

NAME: Generic / TRADE g=generic availability T _{1/2} = half-life		RECEPTOR AFFINITY	SIDE EFFECTS		COMMENTS & ADDITIONAL USES (Bold & ✓ indicates official indication in Canada)	INITIAL & MAX. DOSE	USUAL ADULT DOSE RANGE	\$  /Month		
			ACH.	SED.	OTHER					
Citalopram CELEXA _g T _{1/2} =35hr (20,40mg scored tab (10&30mg ^x ▼)abr=CC elderly: 10mg/d; ↑QT Melitz @ 5,10,15, 20mg ODT.	escitalopram CIPRALEX ^x ▼ (S+) citalopram 10 ⁵ -20 ⁵ mg od -\$65 Max		+	+	SSRIs SE in General nausea {21%(F) - 36%(X)}, anxiety, insomnia {-14%}, agitation,anorexia, tremor somnolence ^{11-26%} , yawning, sweating (all), dry mouth, headache , dizziness, enuresis diarrhea {12%(F,P)-17%(S)}, constipation {13-18%}, EPS sexual dysfx. >30% ^{8,9} , SIADH Toxicity can ↑ depression {D/C Syndrome ¹⁰ → flu-like Sx's ' FINISH ' flu, insomnia, nausea,imbalance,sensory Δ's, hyper}	•fewest drug interactions •?benefit heart dx pt 11,but ↑QT>40mg/d •most anorexic & stimulating •long half-life (5 wk washout) •90mg weekly in USA •DIs tamoxifen	Therapeutic Uses ^{12,13} ✓ OCD (esp. F, P,S,X) ✓ Panic (esp. P,S,F,CC,X) ✓ GAD (P,ES);?others ✓ Bulimia nervosa (F) ✓ Diabetic neurop.(CC) & deter use of EtOH ✓ PTSD(P,S),✓PMDD(F,P,S) ✓ Social Phobia (P,S) ✓ Pediatric (ES,F,S,X) +ve effect on headache? •flat dose response (majority of depressed pts respond at the lowest effective dose) •useful if comorbid dx	10-20mg am 40-60 mg/d 20mg elderly	20mg po od STAART NS Autism 40mg po od Star*D -40-60mg/d	25 25
Fluoxetine PROZAC _g (10,20,40 ^x ▼mg cap & 4mg/ml soln) abr=F T _{1/2} =4-6days, plus norfluoxetine 4-16days (Approved 1989)	5HT SELECTIVE	0	0	•most nauseating , constipating & sedating SSRI; ↑ DIs ^{1A2,2C19}		10-20mg od 60mg Hollander-Autism 80mg/d	(10mg po od) Flame (Sol'n= \$99) 20mg od am 40mg po od am	36 29 50		
Fluvoxamine LUVOX _g (50,100mg scored tabs) abr=X T _{1/2} =15-26hr	SSRIs	0/+	++			25-50mg hs 300mg/d	100mg po hs 150mg po hs 50mg am & 150mg hs	24 33 43		
Paroxetine PAXIL _g T _{1/2} =21-31hr (10 ⁵ ,20 ⁵ , 30mg tab)(40mg tab ^x ▼) abr=P {Paxil CR 12.5,25,37.5mg tab ^x @ } 	(blocks dopamine at high doses: P,S) {Women may respond better than ♂}	+	+			10-20mg am 60mg/d	10-20mg po od am 30mg po od am 40mg po od am 12.5-25mg CR od am ^x @	26-28 29 49 54-60		
Sertraline ZOLOFT _g (25,50,100mg cap) abr=S T _{1/2} =26hr, plus desmethyl 66hr	Vilazodone Viibryd ^x @ in USA only: 10,20,40mg tab od with food; ?wt neutral,?↓sex dysfx	0	+			25-50mg am ^{-95mg/day} HTA-SADD NS 200mg/d	100mg po od cc DIADS-2 NS 50mg am & 100mg pm ^{StarD} 100mg po bid cc	26 45 46		
Nefazodone SERZONE T _{1/2} =2-4hr abr=Z	SARI 5HT Selective	+	+++	As for SSRIs, + ↓ BP Rare: hepatotoxicity ¹⁷ , visual Δ's		50-100mg bid 600mg/d	100mg po bid 150mg po bid	DISCONTINUED Canada NOV03		
Trazodone DESYREL _g T _{1/2} =6-11hr (50;75 ^x ▼;100mg scored tabs) (150mg Dividose tab:50/75/100/150mg ^x ▼)	SSRI+5HT₂ rec. antagonism	0	++++	↓↓ BP, dizzy, headache, nausea; (α ₁ blockade); priapism 1/6000, (Tx epi)	✓dementia 50mg hs (insomnia , sundowning , aggression); less cardiac effects than TCAs	25-50mg bid 600mg/d	25-50mg po hs 100mg po bid pc 200mg po bid pc	10 17 25		
Amitriptyline ELAVIL _g T _{1/2} =9-44hr & noramitriptyline (10, 25,50mg; 75mg ^x ▼tab)	5HT & NE EFFECTS tertiary (3°) amine TCA's {Men may respond better than ♀}	+++++	+++++	General TCA SE: ↑HR, ↓BP (Tx: fluid+/- Florinef), ↑weight, sexual dysfx, sweating, rash, tremors, SIADH, ECG abnormalities, seizures , •fatal in overdose ¹⁸ (≥2gm) due to cardiac & neurologic toxicity. •? rare: anticonvulsant hypersensitivity cross reactions •2° amines generally better tolerated then 3° amines (less dry mouth, dizziness & weight gain) •As dose ↑: ↑BP ^{8,HR} , agitation, tremor,sweating,nausea-37%, headache, sleep disturbances •caution: withdrawal effects	•often 10-30⁺ mg hs for sleep, IBS & chronic