

Handy Hints When Prescribing Antidepressants

*N.B. all drugs in each group are included for completeness – please check formulary status before prescribing
The order of drugs listed does not imply an order of preference – please refer to age-relevant treatment algorithm
for specific recommendations on treatment choice*

SELECTIVE SEROTONIN REUPTAKE INHIBITORS (SSRIs)

ACTION: Delayed disinhibition of serotonin neurotransmission via 4 key pathways – the somatodendritic serotonin autoreceptors, neuronal impulse flow and postsynaptic serotonin receptors, and inhibition of the serotonin reuptake pump

| DRUG | SPECIFIC INFORMATION | COMMON SIDE EFFECTS & ADVICE |
|--------------|---|--|
| Sertraline | <ul style="list-style-type: none"> Causes activation of the central nervous system and may be more useful for patients with fatigue and apathy. May be more useful for depressions with psychosis, the elderly/cognitively impaired and women. Fewer clinically significant interactions. Less suitable for patients with anxious and panicky presentation. Avoid in agitated patients or those with gastrointestinal problems. Post-natal depression. Drug of choice in pregnancy (lowest placental exposure), breast-feeding (undetectable or low levels in infant) and in patients with cardiac disease | <ul style="list-style-type: none"> Before initiating treatment, discuss the possibility of discontinuation symptoms when treatment is stopped Upon initiation – headache, nausea, insomnia, sexual dysfunction, gastro intestinal upset. Most common cause of poor compliance or stopping medication (especially in first 2 weeks). Side effects self-limiting and occur usually in first 2 weeks. Agitation and anxiety can increase / occur in first 2 weeks – if extreme use short term benzodiazepine (remember to discontinue) for approximately 2 weeks. Increased risk of GI bleeds; consider co-prescription of PPI, especially in elderly and/or in combination with aspirin or NSAID |
| Fluoxetine | <ul style="list-style-type: none"> Longer half-life – less discontinuation side effects; but more drug interactions; more likely to cause agitation and insomnia. Can alter insulin requirements. Causes activation of the central nervous system and may be more useful for patients with fatigue and apathy and hypersomnia. Consider for atypical depression, the overweight patient, bulimia, or use in pregnancy. Higher risk of drug interactions, avoid if taking other medications Watch for early and late onset side effects | |
| Citalopram | <ul style="list-style-type: none"> ECG required before initiation to rule out pre-existing QT-prolongation – see Trust guidelines; maximum doses reduced by MHRA to minimise risk of dose-dependent QT-prolongation | |
| Escitalopram | <ul style="list-style-type: none"> More selective in the way they work and, therefore, generally have fewer side effects or secondary properties. May suit medically ill patients or those where there is polypharmacy | |
| Fluvoxamine | <ul style="list-style-type: none"> Nausea more common. Drug interactions more common than with other SSRIs (potent inhibitor of hepatic cytochrome P450 enzymes) Has more anxiolytic and sedative properties and may be useful in patients with agitation and insomnia. | |
| Paroxetine | <ul style="list-style-type: none"> Not recommended by TEWV due to common discontinuation and antimuscarinic effects. | |

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SEROTONIN / NOREPINEPHRINE REUPTAKE INHIBITORS (SNRIs)

ACTION: Acts as an SSRI, but with additional norepinephrine reuptake inhibition, and some dopamine reuptake inhibition.

| DRUG | SPECIFIC INFORMATION | COMMON SIDE EFFECTS & ADVICE |
|---------------------------|--|---|
| Venlafaxine | <ul style="list-style-type: none"> Withdraw slowly – higher risk of discontinuation effects Venlafaxine MR – take in morning, less chance of insomnia Norepinephrine effect generally only seen in doses >150mg so acts as SSRI in lower doses Doses >225mg, of any preparation - secondary care initiation, monitoring and stabilisation, before transfer back to primary care. Monitor BP 6 monthly. Be aware of higher toxicity in overdose so assess risk | <ul style="list-style-type: none"> Similar side effects to SSRIs upon initiation – nausea / headache / insomnia / sexual dysfunction (see SSRI section). Discontinuation effects more likely due to short half-life. Sexual dysfunction – problematic, but less so with duloxetine |
| Duloxetine (in all doses) | <ul style="list-style-type: none"> May be of benefit to patients experiencing pain or frequency of micturition | |

NORADRENERGIC and SPECIFIC SEROTINERGIC ANTIDEPRESSANT (NaSSA)

ACTION: Pre-synaptic alpha 2 adrenoreceptor antagonist - enhances both serotonin and norepinephrine neurotransmission, and has antihistamine properties

| DRUG | SPECIFIC INFORMATION | COMMON SIDE EFFECTS & ADVICE |
|-------------|--|--|
| Mirtazapine | <ul style="list-style-type: none"> Monitor FBC if sign of infection. Sedation – paradoxically lower dose more likely to cause sedation than higher doses | <ul style="list-style-type: none"> Can cause weight gain and sedation. Can cause blood dyscrasias. Sexual dysfunction uncommon. |

