monitoring recommendations).

- If no withdrawal symptoms occur, continue to wean and stop.
- Consider slower weaning (e.g. 12.5%) when reducing to the final lowest dose. End treatment 2 weeks after administering the lowest dose.
- Consider alternate day dosing to aid with weaning if dosage forms are limited.

Adjustments in the case of recurrent symptoms

In the case of recurrent/withdrawal symptoms, revert to the previous lowest tolerated dose. Recommence weaning after 6-12 weeks at a lower weaning rate (e.g. 5-12.5% of daily dose each month) then stop.

(Based on recommendations in References[2-8])

PREFERRED LANGUAGE:

(Adapt for each patient and medicine as appropriate)

Recommend non-pharmacological replacement therapy to reduce reliance on antidepressants.

Recommend gradually reducing to _____ (drug: e.g. amitriptyline 5mg daily) **for** _____ (timeframe e.g. 2 weeks) **and reassess,**

then reduce to _____ (e.g. amitriptyline 5mg daily on alternating days) **for** _____ (e.g. 2 weeks) **and stop.**

Follow up with GP _____ (e.g. fortnightly) **after discharge.**

2b) Alternative management

Non-pharmacological support

Psychological therapy, social support, sleep hygiene practices or cognitive behavioural therapy.[12]

For sleep hygiene advice, refer to [AMH Aged Care Companion-Depression].

Switching within drug class or consider alternative therapy

All TCAs are equally effective in major depression.[2]
To consider other options, refer to [AMH-Antidepressants]

PREFERRED LANGUAGE:

Use **psychological therapy (e.g. counselling) therapy, social support or sleep hygiene practices** concurrently.

2c) Monitoring

Monitor short term (within 1-3 days)	Monitor long term (>7 days)
Monitor for withdrawal symptoms Symptoms can occur within 1-3 days of dose reduction.	**Monitor for recurrence of symptoms** Recurrence of previous or new symptoms (e.g. anxiety, depression) may occur within 1-2 weeks of dose reduction.

- Common withdrawal symptoms (e.g. agitation, headache, hypersalivation, rhinorrhoea, abdominal cramping, diarrhoea, insomnia) are usually mild, highly variable and can last up to 6-8 weeks.
- If severe symptoms (e.g. psychosis, hypertension, tachycardia, tremors and seizures, profuse and persistent sweating, severe anxiety, or severe insomnia) occur, restart at the previous lowest effective dose.
- Amitriptyline discontinuation is more likely to have cholinergic rebound (e.g. agitation, headache, sweating, gastrointestinal symptoms).

PREFERRED LANGUAGE:

Within 1-3 days of dose reduction, monitor for **withdrawal** symptoms which can be **mild** (e.g. *agitation, headache, hypersalivation, runny nose, abdominal cramping, diarrhoea, insomnia*) or **severe** (e.g. *psychosis, hypertension, tachycardia, tremors and seizures, profuse and persistent sweating, severe anxiety, or severe insomnia*).

Monitor for **recurrence** of symptoms within 1-2 weeks of dose reduction, including anxiety or depression.

Restart at the lowest effective dose with retrial weaning at *6-12 weeks*.

EVIDENCE-BASED ADVICE

Effectiveness and safety

A Cochrane meta-analysis of studies predominantly lasting 6-8 weeks, estimated that nine patients with depression needed to be treated with a TCA in order to obtain a benefit in one (number needed to treat [NNT] = 9).[9]

Compared to placebo, 4-30 patients needed to be treated with a TCA in order to suffer harm in one (withdrawal due to side effects) (number needed to harm [NNH] = 4-30). Improvement with TCAs compared with placebo showed a relative risk (RR) of 1.24 (95% CI, 1.11–1.38).[9]

Compared to placebo, TCAs had a higher risk of adverse effects, with a RR for harm of 2.01 (RR 2.01; 95% CI 1.59 to 2.55).[9]

In bipolar disorder, a limited number of trials found TCAs were associated with a higher rate of switching to mania (10%) than with other antidepressants (3%), with a RR of 2.9 (95% CI 1.3-6.7).[10,11]

Over 90% of people would be willing to stop their medicines if recommended by their physician.[13]

Recommended duration of use

Limit drug treatment to short-term use. TCAs are associated with significant harm (e.g. falls, fractures), and long-term use is not recommended, especially in older adults.

SUMMARISED PHRASING DURING HOSPITAL ADMISSION AND/OR AT DISCHARGE

When communicating deprescribing decisions to GPs at discharge, written and verbal communication should include information in the sequence of:

"Medicine, Intention, Rationale, Clear Plan (dose change, duration, follow up), Patient agreement"

PREFERRED LANGUAGE

(write in GP follow up plan and medication list):

_____ : _____ due to_____ outweighing effects _____.

current medication e.g. amitriptyline | stopped/ reduced with aim of stopping | specific rationale (e.g. dry mouth) | of/on current indication (e.g. depression)

_____ reduced to _____ for _____, then _____. Patient/Carer agreed.

If weaning, old dose changed to new dose (e.g. amitriptyline 10mg nocte reduced to amitriptyline 5mg nocte) | if weaning, time frame (e.g. 2 weeks) | follow-up action (e.g. follow up by GP, GP to consider HMR referral)

Refer to www.nswtag.org.au/deprescribing-tools/

Example:

Amitriptyline: reduced with aim of stopping due to dry mouth outweighing effects on depression. Amitriptyline 10mg nocte reduced to amitriptyline 5mg nocte for 2 weeks then follow up with GP. GP to consider HMR referral. Patient agreed. Refer to www.nswtag.org.au/deprescribing-tools/

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