pain •Cp •↑QT •esp. effective for OCD ^{210yrs} •Most serotonergic TCA; •Cp •↑ risk of seizures •DI: grapefruit •Most histamine block •Cp • Breastfeed concern •✓ psychoneurotic/anxious dep. •Cp ✓ Childhood enuresis (age 6+) •Most NE activity •caution CV hx • Least ACH side effects •Cp (used in IBS irritable bowel syndrome) •Least hypotensive TCA. ✓IBS •Cp (response may be higher at low end ~50mg of dose range ²³)	Therapeutic Uses ¹⁹ ✓ IBS, Pain Syndromes ²⁰ & sleep disorders ²¹ (amitriptyline; but nortriptyline ^{2°TCA} useful & less SE) ✓ Neuropathy ✓ Agitation & insomnia ✓ Panic→ imipramine ✓ Migraine prophylaxis ²² (esp. amitrip./nortriptyline) ✓ D/C Smoking → nortrip. ✓ ADHD (ie. desipramine)	10-25mg hs 300mg/d	50 mg po hs 200mg po hs	12 38	
Clomipramine ANAFRANIL _g (10, 25, 50mg tab) T _{1/2} =20-32hr & desmethyl 66hr		+++++	++++			10-25mg hs 300mg/d	50 mg po hs 150mg po hs 200mg po hs	18 39 50		
Doxepin  SINEQUAN _g (10,25,50,75,100,150mg cap) T _{1/2} =8-52hr with desmethyl		+++	++++			10-25mg hs 300mg/d	50 mg po hs 200mg po hs	17 41		
Imipramine  TOFRANIL _g (10, 25, 50; 75 ^x ▼mg tab) T _{1/2} =6-34hr with desipramine & hydroxy		+++	+++			10-25mg hs 300mg/d	50 mg po hs 150-200mg po hs	24 55-71		
Desipramine NORPRAMIN _g (10,25,50,75,100mg tab)-imipramine derivative T _{1/2} =12-46hr with hydroxy		++	++			10-25mg hs 300mg/d	50 mg po hs 150mg po hs (2x75mg) 200mg po hs (2x100mg)	29 66 66		
Nortriptyline AVENTYL _g (10, 25mg cap) -amitriptyline derivative T _{1/2} =16-88hr & hydroxy		secondary (2°) amine TCA's	+++		++		10mg hs 150mg/d Star*D <200mg/d	25mg po hs 50mg po hs 100mg po hs 75-100mg/d for neuropathic pain	15 21 28	
Venlafaxine EFFEXOR _g (XR 37.5mg, 75mg, 150mg cap) g  (Reg 37.5,75mg scored tabs-Co D/C Jul04) -XR cap content may be sprinkled T _{1/2} =5hr & desmethyl 11hr		Desvenlafaxine ER ghost tab Pristiq ^x @ 50-100mg po od new ; DI: CYP 3A4 (?clarithromycin),allergic rxn \$85	++	+			18.75-37.5mg 375mg/d	37.5mg XR po od 75mg XR po od 150mg XR od Star*D ~200mg/d 225mg XR od (150mg+75mg cap)	13 18 19 36	
DULoxetine CYMBALTA SNRI 30,60mg cap on SPDP  SE: nausea, insomnia,somnolence,headache,diarrhea, ↓appetite, fatigue, ↑sweat, ↑BP, ↑LFT, ↑DIA2D6, dry mouth; urinary retentionFDA?; ✓depression adult & maintenance ²⁰ , GAD, diabetic neuropathic pain ²¹ , fibromyalgia & ?stress incontinence ²² @ 30-60mg/d ⁵⁶⁹⁻¹³² Max 120mg.										
Bupropion SR WELLBUTRIN _g (100,150mg tab).(150,300mg XL ghost tab) T _{1/2} =21hr	NDRI DA & NE	0	0	agitation,insomnia,tremor,sweating, ↓appetite, GI upset, psychos.	•↑d risk of seizure ~0.4% 400mg/d •less sex dysfx, low wt. gain	= ZYBAN ^{SK} ^x ▼ → D/C smoking; ✓ BPAD & Seasonal AD	100mg od am 450mg/d ^x <300mg/d	100-150mg bid Star*D -300mg/d 150-300mg XL po od	22-28 25-44	
MAOIs: non-selective & irreversible; ✓ atypical/refractory depression; enzyme effect ~10days; many DIs & food cautions (tyramine-hypertensive crisis);phenelzine NARDIL 15mg tab bid-tid; tranylcypromine PARNATE 10mg tab bid-tid										
Mirtazapine REMERON _g T _{1/2} =20-40hr 15 ⁵ ,30 ⁵ ,45mg tabs (Remeron RD 15,30,45mg tab)	NaSSA_{5HT} & NE	+++	++++	Dry mouth, sedation , edema, arthralgias, dizzy, ↑lipid. DI-clonidine	↑appetite& weight ↓;sexual dysfx; rare neutropenia; RD if difficulty swallowing	✓Anxiety,Somatization	≤7.5-45mg/day Star*D <60mg/d ~30mg/day HTA-SADD NS	15-30mg po hs RD 15-30mg po hs regular	12-16 16-25	
Moclobemide MANERIX _g T _{1/2} =1-2hr (100,150,300mg scored tabs) (2x150mg tabs cheaper than 300mg tab)	RIMA Selective & Reversible	+	0	Dry mouth, dizzy, headache, nausea, tremor, restless, less sex dysfx	•no tyramine dietary precaution if <600mg/d •enzyme effect lasts ~24hrs DI: meperidine,sympathomimetics,DM...	✓Atypical, ✓ Anxious-phobic , ✓Co-morbid anxiety	100mg bid 600-900mg/d	150mg po bid pc 300mg am&150pm pc 300mg po bid pc	22 28 34	

