withdrawal or changing of antidepressant treatment

Stopping antidepressant treatment

- the timing of when to stop antidepressant treatment is discussed in menu item below (length of antidepressant treatment)
- patients should be advised not to stop treatment suddenly or omit doses - patients should also be forewarned about possible symptoms that may occur when treatment is discontinued
- Drug and Therapeutics Bulletin (1) advises:
  - after a 'standard' 6-8 months treatment it is recommended that treatment should be tapered off over a 6-8 week period
  - if the patient has been on maintenance therapy then an even more gradual tapering e.g. by 1/4 of the treatment dose every 4-6 weeks, is advised
  - if a treatment course has lasted less than 8 weeks then discontinuation over 1-2 weeks is considered safe
- this contrasts with the Maudsley prescribing guidelines (2) which recommend that antidepressants should be withdrawn slowly, preferably over four weeks, by weekly increments for example,

Drug	maintenance dose (mg/day)	dose after 1st week (mg/day)	dose after 2nd week (mg/day)	dose after 3rd week (mg/day)	dose after 4th week (mg/day)
amitriptyline	150	100	50	25	Nil
paroxetine	30	20	10	5 (liquid)	Nil
trazadone	450	300	150	75	Nil

If withdrawal symptoms occur then the rate of drug withdrawal should be slowed or (if the drug has been stopped) the patient should be given reassurance that symptoms rarely last more than 1-2 weeks (2).

- **NICE also suggest a four week period for withdrawal of antidepressant treatment (3):**
  - **stopping or reducing antidepressants**
    - advise people that discontinuation symptoms may occur on stopping, missing doses or, occasionally, reducing the dose of the drug. Explain that these are usually mild and self-limiting over about 1 week, but can be severe, particularly if the drug is stopped abruptly
    - normally, gradually reduce the dose over 4 weeks (this is not necessary with fluoxetine). Reduce the dose over longer periods for drugs with a shorter half-life (for example, paroxetine and venlafaxine)
    - advise the person to see their practitioner if they experience significant discontinuation symptoms. If symptoms occur:
      - monitor them and reassure the person if symptoms are mild
      - consider reintroducing the original antidepressant at the dose that was effective (or another antidepressant with a longer half-life from the same class) if symptoms are severe, and reduce the dose gradually while monitoring symptoms
    - for detailed guidance then consult the full guideline (3)

Swapping antidepressant treatment (2):

- when swapping from one antidepressant to another, abrupt withdrawal should usually be avoided. Cross-tapering is preferred, where the dose of the ineffective or poorly tolerated drug is slowly reduced while the new drug is slowly introduced for example,

		week 1	week 2	week 3	week 4
withdrawing dosulepin	150 mg od	100mg od	50 mg od	25 mg od	Nil
introducing citalopram	Nil	10 mg od	10mg od	20 mg od	20 mg od

Antidepressant use: swapping and stopping

The table below has been adapted from the Maudsley prescribing guidelines (2). However it is recommended that local prescribing guidelines and/or specialist psychiatric advice must be consulted when swapping antidepressant medication. Also the specific summary of product characteristics for each of the antidepressants involved should be consulted. It has been noted that there are no clear guidelines on switching antidepressants, so caution is required (2).

changing from	to tricyclics	to citalopram/escitalopram	to fluoxetine	to paroxetine	to sertraline	to venlafaxine	to mirtazapine
tricyclics (TCA)	cross taper cautiously	halve dose and add citalopram (or escitalopram) then slow withdrawal	halve dose and add fluoxetine then slow withdrawal	halve dose and add paroxetine then slow withdrawal	halve dose and add sertraline then slow withdrawal	cross taper cautiously starting with 37.5 mg per day	cautious cross-tapering recommended (4)
citalopram/escitalopram	cross taper cautiously		withdraw citalopram (escitalopram) then start fluoxetine	withdraw citalopram (escitalopram) and then start paroxetine at 10 mg per day	withdraw citalopram (escitalopram) and then start sertraline at 25 mg per day	withdraw and then start venlafaxine at 37.5 mg per day. Increase very slowly	cautious cross-tapering recommended (4)
fluoxetine	stop fluoxetine. Start tricyclic at very low dose and increase very slowly	stop fluoxetine. Wait 4-7 days; start citalopram at 10mg per day (or escitalopram 5mg per day) and increase slowly		stop fluoxetine. Wait 4-7 days; start paroxetine at 10mg per day and increase slowly	stop fluoxetine. Wait 4-7 days; start sertraline at 25 mg per day and increase slowly	stop fluoxetine. Wait 4-7 days; start venlafaxine at 37.5 mg per day. Increase very slowly	cautious cross-tapering recommended, start mirtazapine at 15mg daily (4)
						withdraw	

