

- **Mode of action** pre synaptic inhibition of serotonin uptake.
- **Direct effects** are related to serotonergic potentiation, e.g. GI symptoms & bleeding esp. in elderly or those on NSAID. May cause SIADH.
- **Drug interactions** can be hazardous :
 - a. Increase in serotonin activity & risk of **serotonin syndrome** due to inhibition of cytochrome P₄₅₀ reactions (phase I). Pethidine, pentazocine & tramadol should be avoided.
 - b. Increased S. levels of drugs metabolized by cytochrome P₄₅₀ care with use of drugs like type I antiarrhythmics, warfarin, propranolol, midazolam & tramadol.
 - c. SSRIs compete with highly protein bound drugs e.g. lidocaine, midazolam, fentanyl, resulting in increased free fraction.
- **Withdrawal S/S** - dizziness, lethargy, palpitation, flu like syndrome, sensory & sleep problems & psychic phenomenon.

Discontinuation leads to withdrawal & continuation leads to drug interactions. SSRIs can be **continued** during surgery. Precautions to be taken are- avoid drugs known to cause drug interactions. In elderly, on NSAIDs, need to weigh against risk of withdrawal.

Serotonin Syndrome - is a clinical syndrome due to excessive stimulation of central & peripheral serotonergic receptors, usually due to drug interactions / overdose.

- S/S - restlessness, hypomania, hallucination, motor & autonomic changes. Life threatening acute complication like coma, seizures, rhabdomyolysis & DIC may occur.
- **Drugs** associated with serotonin syndrome include antipsychotics (SSRI, MAOI, TCA, Li, venlafaxine), tryptophan containing items, amphetamines, bromocriptine, l-DOPA, narcotics (pethidine, fentanyl, tramadol, pentazocine), valproate, antiemetics (ondansetron, granisetron, metoclopramide), sumatriptan, dextromethorphan, antibiotics (linezolid), antiviral (ritonavir).
- **Investigations** - to exclude other diagnosis.
- **Treatment** - Discontinue drug, symptomatic & supportive management.
- Specific agent - cyproheptadine, chlorpromazine

Other Antidepressants

Drug	Brand name	Initial daily doses p.o.	Other Details
Maprotiline	Ludomil	75mg o.d. (upto 200 mg), IV 1-2 mg over 2 min	similar to TCA. No specific complications
Mianserine	Tetradep, Seridac	10-30 mg	<ul style="list-style-type: none"> • α_2 antagonist • α_1 serotonin, histamine agonist • Cardiac safe (hypotension is reported in combination with amantidine) • Neutropenia esp. in elderly
Mirtazapine	Mirt, Mirtaz	7.5 mg	<ul style="list-style-type: none"> • α_2 antagonist • block serotonin & histamine receptors • Sedation • No inhibition of cytochrome P₄₅₀
Venlafaxine	Flavix, Veniz XR	25-37.5 mg	<ul style="list-style-type: none"> • serotonin & NE reuptake inhibitor • High doses - inhibits dopamine uptake • Less cardiac & metabolic effects • may contribute to serotonin syndrome • Dose dependent increase in toxicity
Trazodone	Depryl, Trazonil, Tazodac	10 mg	<ul style="list-style-type: none"> • Hypotension, nausea, sedation
Nefazodone	Serzone	50-100 mg (upto 600 mg /day)	<ul style="list-style-type: none"> • Sedation, ataxia. Inhibits Cytochrome P₄₅₀
Bupropion	Smoquit, Wellbutrin	75-150 mg (max 450 mg/day)	<ul style="list-style-type: none"> • not cardiotoxic • can cause seizures
Alprazolam	Alprax, Trika, Anxit	0.25-0.5 mg	<ul style="list-style-type: none"> • No cardiac / anticholinergic side effects

Atypical antidepressants also have withdrawal S/S and should be **discontinued** preop. Psychiatric consultation for unstable patients.