↓ = ↓ dose for renal dysfx <= scored tab ^x = n-formulary in SK ² = prior approval NIHB [▼] = covered by NIHB [⊗] = not NIHB **COST**=total cost **5HT**=serotonin **ACH**=anticholinergic effects (dry mouth, constipation, urinary hesitancy, blurred vision) **ADD**=attention deficit disorder
BP=blood pressure **Cp**=plasma level avail **DA**=dopamine **D/C**=discontinuation **DI**=drug interactions **epi**=epinephrine **GI**=stomach **HR**=heart rate **MAOI**=monoamine oxidase inhibitors **NE**=norepinephrine **OCD**=obsessive compulsive dx **RIMA**=reversible inhibitor of
MAO-A **SE**=side effect **SED**=sedation **SSRI**=selective 5HT reuptake inhibitor **Sx**=symptoms **TCA**=tricyclic antidepressant **Tx**=treatment **wk**=week **wt**=weight **INITIAL DOSE** -Lower initial dose for elderly/sensitive pts ¹ =initial dose lower than usual effective dose.
Suicidal Thoughts/Behavior: ↑ by all agents if ≤24yrs **Pregnancy:** SSRI most safety data (fluoxetine most clinical experience), bupropion or select TCAs. **Treatment Duration:** full dose for at least ≥6-12months after remission (if recurrence tx longer)

Add-on Augment/Combo → if **partial** response: some evidence ECT; (esp. with TCA + lithium ≥600mg/d or l-thyroxine ≤100ug/d; buspirone ^{Star*D}, pindolol, quetiapine XR/olanzapine/risperidone/aripiprazole, tryptophan & ?folic ≤1mg/d with SSRI). Bupropion ^{Star*D} or mirtazapine (with SSRI or venlafaxine).