paroxetine	cross taper cautiously with very low dose of tricyclic	withdraw paroxetine then start citalopram 10mg per day (or escitalopram 5mg per day)	withdraw paroxetine then start fluoxetine		withdraw paroxetine then start sertraline at 25 mg per day	paroxetine. Start venlafaxine at 37.5 mg per day. Increase very slowly	cautious cross-tapering recommended (4)
sertraline	cross taper cautiously with very low dose of tricyclic	withdraw sertraline then start citalopram 10mg per day (or escitalopram 5mg per day)	withdraw sertraline then start fluoxetine	withdraw sertraline then start paroxetine 10mg per day		withdraw sertraline then start venlafaxine at 37.5 mg per day	cautious cross-tapering recommended (4)
venlafaxine	cross taper cautiously with very low dose of tricycli	cross taper cautiously. Start with citalopram 10 mg per day (or escitalopram 5mg per day)	crosss taper cautiously. Start with 20 mg every other day	cross taper cautiously. Start with 10 mg per day.	cross taper cautiously. Start with 25 mg per day		cautious cross-tapering recommended (4)
mirtazapine	cautious cross-tapering recommended, using very low starting dose for tricyclic (4)	cautious cross-tapering recommended (4)	cautious cross-tapering recommended (4)	cautious cross-tapering recommended (4)	cautious cross-tapering recommended (4)	cautious cross-tapering recommended (4)	
stopping/withdrawing of particular antidepressants	**ticyclics** reduce over four weeks (4)	**citalopram/escitalopram** reduce over one to four weeks (4)	**fluoxetine** at 20mg per day - just stop at 40 mg per day, reduce over four weeks	**paroxetine** reduce over four weeks, or longer if necessary *	**sertraline** reduce dose gradually over one to four weeks (4)	**venlafaxine** reduce over four weeks or longer if necessary (2,4)	**mirtazapine** reduce dose gradually over 4 weeks (4)

NICE guidance regarding switching antidepressants is less detailed (3):

- do not switch to, or start, dosulepin
  - because evidence supporting its tolerability relative to other antidepressants is outweighed by the increased cardiac risk and toxicity in overdose
- **when switching to another antidepressant, which can normally be achieved within 1 week when switching from drugs with a short half life, consider the potential for interactions in determining the choice of new drug and the nature and duration of the transition.** Exercise particular caution when switching:
  - from fluoxetine to other antidepressants, because fluoxetine has a long half-life (approximately 1 week)
  - from fluoxetine or paroxetine to a TCA, because both of these drugs inhibit the metabolism of TCAs; a lower starting dose of the TCA will be required, particularly if switching from fluoxetine because of its long half-life
  - to a new serotonergic antidepressant or MAOI, because of the risk of serotonin syndrome
  - from a non-reversible MAOI: a 2-week washout period is required (other antidepressants should not be prescribed routinely during this period).

Notes:

- **do not co-administer clomipramine and SSRIs or venlafaxine**

- **when switching between one SSRI and another, some consider cross-tapering the doses generally not to be necessary (5,6)**
  - selective serotonin reuptake inhibitors (SSRIs) overlap in their mechanism of action, and the new SSRI will usually prevent discontinuation symptoms that may occur when the first SSRI is stopped. Substituting a new SSRI at the relatively equivalent dose of the former SSRI is typically well-tolerated , though starting the new SSRI at a lower dose may also be considered since patients occasionally have idiosyncratic side effects to particular SSRIs (5)
  - the New Zealand formularly guidance (6) supports no need for cross-tapering for switching between short acting SSRIs (citalopram, escitalopram, paroxetine, sertraline) - but for switches from fluoxetine then it supports the Maudsley guidance and states
    - stop fluoxetine, wait 4 - 7 days, start SSRI at low dose (low dose= citalopram 10mg/day; escitalopram 5mg/day; paroxetine 10mg/day; sertraline 25mg/day)
  - the effects of the first SSRI are likely to be so similar to that of the second one, that the second SSRI will reduce the discontinuation effects of the first (2). The abrupt switch between SSRIs may still produce discontinuation symptoms, and vigilance is still advised. In cases where discontinuation symptoms arise a short period of dose tapering is recommended before starting a different SSRI

- * withdrawal effects may be more pronounced. Slow withdrawal over 1-2 months may be necessary

Reference:

- Drug and Therapeutics Bulletin (1999); 37 (7):49-52.
- The Maudsley Prescribing Guidelines 2001; 6th Ed, p64 - 65.
- NICE (October 2009). Depression
- MIMS - Switching and Withdrawing Antidepressants (Accessed 6/8/13).
- UptoDate - Antidepressant medication in adults: Switching and discontinuing medication (Accessed 6/8/13)
- Using the New Zealand Formulary : Guide for switching antidepressants (Accessed 6/8/13)

Links:

- **discontinuation syndromes with antidepressants**
- **length of treatment/continuation of antidepressant Rx**
- **antidepressant treatment**
- **stopping or switching treatment with an SSRI**
- **NICE guidance - management of depression in primary and secondary care**