Behavioral & Psychological Symptoms of DEMENTIA (BPSD) Treatment Chart [1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20,21] www.RxFiles.ca Brent Jensen BSP Sept 04

Generic/TRADE (Strength & forms)	Class / Symptoms / Tips	Side effects	Comments / Drug Interactions (DI [3,22,23]) (√ = therapeutic use)	INITIAL & MAX DOSE	USUAL DOSE RANGE geriatric	$ /Month
Donepezil ☎ ⊗ **ARICEPT** [24,25,26,27,28,29,30,31,32,33,34,35,36,37] 5ˢ, 10ˢ mg tab acetycholinesterase activity t ½ ~75hr	**May** temp. stabilize dementia & behavior (& may help apathy, hallucinations & delusions) Slows rate of functional loss Not delay institutionalisation[35] AD2000	(Nausea, vomiting, diarrhea) ~10%; ↑with ↑dose, anorexia, muscle cramps, insomnia, fatigue, wt loss~3%,other cholinergic effects, agitation initially	√Mild to moderate Alzheimer's (MMSE 10-26); ? for mod-severe Alzheimer's [38,39]; ↑ dose **q 1month** if needed DI: ↑ level by erythromycin, grapefruit juice, ketoconazole, paroxetine & quinidine ; ↓ level by carbamazepine, dexamethasone, phenytoin, phenobarbital & rifampin.	5mg 10mg	5mg po **od** in **am** 10mg po **od** in am (with food may ↓SE)	171 171 ☎ ⊗
Galantamine ☎⊗ **REMINYL** [40,41,4243,44,45,46,47,48,49,50,51] 4,8,12ˢ mg tab acetycholinesterase & nicotinic activity t ½ ~6hr	NNT **12** minimal improvement [12] NNT **42** marked improvement [12] NNH **16** adverse event-dropout [12] ↑ADAS-Cog ~2-3pts vs placebo [8] (~20% ↑ 4pts; ~10% ↑ 7pts vs placebo)	(Nausea, vomiting, diarrhea)~>10%; ↑with ↑dose,↓HR, anorexia, wt loss~3%, insomnia,abdominal pain	√ Mild to mod Alzheimer's & to reverse neuromuscular blockers (not effective for mild cognitive impairment; ↑mortality 1.5vs0.5%)[52] ↑ dose **q 1month** if needed; ↓ dose in hepatic/renal dysfx DI:↑level by antidepressants (amitriptyline,fluoxetine,fluvoxamine,paroxetine ~30%), cimetidine 16%, erythromycin 10%, ketoconazole 30% & quinidine 30%	4mg 24-32mg	4mg po bid cc 8-12mg po bid cc	178 178 ☎ ⊗
Rivastigmine **EXELON** [53,54,55,56,57,58,59] ☎ ⊗ 1.5, 3, 4.5, 6 mg cap; 2mg/ml soln acetyl & butrylcholinesterase activity t ½ ~2hr	↑ MMSE ~1pt vs placebo [8,35] Takes~**3months** Tx→?modest benefit Taper dose to reduce withdrawal SE Acetylcholinesterase Inhibitor (**ChEIs**)	(Nausea, vomiting, diarrhea) ~>10%; ↑with ↑dose, anorexia, muscle cramps, insomnia, fatigue, wt loss~3%,asthenia,headache, confusion, other cholinergic effects (stomach,↓HR,nightmares..)	√Mild to mod Alzheimer's(MMSE 10-26),?Lewy body [60,61] If Tx interrupted for several days→**restart** 1.5mg bid Oral soln: stable for **4hrs** when mixed with juice/soda ↑ dose **q 1month** if needed. ↓↓ DI's but smoking ↓levels.	3mg 12mg	1.5-3mg po bid cc 4.5-6mg po bid cc 4.5mg(2.25ml) bid	178 178 212 ☎ ⊗

Relative Contraindications: bradycardia, sick sinus syndrome, active peptic ulcer, severe asthma, anesthesia ↑succinylcholine effect, **anticholinergic meds** antagonistic effects, Parkinson's ↑EPS, Epilepsy ?↓Sz threshold & B-blockers ?↑bradycardia

☎ = **EDS** **New pts**: a) Dx of probable Alzheimer's b) MMSE 10-26 within 60 day before coverage c) Functional Activities Questionnaire (FAQ) within 60 days before coverage d) Stop all anticholinergic meds 14 days before MMSE & FAQ e) if intolerant: may switch to another ChEIs. **To continue coverage** must **not** have **both** >2pt ↓MMSE & 1pt ↑ FAQ in a 6month period. **MMSE** must **always** be **≥10**. Patients who do not meet criteria to continue can be re-evaluated within 3 months to confirm deterioration before coverage is discontinued. **Re-evaluate q 6 months**.