Antidepressants – Supplementary Tables

Table 1: Adverse Effects: Management Options 24,25

• **Dizziness** ☞ check BP for **orthostatic hypotension**; mild symptoms may attenuate over several weeks; ↓ dose or switch agent; encourage adequate fluid intake & avoid excessive salt restriction; **Florinef** 0.1mg po od & titrate

• **Sedation/foggy** ☞ may attenuate over 1-2 weeks; give single dose 1-2 hr prior to bedtime; ↓ dose or choose alternative; select pts modafinil or methylphenidate / atomoxetine

• **Peripheral anticholinergic effects** ☞ tolerance may develop over several weeks; switch to alternative agent; treatment options for some Sx:

- **blurry vision** - pilocarpine eye drops; methylcellulose drops for dry eyes
- **urinary hesitancy** - bethanechol 25-50mg po tid-qid
- **abdominal cramps, nausea, diarrhea** - adjust dose
- **dry mouth** - sugarless gum; saliva substitutes
- **constipation** - adequate hydration, activity, bulk forming laxatives

• **Sweating** ☞ ↓ dose or change antidepressant; benzotropine, cyproheptadine, clonidine

• **Weight gain** ☞ modify & monitor diet & activity; switch to alternate agent

• **Sexual dysfunction** ☞ distinguish etiology (drug vs illness); switch to: (bupropion, mirtazapine, citalopram, moclobemide, venlafaxine^{↓ dose}); adjust dose; 1 day/wk drug holiday, amantadine;

Other: • ↓ libido → neostigmine 7.5-15mg 30min prior to intercourse

- impaired erection → bethanechol 10mg po tid, ? buspirone
- anorgasmia → amantadine; cyproheptadine 4mg po qam, ?sildenafil in ♀
- antidepressant induced erectile dysfunction → sildenafil may help²⁶

• **Myoclonus** ☞ ?TCA toxicity; reassess dose/levels; clonazepam 0.25mg tid

• **Insomnia & anxiety (5HT related)** ☞ ↓ dose; administer in am; + short course of trazodone 50-100mg hs; switch to alternate agent

• **SIADH (syndrome of inappropriate antidiuretic hormone secretion esp in elderly)**: assoc. with hyponatremia ☞ DC causative med; fluid restrict (1 liter/d) ? demeclocycline-not CDN, tolvaptan

• **Serotonin Syndrome**²⁷: excitement, anxiety, diaphoresis, rigidity, ↑ temp, tremor, clonus, ↑ reflexes, ↑ HR & ↑ BP, delirium; Tx: D/C serotonergic meds; cyproheptadine 8mg po q4h, diazepam

• **Discontinuation syndrome** with abrupt withdrawal eg. **paroxetine & venlafaxine** a flu-like Sx ~10day (FINISH: flu, insomnia, nausea, imbalance, sensory disturbances & hyperactivity) may occur: Tx: **TAPER** off original antidepressant slowly over several days⁷ even weeks; for venlafaxine may dose q36-48hr when at 37.5mg daily or benzotropine (for cholinergic rebound → nausea/vomiting Gravidol, sweating), lorazepam (for agitation/insomnia), propranolol (for akathisia) as necessary.

Table 4: Individualizing Therapy Considerations 28

Anxiety/Panic ✓ SSRI, venlafaxine, mirtazapine

Anxiety, Comorbid ✓ SSRI, moclobemide, mirtazapine, duloxetine, ?buspirone

Atypical ✓ moclobemide, MAOIs, SSRI

Bipolar ✓ mood stabilizer e.g. lithium, valproic acid, carbamazepine, quetiapine +/- antidepressant

Cardiac Dx: ✓ SSRIs[?] low dose-citalopram, sertraline, MAOIs, bupropion; **Catatonic**: ECT

Chronic Pain/Neuropathy²⁹ ✓ TCAs: amitriptyline, nortriptyline; venlafaxine, duloxetine

Drug Induced^{30,31} stop or reduce offending agent (see bottom)

Elderly^{32,33} ✓ SSRI (CC,P,S); venlafaxine; mirtazapine; bupropion; RIMA; 2°TCA eg. nortriptyline

Migraine³⁴ ✓ amitriptyline, nortriptyline

Obsessive Compulsive ✓ SSRI (high dose), clomipramine

Orthostatic Hypotension ✓ venlafaxine(↑BP); nortriptyline, SSRIs (ambulation, hydration, gradual dose titration)

Phobic ✓ moclobemide, MAOI, paroxetine?

