**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

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| **Sertraline** | - 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.  
- Before initiating treatment, discuss the possibility of discontinuation symptoms when treatment is stopped.  
- Upon initiation – headache, nausea, insomnia, sexual dysfunction, gastrointestinal 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** | - 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. |
|           | Before initiating treatment, discuss the possibility of discontinuation symptoms when treatment is stopped.  
| **Citalopram** | - 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.  
- 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. |
|           | - Increased risk of GI bleeds; consider co-prescription of PPI, especially in elderly and/or in combination with aspirin or NSAID. |
| **Escitalopram** | - 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. |
|           | Before initiating treatment, discuss the possibility of discontinuation symptoms when treatment is stopped.  
| **Fluvoxamine** | - Not recommended by TEWV due to common discontinuation and antimuscarinic effects. |
| **Paroxetine** | Not recommended by TEWV due to common discontinuation and antimuscarinic effects. |
### SEROTONIN / NOREPINEPHRINE REUPTAKE INHIBITORS (SNRIs)

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

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| Venlafaxine | - 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 | - 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) | - 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.

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| Mirtazapine | - Monitor FBC if sign of infection.  
- Sedation – paradoxically lower dose more likely to cause sedation than higher doses | - 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-HT₁a receptors.

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| Vortioxetine | - 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 | - 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.

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| Trazodone | - Low anticholinergic and cardiotoxicity.  
- Take with food to reduce peak blood levels  
- Can add to SSRI to aid sleep | - Increased sedation (used off-licence as a hypnotic) and nausea.  
- Tremor, postural hypotension, tachycardia. |
**SELECTIVE NOREPINEPHRINE REUPTAKE INHIBITORs (NRIs)**

**ACTION:** Selective inhibition of norepinephrine reuptake

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| Reboxetine | • 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 if SSRI and SNRI  
• Use only in severe depression or if patient is unable to tolerate serotonergic medications | • 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).

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| Amitriptyline | • Has shown additional effects on pain relief in low dose | • 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 | • Less cardiotoxic than other TCAs and therefore less toxic in overdose.  
• May have increased risk of hepatic toxicity | |
| Doxepin | • Very sedating, good for patients with sleep problems | |
| Clomipramine | • More activating, has also demonstrated efficacy in anxiety | |
| Imipramine | • Anxiolytic and sedative, reasonable choice in patients with sleep problems | |
| Nortriptyline | • Usually better tolerated than other TCAs with less cardiac and orthostatic side effects, often used in the elderly | |
| Trimipramine | | |
| Dosulepin | • **DO NOT PRESCRIBE** – see NHS England guidance | |

**AGOMELATINE**

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

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| Agomelatine | • 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 | • 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 |