Haloperidol [62] **HALDOL** 0.5ˢ, 1ˢ, 2ˢ, 5ˢ, 10ˢ mg tab; 2mg/ml soln; **DEPOT** 250 & 500mg/5ml Vials, 100mg/1ml Amp ✗⊗; 5mg/ml amp	Helps delusions & hallucinations & agitation: these occur esp. early in **Lewy body** ↑EPS, ↑ALT ≤16%, **Weight gain** ≤ 1 kg **Antipsychotics**	Delirium, confusion, anticholinergic, sedation, constipation,↓BP,↑weight,EPS (extrapyramidal) esp. parkinsonian, akathisia, falls, neuroleptic malignant syndrome & tardive dyskinesia.	Start low dose, go slow Aim for **improvement** not resolution of hallucinations/delusions Least EPS/Parkinson effect with **quetiapine** & clozapine	**0.25**-100mg po 25-300mg IM q4w	0.25mg po bid 1mg po bid 50-100mgIMq2-**4w**	10 10 20
Olanzapine ☎ ▼ **ZYPREXA** [63,64,65,66,67,68,69] 2.5, 5, 7.5, 10, 15mg tab; ZYDIS 5, 10, 15⊗mg tab; 10mg IM ✗⊗ vial (For IM use sterile water for injection; do not mix in same syringe with diazepam, haloperidol or lorazepam)	SE:somnolence, dry mouth, dizzy, headache, asthenia, constipation, blurred vision, urinary incontinence, dyspepsia, ↑ ALT ≤ 6%, **diabetes**, **weight ↑↑**, **akathesia** >10%, postural hypotension, seizures 0.9%, ?↑ stroke/death, ↑ triglycerides, ↑ cholesterol, ↔↑ **prolactin** effect		Antipsychotics in Lewy body dementia cause significant ↑ in EPS side effects ↑ weight gain/diabetes esp. with **clozapine** & olanzapine [70]	**1.25**-5mg 10-20mg	2.5mg po od 5-7.5mg po od	67 128-188 ☎ ⊗
Quetiapine **SEROQUEL** 25, 100, 150, 200, 300mg tab [71,72]	SE**: somnolence**, dizzy, drowsy, constipation, dry mouth, **lens changes** in beagles-annual slit lamp exam, ↓ BP, **weight ↑**, seizures ≤0.8%, dyspepsia, headache, urinary incontinence, diabetes, ↑ALT ≤ 9%, akathisia >**2**%, ↑ triglyceride 17%, ↑ cholesterol 11%, hypothyroidism 0.4%, **low EPS** effect ↔ **prolactin** effect			**12.5**mg 150-750mg	25mg po hs 50-100mg po hs	25 42-54
Risperidone **RISPERDAL** [73,74,75,76] 0.25, 0.5ˢ, 1, 2ˢ, 3ˢ, 4ˢ mg tab; M-TAB⊗ 0.5,1,2mg tab ; 1mg/ml soln; **Consta** 25,37.5,50mg vial.	SE: sedation, headache, dry mouth, constipation, blurred vision, urinary incontinence, insomnia, asthenia, **↓BP,** akathisia >10%, ↓ appetite, TTP, seizures ≤0.3%, photosensitive, ?↑ stroke, **weight ↑**. Oral liquid **not** mix with cola or tea. **↑ EPS at doses > 2-4mg/day &** ↑ **prolactin** effect			**0.25**-1mg 2-6mg	0.5mg po hs 1-2mg po hs	34 46-84