Psychotic ✓ +antipsychotic quetiapine, aripiprazole, olanzapine, amoxapine etc., ECT Navarro'08

Seizure History ✓ trazodone, SSRIs, moclobemide, venlafaxine

Sleep Disorders³⁵ ✓ trazodone, amitriptyline, other TCAs (nortriptyline)

Smoking Cessation³⁶ ✓ bupropion **ZYBAN** 300mg/d, nortriptyline 25-75mg/d

Weight Gain, Less³⁷ ✓ bupropion, SSRI, RIMA, venlafaxine, duloxetine

Table 2: Precautions 38,39,40

TCAs: benign prostatic hypertrophy, history of urinary retention, uncorrected angle closure glaucoma, seizure history, post-MI - acute recovery phase, cardiovascular disease, cholinergic rebound upon withdrawal from high doses (dizziness, nausea, diarrhea, insomnia, restlessness, cardiac conduction delays, heart block; arrhythmias)

SSRIs: ↑ levels & half-life, irritable bowel syndrome, CNS over-stimulation (e.g. **serotonin syndrome**)⁴¹ esp. if used with other serotonergic drugs (buspirone, dextromethorphan, lithium, MAOI, meperidine, methylene blue, mirtazapine, MDMA, ondansetron, sibutramine, St. Johns Wort, sumatriptan, tramadol, tryptophan, TCA)⁴²; withdrawal syndrome: dizziness, GI upset, headache, sleep disturbance, agitation/restlessness (usually mild & transient; less with fluoxetine)⁴³

Bleeding & ↑Fractures: assoc. by SSRI; risk of bleeding <0.5%; ↑ with NSAIDs, OACs⁴⁴

MAOIs: hypertensive crisis can occur secondary to foods containing tyramine (e.g. HIGH → Unpasteurized cheese (cheddar, camembert, blue), yeast extract, herring, aged unpasteurized meats, broad bean pods; **MODERATE** → avocado, meat extract, certain ales & beer, wine; **LOW** → fruit, cream & cottage cheese, distilled spirits, chocolate);

CI: Stroke/heart dx, geriatric or debilitated, pheochromocytoma, or hx of severe headache.

Bupropion: avoid if hx of seizures, bulimia or anorexia nervosa

Pediatrics: Safety & efficacy **not** well established.^{45,46,47,48} CBT, IPT, fluoxetine & citalopram 1st line option.⁴⁹ (Concern → suicide^{idea < 25yr}, aggression & agitation) NNH=143.

Imipramine for enuresis^{kids ≥ 6 yrs}. FDA: Fluoxetine^c depression⁽⁴⁹⁾ & OCD; clomipramine, fluvoxamine & sertraline^{OCD, 50}. TCAs: little to no depression benefit.^{Hazell'02}

Pregnancy: Consider risk vs benefit! ECT & psychotherapy are non-drug options. TCAs^{desipramine} & SSRIs: most clinical safety data.

SSRIs: **fluoxetine** most experience, paroxetine (no active metabolite, but ?harm⁵¹), sertraline^{?septal defects}, bupropion **but** less clinical experience, citalopram^{?septal defects- ?↑ Autism disorders with SSRIs/TCAs.^{51,53} Only if low depression risk,}

consider ↓ dose & /or taper off over weeks before delivery.⁵² Neonate may have **withdrawal**⁵³ & pulmonary HTN with SSRI^{rare}.⁵⁴ Depression serious risk for relapse, hospitalization, suicide; inform ?malformations, monitor u/s, echo. (See RxFiles Q&A Antidep during Preg/Lact)

Breastfeeding: consider risk vs benefit; psychotherapy; levels often <10% of maternal dose; esp. SSRIs & TCAs used: ↓ levels & no reported adverse effects^{sertraline, paroxetine & fluvoxamine}, ↓ breast milk level: fluoxetine, ?citalopram & venlafaxine⁵⁵; CanPedsSoc²⁰¹¹: SSRIs considered compatible.⁵¹ [See pg 91b]

TCAs: amitriptyline, nortriptyline, desipramine, imipramine, clomipramine.