MULTIMODAL SEROTINERGIC AGENT

ACTION: Inhibits re-uptake of serotonin, an antagonist at 5HT₃ receptors and an agonist at 5-HT_{1A} receptors

| DRUG | SPECIFIC INFORMATION | COMMON SIDE EFFECTS & ADVICE |
|--------------|--|--|
| Vortioxetine | <ul style="list-style-type: none"> Enhanced release of 5HT, norepinephrine, dopamine, acetylcholine and histamine could theoretically improve the efficiency of information processing in maladaptive brain circuits by facilitating long-term potentiation, synaptic plasticity, and enhanced pyramidal neuron activity leading to improvement not only of mood, but also of cognitive symptoms in major depressive disorder. Glutamate action should help with anxiety, but trials in GAD have been variable | <ul style="list-style-type: none"> Nausea seems to be particularly prevalent No cardiovascular effects |

SEROTONIN ANTAGONIST REUPTAKE INHIBITORS (SARIs)

ACTION: Similar to SSRIs but blocks serotonin receptors rather than stimulating them

| DRUG | SPECIFIC INFORMATION | COMMON SIDE EFFECTS & ADVICE |
|-----------|---|---|
| Trazodone | <ul style="list-style-type: none"> Low anticholinergic and cardiotoxicity. Take with food to reduce peak blood levels Can add to SSRI to aid sleep | <ul style="list-style-type: none"> Increased sedation (used off-licence as a hypnotic) and nausea. Tremor, postural hypotension, tachycardia. |

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SELECTIVE NOREPINEPHRINE REUPTAKE INHIBITORS (NRIs)

ACTION: Selective inhibition of norepinephrine reuptake

| DRUG NAME | SPECIFIC INFORMATION | COMMON SIDE EFFECTS & ADVICE |
|------------|--|--|
| Reboxetine | <ul style="list-style-type: none"> Has also shown antinociceptive properties (reducing sensitivity to painful stimuli). Reasonable alternative in patients intolerant to serotonergic side effects from SSRI or TCA Reboxetine might be less effective than SSRI and SNRI Use only in severe depression or if patient is unable to tolerate serotonergic medications | <ul style="list-style-type: none"> Side effects (less than with TCA) - insomnia, sweating, dizziness, dry mouth, constipation, tachycardia, urinary hesitancy may occur. Sexual dysfunction uncommon. Can cause hypokalaemia. |

TRI- AND TETRACYCLIC ANTIDEPRESSANTS (TCAs)

ACTION: Serotonin and norepinephrine reuptake inhibitor (therapeutic action), with anticholinergic properties, antihistamine and adrenergic antagonism (side effects).

| DRUG NAME | SPECIFIC INFORMATION | COMMON SIDE EFFECTS & ADVICE |
|---------------|---|---|
| Amitriptyline | <ul style="list-style-type: none"> Has shown additional effects on pain relief in low dose | <ul style="list-style-type: none"> Antimuscarinic, sedation (often with hangover effects), weight gain. Very cardiotoxic – arrhythmias, tachycardia / heart block. Very toxic in overdose as they inhibit sodium channels. Postural hypotension. Women less tolerant of TCA side effects than men Titrate to effective dose. Caution in patients with cardiac disease. Don't give to patients with suicide ideation or prescribe only a few days' supply at a time. Studies demonstrated more rapid onset of action than with SSRI's especially in male patients |
| Lofepramine | <ul style="list-style-type: none"> Less cardiotoxic than other TCAs and therefore less toxic in overdose. May have increased risk of hepatic toxicity | |
| Doxepin | <ul style="list-style-type: none"> Very sedating, good for patients with sleep problems | |
| Clomipramine | <ul style="list-style-type: none"> More activating, has also demonstrated efficacy in anxiety | |
| Imipramine | <ul style="list-style-type: none"> Anxiolytic and sedative, reasonable choice in patients with sleep problems | |
| Nortriptyline | <ul style="list-style-type: none"> Usually better tolerated than other TCAs with less cardiac and orthostatic side effects, often used in the elderly | |
| Trimipramine | <ul style="list-style-type: none"> DO NOT PRESCRIBE – see NHS England guidance | |
| Dosulepin | | |

AGOMELATINE

ACTION: Melatonin receptor agonist and a selective serotonin-receptor antagonist; does not affect the uptake of serotonin, noradrenaline or dopamine

| DRUG NAME | SPECIFIC INFORMATION | COMMON SIDE EFFECTS & ADVICE |
|-------------|---|--|
| Agomelatine | <ul style="list-style-type: none"> Restricted formulary in TEWV – see NTAG recommendation; requires approval before initiation RED drug – secondary care prescribing only Melatonin activity useful if insomnia is a feature | <ul style="list-style-type: none"> Relatively free of side-effects Minimal cardiovascular effects Rare reports of liver damage and failure – LFT monitoring required before initiation and after 3, 6, 12 and 24 weeks, then regularly thereafter when clinically indicated |

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