Continued on page 53 & 54

Generic/TRADE (Strength & forms)	Class / Symptoms / Tips	Side effects	Comments / Drug Interactions (DI [3,77,78]) (√ = therapeutic use)	INITIAL & MAX DOSE	USUAL DOSE RANGE geriatric	$ /Month
Citalopram [79,80,81] =**CC** **CELEXA** 20, 40mg **scored** tabs **Fluoxetine** [82] =**F** **PROZAC** 10,20,40✗▼mg cap & 4mg/ml soln **Fluvoxamine** [83] =**X** **LUVOX** 50ς, 100ς mg scored tabs **Paroxetine** [84,85] =**P** **PAXIL** 10ς,20ς, 30mg tab **Sertraline** [86,87] =**S** **ZOLOFT** 25, 50, 100mg cap	Helps depression (mood, appetite, sleep or energy) & apathy which often occurs early in dementia **SSRI'S** (not too useful for specific phobias)	**SSRIs SE in General (GI & CNS)** **nausea** {21%(F) - 36% (X)}, anxiety, insomnia {~14%}, agitation, anorexia, tremor, somnolence {11-26%}, sweating, dry mouth, headache, dizziness, falls, diarrhea {12% (F,P)-17% (S)}, constipation {13-18%}, sexual dysfx.[88,89], **D/C Syndrome** **Serotonergic syndrome** with MAOI's -↓BP, tremor, agitation, hypomania	CC & S -**few drug interactions** F–most **anorexic** & stimulating;long half-life [5week washout] X-most **nausea**,constipating & sedating SSRI, ↑ DI's P -most anticholinergic of SSRI's •↑weight & D/C reaction possible [90] S -most diarrhea & male sexual dysfx of SSRIs **Trazadone** 25-50mg hs (helps sleep, sun downing & depression) **-flat dose response curve for depression**; however titration to ↑ doses sometimes required for anxiety. **Start low, slow but go**. Elderly may need **>8week trial**.	**CC** 10-20mg am 60mg/d **F** 10-20mg od 80mg/d **X** 25-50mg hs 300mg/d **P** 10-20mg am 60mg/d **S** 25-50mg am 200mg/d	20mg po od 40mg po od 20mg po od am 40mg po od am 100mg po hs 150mg po hs 20mg po od am 40mg po od am 100mg po od cc 100mg po bid cc	**29** 29 **28** 49 **33** 45 **32** 57 **34** 61
Venlafaxine **EFFEXOR** (**Reg** 37.5,75mg tab-Co **D/C** Jul04) **XR** 37.5, 75, 150mg caps (contents of XR may be sprinkled)	**SNRI** **5HT & NE** (also some dopamine)	**As dose↑: ↑BP**, agitation, tremor, sweating, nausea {~37%},sleep disturbances, headache, "clean TCA", SE similar to SSRIs	**Less weight** gain; **few drug** interactions Caution: **D/C Syndrome** (e.g. agitation, nausea, fatigue, dizziness, headache, etc.)	18.75-37.5mg bid 375mg/d	75-150mg **XR** po od 225mg **XR** po od (if 2-3 cap)	**65** 126-181
Desipramine =**D** **NORPRAMIN** 10, 25, 50, 75, 100mg tab **Nortriptyline** =**N** **AVENTYL** 10, 25mg cap [91]	**TCA's**	**CNS**: agitation initially, confusion, drowsiness, headache, tremors, seizures, **anticholinergic**: dry mouth, blurred vision, constipation etc.; nausea, sweating, rash, **cardiovascular**: ↑ heart rate, arrhythmias, ↓ BP; anorgasmia	May ↑ effect of anticholinergic & CNS meds. ~2-3 months for max effect. Trough plasma levels avail. Fatal (≥2gm) **overdose** → to heart & CNS •desipramine (the least anticholinergic, helps **apathy**) & notriptyline are generally **better tolerated** than other TCA's	10-25mg 150-300mg	D 50mg po hs D 75mg po hs N 25mg po hs N 50mg po hs	20 **30** 15 **21**
Buspirone **BUSPAR** 5,10ς mg tab	**Azapirone** 5 HT_{1a} agonist	Nausea, headache, dizzy; Onset 1wk; Max effect 6 wks	√ Anxiety in Bz naive pt & for alcohol withdrawal; Non-addicting, DI's	5mg; 60-90mg	5-10mg po tid-qid	⊗ 50-69
Clonazepam **RIVOTRIL** 0.25✗▼,0.5ς, 1, 2ς mg tab -long acting benzodiazepine	May help severe anxiety (use **cautiously**) **Benzodiazepines**	**Drowsiness** (tolerance develops), **dizziness**, ↓ concentration, anterograde amnesia, ↑ traffic **accidents**, physical **dependence** & paradoxical anger/hostility (disinhibition). Taper off slowly to ↓ rebound anxiety.	√ Anticonvulsant, Panic attack; Other uses: s**edative,** social phobia & akathisia, acute mania & neuralgic pain	0.25mg 10-20mg	0.5mg po tid 1mg po bid	**15** 21
Lorazepam **ATIVAN** 0.5, 1ς, 2ς mg tab; (0.5,1,2mg sl▼tab;4mg/ml **amp**⊗)✗ -short acting benzodiazepine			√ Anxiety, Preanesthetic, Status epilepticus; ↓ **DI's;** Other uses: **sedative**, muscle relaxant, alcohol withdrawal	0.5mg 10mg	0.5mg po tid 1mg po tid	11 **12**