QT: concern esp. if cardiac/QT history, ↓ heart rate, ↓ Mg²⁺/K⁺, or DIs eg. 2C19.

Elderly: extra caution required; med dose: start low & go slow

Relative Seizure Risk:⁵⁶

HIGH → maprotiline, amoxapine, clomipramine, bupropion

LOW → amitriptyline, imipramine, trimipramine, nortriptyline, desipramine, doxepin

LOWEST → trazodone, SSRI, MAOI'S, moclobemide, venlafaxine

***Atypical depression** defined as: mood reactivity; irritability; hypersomnia; hyperphagia; psychomotor agitation & hypersensitivity to rejection.

DRUG INTERACTIONS: Various cytochrome **P450 inhibition**⁵⁷ by SSRIs.

Less DI's⁵⁸: citalopram, escitalopram, mirtazapine, moclobemide, sertraline, venlafaxine, desvenlafaxine

Drug	CYP450 1A2	CYP450 2C9	CYP450 2C19	CYP450 2D6	CYP450 3A4
citalopram	0	0	0 to ++	+	0
fluoxetine	+	++	+ to ++	+++	+ to ++
fluvoxamine	+++	++	+++	+	++
paroxetine	+	+	+	+++	+
sertraline	+	+	+	+ to ++	+

Table 3: Switching Antidepressants: Taper or Washout periods in DAYS for outpatients 59,60,61

FROM						
amitriptyline	1*	1 [#]	1-7 [†]	7 [†]	1 [†]	1-7 [†]
clomipramine	1*	1 [#]	7-14 [†]	7 [†]	1 [†]	7-14 [†]
doxepin, imipramine	1*	1 [#]	1-7 [†]	7 [†]	1 [†]	1-7 [†]
desipramine	1*	1 [#]	1-7 [†]	7 [†]	1 [†]	1-7 [†]
nortriptyline	1*	1 [#]	1-7 [†]	7 [†]	1 [†]	1-7 [†]
mirtazapine	1 [#]	1 [†]	3 [†]	7 [†]	3 [†]	3 [†]
duloxetine ††	7 [#]	5 [†]	5 [†]	5 [†]	5 [†]	5 [†]
venlafaxine ††	7 [#]	7 [†]	7 [†]	7 [†]	7 [†]	7 [†]
fluoxetine	35 ¹	35 ¹	7 ¹	35 ¹	35 ¹	7 ¹
fluvoxamine	1-7 [†]	7 [†]	1 [#]	7 [†]	1 [†]	1+
paroxetine ††	7 [†]	7 [†]	7 [#]	10 [†]	7 [†]	7+
citalopram/sertraline	1-7 [†]	7 [†]	1 [#]	10 [†]	1 [†]	1+
nefazodone	1-3 [†]	3 [†]	1 [#]	7 [†]	1 [†]	1+
trazodone	1-7 [†]	7 [†]	1 [#]	7 [†]	2 [†]	1+
phenelzine	10-14	14	10-14		14	2 ^{##} 14
tranylcypromine	10-14	14	10-14	14		2 ^{##} 14
bupropion	1-3 [†]	1 [†]	1 [†]	7 [†]	3 [†]	
moclobemide	2	2	2	2		2
SWITCH TO New agent	amitriptyline, clomipramine doxepin, imipramine desipramine, nortriptyline mirtazapine, venlafaxine, duloxetine fluoxetine, fluvoxamine, paroxetine citalopram, sertraline, nefazodone, trazodone			phenelzine tranylcypromine moclobemide bupropion		

The **more critical** recommendations are in **bold**; risks of toxicity are greater with higher dosage regimens and inadequate washout period. **Some urgent cases may necessitate shorter delays in switching.**

* no washout required; use equivalent dose;
† taper first drug; start 2nd new drug at a low dose;
taper 1st med over 3-7day if on high dose prior to initiating 2nd new med;
taper if high dose; maintain dietary restriction for 10d;
! use lower doses of 2nd new drug initially; longer taper (up to 8wk) may be required if high dose fluoxetine^{no taper be long t-1/2 if only 20mg od}
†† paroxetine & venlafaxine tapered slowly ↓ discontinuation rx's.

