# 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) | | |
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| **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 | • Causes activation of the central nervous system and may be more useful for patients with fatigue and apathy.<br>• May be more useful for depressions with psychosis, the elderly/cognitively impaired and women.<br>• Fewer clinically significant interactions.<br>• Less suitable for patients with anxious and panicky presentation.<br>• Avoid in agitated patients or those with gastrointestinal problems.<br>• Post-natal depression.<br>• 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<br>• Upon initiation – headache, nausea, insomnia, sexual dysfunction, gastro intestinal upset.<br>• Most common cause of poor compliance or stopping medication (especially in first 2 weeks).<br>• Side effects self-limiting and occur usually in first 2 weeks.<br>• Agitation and anxiety can increase / occur in first 2 weeks – if extreme use short term benzodiazepine (remember to discontinue) for approximately 2 weeks.<br>• 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.<br>• Causes activation of the central nervous system and may be more useful for patients with fatigue and apathy and hypersomnia.<br>• Consider for atypical depression, the overweight patient, bulimia, or use in pregnancy.<br>• Higher risk of drug interactions, avoid if taking other medications<br>• Watch for early and late onset side effects | |
| Citalopram<br>Escitalopram | • 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<br>• More selective in the way they work and, therefore, generally have fewer side effects or secondary properties.<br>• May suit medically ill patients or those where there is polypharmacy | |
| Fluvoxamine | • Nausea more common.<br>• Drug interactions more common than with other SSRIs (potent inhibitor of hepatic cytochrome P450 enzymes)<br>• Has more anxiolytic and sedative properties and may be useful in patients with agitation and insomnia. | |
| Paroxetine | • Not recommended by TEWV due to common discontinuation and antimuscarinic effects. | |

| SEROTONIN / NOREPINEPHRINE REUPTAKE INHIBITORS (SNRIs) | | |
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| **ACTION**: Acts as an SSRI, but with additional norepinephrine reuptake inhibition, and some dopamine reuptake inhibition. | | |
| **DRUG** | **SPECIFIC INFORMATION** | **COMMON SIDE EFFECTS & ADVICE** |
| Venlafaxine | • Withdraw slowly – higher risk of discontinuation effects<br>• Venlafaxine MR – take in morning, less chance of insomnia<br>• Norepinephrine effect generally only seen in doses >150mg so acts as SSRI in lower doses<br>• Doses >225mg, of any preparation - secondary care initiation, monitoring and stabilisation, before transfer back to primary care. Monitor BP 6 monthly.<br>• 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).<br>• Discontinuation effects more likely due to short half-life.<br>• 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) | | |
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| **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 | • Monitor FBC if sign of infection.<br>• Sedation – paradoxically lower dose more likely to cause sedation than higher doses | • Can cause weight gain and sedation.<br>• Can cause blood dyscrasias.<br>• Sexual dysfunction uncommon. |

| MULTIMODAL SEROTINERGIC AGENT | | |
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| **ACTION:** Inhibits re-uptake of serotonin, an antagonist at $5HT_3$ receptors and an agonist at $5\text{-}HT_{1A}$ receptors | | |
| **DRUG** | **SPECIFIC INFORMATION** | **COMMON SIDE EFFECTS & ADVICE** |
| 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.<br>• Glutamate action should help with anxiety, but trials in GAD have been variable | • Nausea seems to be particularly prevalent<br>• No cardiovascular effects |

| SEROTONIN ANTAGONIST REUPTAKE INHIBITORs (SARIs) | | |
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| **ACTION**: Similar to SSRIs but blocks serotonin receptors rather than stimulating them | | |
| **DRUG** | **SPECIFIC INFORMATION** | **COMMON SIDE EFFECTS & ADVICE** |
| Trazodone | • Low anticholinergic and cardiotoxicity.<br>• Take with food to reduce peak blood levels<br>• Can add to SSRI to aid sleep | • Increased sedation (used off-licence as a hypnotic) and nausea.<br>• Tremor, postural hypotension, tachycardia. |

| SELECTIVE NOREPINEPHRINE REUPTAKE INHIBITORs (NRIs) | | |
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| **ACTION**: Selective inhibition of norepinephrine reuptake | | |
| **DRUG NAME** | **SPECIFIC INFORMATION** | **COMMON SIDE EFFECTS & ADVICE** |
| Reboxetine | • Has also shown antinociceptive properties (reducing sensitivity to painful stimuli).<br>• Reasonable alternative in patients intolerant to serotonergic side effects from SSRI or TCA<br>• Reboxetine might be less effective than SSRI and SNRI<br>• Use only in severe depression or if patient is unable to tolerate serotinergic medications | • Side effects (less than with TCA) - insomnia, sweating, dizziness, dry mouth, constipation, tachycardia, urinary hesitancy may occur.<br>• Sexual dysfunction uncommon.<br>• Can cause hypokalaemia. |

| TRI- AND TETRACYCLIC ANTIDEPRESSANTs (TCAs) | | |
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| **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 | • Has shown additional effects on pain relief in low dose | • Antimuscarinic, sedation (often with hangover effects), weight gain.<br>• Very cardiotoxic – arrhythmias, tachycardia / heart block.<br>• Very toxic in overdose as they inhibit sodium channels.<br>• Postural hypotension.<br>• Women less tolerant of TCA side effects than men<br>• Titrate to effective dose.<br>• Caution in patients with cardiac disease.<br>• Don't give to patients with suicide ideation or prescribe only a few days' supply at a time.<br>• 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.<br>• 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 | • **DO NOT PRESCRIBE** – see NHS England guidance | |
| Dosulepin | | |

| AGOMELATINE | | |
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| **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 | • Restricted formulary in TEWV – see NTAG recommendation; requires approval before initiation<br>• RED drug – secondary care prescribing only<br>• Melatonin activity useful if insomnia is a feature | • Relatively free of side-effects<br>• Minimal cardiovascular effects<br>• 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 |