=↓ dose for renal dysfunction ς=scored tab ✗=Non-formulary Sask ☎=Excptional Drug Status Sask. ⊗=not covered by NIHB ▼=covered by NIHB **ADAS-cog**=cognitive section of the 70 point Alzheimer's Disease Assessment Scale **Bz=**benzodiazepine **BP=**blood pressure **cc=**with meal **DI=**drug interaction **Dx**=diagnosis **FAQ**=Functional Activities Questionnaire **HR=**heart rate **MMSE**=Mini-mental state examination (Scale 0-30) **NNH**=number needed to harm **NNT**=number needed to treat **Pt**=patient **Sz**=seizure **SE**=side effect **T½**=half life **Tx**=treatment **wt**=weight

Other Meds: See **RxFiles** Charts: Mood Stabilizers (Carbamazepine, Divalproex, Lithium,…); Antidepressants (Bupropion, Mirtazapine,…).
Options: NOT estrogen[92,93],?ginkgo[94,95,96], ?NSAIDs[97,98,99], ?statins[100,101], ?Vit E[102] & ?B_{12}[103]

Memantine **NAMENDA/EBIXA** ✗⊗ 10mg scored tab: NMDA antagonist that is available for mod-severe Alzheimer's; 5mg od (↑ q1-2week) →10mg bid $160 [104,105,106,107,108,109,110]
SE: dizziness, drowsiness, confusion, insomnia, headache, inner & motor restlessness, akathisia, nausea,?Cornea changes & over excitation. DI's: amantadine, DM & ketamine since also NMDA antagonists; sodium bicarbonate & acetazolamide.

Prevention of Dementia: ↓ cardiovascular risk factors if present by (↓BP[111], ↓cholesterol, stop smoking, ↑ exercise & use ASA in high risk pts)

Epidemiologic: 1.5% of age 65 affected; doubles q4yr; 30% by age 80; average survival 8yr from Dx [6]

Dementia: Types: Alzheimer's (short term memory, word finding & way finding), vascular, mixture of these, Lewy body (fluctuations in cognition, hallucinations & spontaneous motor features of Parkinsonism), Frontotemporal (disinhibition, behavioral issues, social tactlessness & language changes) & Normal pressure hydrocephalos (rapid progressing, early gait abnormalities & incontinence). Progessive deterioration which requires interventions to ↓ disease progression, ↓ symptoms (cognitive, behavioral & psychological) & ↓ caregiver burden.

Non Drug: involve family & other caregivers in environmental & behavioral therapy, plan advance health care directive & discourage driving.

Management of Behavioral & Psychological Symptoms of DEMENTIA (BPSD) [112]

-very common (up to 90% during course of dementia) & cause significant distress to patients, families & caregivers
-not just agitation but non-agitated Sx (apathy, withdrawal, daytime somnolence {circadian rhythm disturbances}, depression etc.)

Diagnosis:

◆History, physical exam & nurse observations; collateral evidence from family also essential! ◆Lab Tests-Recommended: CBC, electrolytes, calcium, serum glucose & TSH; Optional: BUN & SCr, magnesium, B12, LFTs, arterial blood gases, ECG, CT if suggestion of structural lesion present ◆Eliminate any source of delirium – e.g. **medication intoxication/withdrawal reactions/ drug interactions**, dehydration & infections (if indicated: urinalysis/C&S, chest x-ray, lumbar puncture if suspicion of meningitis)

Treatment:

◆Appropriate **environmental & behavioral** measures should be explored! Reserve **drug therapy for situations** where non-pharmacological interventions have been fully explored & implemented or in cases of severe dangerous Sx. Specify the problem behavior (eg. "agitation" is less useful than "screaming", "hitting when bathed"). Identify what brings it on & what makes it go away. Identify whom the behavior is bothering (patient, caregiver/staff or other patients).

◆If drug treatment (ie. Sx have no physical cause, are unrelated to other medications or unresponsive to non-pharmacological interventions), start with **1/3 to 1/2 of usual adult** dose & titrate up slowly individualizing dosages for each patient

Start Low, Go Slow!