Antidepressant Drug Interactions: page **106**
Other non P450 reactions possible (eg. Serotonin Sx)

Drug induced depression: ACEI, acetazolamide, amphetamine/ cocaine withdrawal, anticonvulsants, amantadine, barbiturates, BCPs, belimumab, benzos, bromocriptine, caffeine, chemotherapy^{some}, cimetidine, clonidine, dapsone, digoxin, disulfiram, efavirenz, ethambutol, ethanol, finasteride, griseofulvin, haloperidol, hydralazine, interferon, isoniazid, isotretinoin, levodopa, mefloquine, methylphenidate, methysergide, metoprolol, metoprolamide, metronidazole, nitrofurantoin, NSAIDs, opiates, physostigmine, procainamide, progestins, propranolol, reserpine, rilpivirine, streptomycin, steroids, sulfas, tetracycline & thiazides.

General:⁶⁰ Remission ~30%, Response ~50%, Eventually ~80% respond to drug (2-4wk some & 6-8wk for major improvement). **Psychotherapy, cognitive behavioral therapy (CBT) +/- drug tx also effective!** ECT may be effective 6-12 txs over 2-4wk. New: Vagus nerve & transcranial magnetic stimulation

ACP Guide 2008: Since drugs are ~equally effective; consider SE, cost, & pt preference. Assess after 1-2 wks & regularly (SE eg. suicidal effect). Modify tx if no response within 6-8wks. Tx Duration: **1st episodes** → continue for ~6 months 4-9months after response; pts with a hx of 2+ episodes → tx longer (years -lifelong)! CANMAT 2009 Canadian: Adult Major Depressive Disorder. Pharmacotherapy. Lam RW, et al. J Affect Disord. 2009 Aug 10. (11% of Canadians at some time, 4% during any given year, acute/maintenance tx, psychotherapy -CBT or IPT, ECT, & Complementary-St John's wort, light tx SAD & exercise.)⁶⁰

APA (American) 2010: Major Depressive Disorder. Acute tx options: meds, psychotherapy, both; ECT, TMS or light therapy. Meds esp for severe depression: most pts a SSRI, SNRI, mirtazapine or bupropion is optimal; but consider SE, DI, cost & pt preference; adjust/augment/combo/ECT as needed.⁶⁰

Assessment Questions: PHQ-9 or 1) In last month, have you often been bothered by "feeling down", depressed or hopeless? 2) In last month, have you been bothered by having little interest or pleasure in doing things? Clinical benefit relates to severity Depression MID-Med NNT=16, Severe NNT=11, Very Severe NNT=4 over ~8 wks Fournier'10

- Assess the patient's status regularly, beginning within 2 weeks after starting therapy.
 - Modify treatment if there's no response within 2 months.
 - Successful treatments of first episodes of major depression should continue for about 6 months; patients with a history of two or more episodes should undergo treatment for much longer periods.
- Qaseem A, Snow V, Denberg TD, et al; Clinical Efficacy Assessment Subcommittee of American College of Physicians. (ACP) Using second-generation antidepressants to treat depressive disorders: a clinical practice guideline from the American College of Physicians. *Ann Intern Med*. 2008 Nov 18;149(10):725-33.

ANTIDEPRESSANT COMPARISON CHART - References

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- Sept/05 Nice:Depression in children & young people <http://www.nice.org.uk/pdf/CG028NICEguideline.pdf> ; (Simon GE, Savarino J, Operskalski B, Wang PS. **Suicide risk during antidepressant treatment**. Am J Psychiatry. 2006 Jan;163(1):41-7. CONCLUSIONS: The risk of suicide during acute-phase antidepressant treatment is approximately one in 3,000 treatment episodes, and risk of serious suicide attempt is approximately one in 1,000. Available data do not indicate a significant increase in risk of suicide or serious suicide attempt after starting treatment with newer antidepressant drugs.) (Cheung AH, et al. The use of antidepressants to treat depression in children and adolescents. CMAJ. 2006 Jan 17;174(2):193-200.) & (Hammad TA, et al. Suicidality in pediatric patients treated with antidepressant drugs. Arch Gen Psychiatry. 2006 Mar;63(3):332-9. CONCLUSION: Use of antidepressant drugs in pediatric patients is associated with a modestly increased risk of suicidality. InfoPOEMs: The use of antidepressant medications in children is associated with an increased risk of suicidal ideation and suicide-related behaviors. It is uncertain what overall effect antidepressant medications have on the morbidity and mortality of treated children. Close monitoring of patients using these medications regarding the risk of suicidality is recommended. (LOE = 1a-)) (Glaxo May/06 Meta analysis: 8958 paroxetine & 5953 placebo pts; suicidal behavior aged 18-24yrs (2.19 vs 0.92%); all ages (0.32 vs 0.05%); all were nonfatal suicide attempts; 8 of 11 attempts were in aged 18-30yrs) Emslie GJ, et al. Paroxetine Treatment in Children and Adolescents With Major Depressive Disorder. A Randomized, Multicenter, Double-Blind, Placebo-Controlled Trial. J Am Acad Child Adolesc Psychiatry. 2006 Jun;45(6):709-719. Paroxetine was not shown to be more efficacious than placebo for treating pediatric major depressive disorder. (Misri S, et al. 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In these high-risk patients, antidepressant drug treatment does not seem to be related to suicide attempts and death in adults but might be related in children and adolescents. These findings support careful clinical monitoring during antidepressant drug treatment of severely depressed young people.) (Tiihonen J, et al. Antidepressants and the risk of suicide, attempted suicide, and overall mortality in a nationwide cohort. Arch Gen Psychiatry. 2006 Dec;63(12):1358-67. Among suicidal subjects who had ever used antidepressants, the current use of any antidepressant was associated with a markedly increased risk of attempted suicide and, at the same time, with a markedly decreased risk of completed suicide and death. Lower mortality was attributable to a decrease in cardiovascular- and cerebrovascular-related deaths during selective serotonin reuptake inhibitor use.) (Simon GE. The antidepressant quandary—considering suicide risk when treating adolescent depression. 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Relationship between antidepressants and suicide attempts: an analysis of the veterans health administration data sets. Am J Psychiatry. 2007 Jul;164(7):1044-9. These findings suggest that SSRI

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Barbui C, Esposito E, Cipriani A. Selective serotonin reuptake inhibitors and risk of suicide: a systematic review of observational studies. *CMAJ*. 2009 Feb 3;180(3):291-7. Based on data from observational studies, use of SSRIs may be associated with a reduced risk of suicide in adults with depression. Among adolescents, use of SSRIs may increase suicidality.

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Hansen RA, Gartlehner G, Lohr KN, et al. **Efficacy and safety of second-generation antidepressants** in the treatment of major depressive disorder. *Ann Intern Med*. 2005 Sep 20;143(6):415-26. **CONCLUSIONS:** Overall, second-generation antidepressants probably do not differ substantially for treatment of major depressive disorder. Choosing the agent that is most appropriate for a given patient is difficult. (InfoPOEMs: When it comes to the new, nontricyclic antidepressants, the medical literature does not give us any clear guidance as to which one is more effective, of faster onset, safer, or better tolerated. Sexual side effects are lower with bupropion and nausea seems to occur more often with venlafaxine. Other research has shown these new drugs to be no more effective or better tolerated than tricyclic antidepressants. For now, start your patient on your favorite antidepressant, with the realization that most patients will need to switch to another drug at least once. (LOE = 1a))

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Health Canada Oct/08 Venlafaxine overdose warning http://www.hc-sc.gc.ca/dhp-mps/medeff/advisories-avis/prof/_2008/venlafaxine_hpc-cps-eng.php

Health Canada Feb/11 **Methylene blue injectable** in combination with serotonin reuptake inhibitors - Association with serotonin toxicity Cases of serotonin toxicity have been reported and published in association with the use of methylene blue injectable in patients exposed to drugs with serotonin reuptake inhibition properties.

Health Canada Jan/12: Lundbeck Canada, in collaboration with Health Canada, would like to inform you that the antidepressant **Celexa® (citalopram hydrobromide; also marketed as generics)**, should no longer be used at doses greater than **40 mg per day** due to study results indicating a dose-dependent potential for QT prolongation.

Health Canada May/12 is informing Canadians of a labelling update for the prescription drug **Ciprallex** (the brand name of the drug **escitalopram**) regarding a dose-related risk of abnormal heart rhythms. Ciprallex is used to treat depression and belongs to a family of drugs known as Selective Serotonin Reuptake Inhibitors (SSRIs). 10 mg per day is the maximum recommended dose for patients who: are 65 years of age or older, or have liver problems, or are taking the heartburn drugs omeprazole or cimetidine which can increase the blood level of Ciprallex. 20 mg per day is still the maximum recommended dose for most other patients.

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