◆If receiving treatment, **reevaluate** drug regimen & non-pharmacologic strategies at regular intervals (ie. **3**-6 months)

◆Consider cholinesterase inhibitors in Alzheimer's (**donepezil**, **galantamine**, **rivastigmine**) ☎ ⊗; SE: n/v, fatigue, anorexia, ↓ heart rate

DEPRESSION:

(anxiety often coexists thus use antidepressants with anxiolytic properties)

- ↓ mood, apathy & amotivation

Mild→ non pharmacologic

Moderate to *severe*→ **ANTIDEPRESSANT Tx**

SSRI/venlafaxine →1st line

In general →good for depression, depression assoc. agitation, emotionality & irritability
Allow >6 week for adequate trial at an adequate dose

⇩

SSRIs: **SE**: nausea, vomiting, restlessness, falls, insomnia, weight loss & hyponatremia
Citalopram 10-30mg/d, **fluvoxamine** 25-150mg/d, **paroxetine** 10-30mg/d, **sertraline** 25-100mg/d
Venlafaxine: 37.5-225mg XR od or **bupropion** ☎ ✆100-150mg bid to activate patients with withdrawal or psychomotor retardation

TCA's: Avoid anticholinergics →less with **nortriptyline** 10-75mg hs & desipramine 25-150mg/d;
SE: hypotension, blurred vision, urinary hesitancy, cardiac conduction changes

Mirtazapine: ⊗ consider if anorexia/anxiety is a problem; 15-45mg/day
Moclobemide: role in anxiety & mood dx but may ↑ stimulation; 100mg od-300mg bid
Trazodone: low doses used for sedation & some anxiolytic effect;
monitor for hypotension, serotonin syndrome & rare priapism in ♂

Start Low, Go Slow, But go!

Consider **ECT** in management of treatment resistant or severe depression

PSYCHOSIS/AGITATION:

Positive Sx -delusions & hallucinations or paranoia
Negative Sx -poverty of thought, apathy & social withdrawal
Agitation -pacing, chanting, psychomotor agitation etc.

ANTIPSYCHOTIC Tx

Start Low, Go Slow!

-first designate target Sx
-try to minimize **sedation**,↑confusion,hypotension & **EPS**
-target Sx (hallucinations, delusions, hostility, aggression, agitation,violent behavior & sleep-wake cycle disturbances)

haloperidol 0.25-2mg/day
risperidone 0.25-2mg/day
quetiapine 12.5-150mg/day
olanzapine ☎ ▼1.25-10mg/day

} monitor for SE & may attempt med tapering q6month

◆Newer agents at least as effective but generally better tolerated. Still monitor for **SE**: sedation, hypotension, falls, anticholinergic side effects (dry mouth constipation & delirium), EPS (drooling, rigidity & akinesia), ↑ weight & tardive dyskinesia
◆Patients with **Lewy bodies** (15% of dementias) demonstrate ↑ sensitivity to neuroleptic medications

ANXIETY:

-use non-pharmacological intervention
-minimize provocation

-consider **antidepressant** therapy if anxiety is secondary to depression or very chronic in nature

-consider
ANTIANXIETY Medication

lorazepam 0.5-2mg/day
oxazepam 5-30mg/day
buspirone 10-30mg/day
trazodone 25-100mg/day
alprazolam 0.125-2mg/day
clonazepam 0.125-3mg/day
(caution long-acting)

Benzodiazepines-SE:
sedation, ataxia, altered sleep architecture, motor & cognitive impairment & propensity to cause withdrawal Sx when D/C. Paradoxical excitation & falls may occur. An intermediate acting such as temazepam/oxazepam/lorazepam can be best used for short term, if possible sleep/anxiety states or before planned anxiety provoking situations

Buspirone: ✆
low sedation, ↓DI's, ↓ withdrawal & ↓ impairment of motor fx; option→ chronic anxiety but onset ~3wk delay

MOOD STABILIZERS: some use in agitation, aggression, hostility, sleep-wake disturbance cycle & mania
◆**divalproex** 125-750mg/day -fewer **SE**: sedation, diarrhea, tremor, nausea, weight gain, hair loss & ↑ liver tests & fewer DI's, but less evidence for use.
◆**carbamazepine** 100-600mg/day -more **SE**: sedation, ataxia, falls, skin rash, headache, leukopenia & ↑ liver tests & multiple DI's
BETA BLOCKER-propranolol 10-80mg/d; possible ↓ aggression; SE:↓ heart rate & hypotension CI: asthma, PVD & possibly depression Hx
CHOLINESTERASE INHIBITORS -modest cognitive, functional & behavioral benefits; may help apathy, hallucinations & delusions
(memantine ✘ ⊗ is a recently approved NMDA receptor antagonist which may have a role similar to cholinesterase inhibitors)

CI contraindication **DI** drug interaction **Dx** disorder **fx** function **HR** heart rate **Hx** history **n/v** nausea/vomiting **PVD** peripheral vascular disease **SE** side effect
Sx symptom **Tx** treatment ☎ Exception Drug Status Sask. ✘ non-formulary in Sask. ⊗not covered by NIHB ▼covered by NIHB ✆prior approval NIHB

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