Generic -TRADE	Equivalent Dose /Class	Peak Levels/ Onset of action	Average t½* /Active Metabolite	COMMENTS	INITIAL & (MAX DOSE)	USUAL SEDATIVE DOSE	$ /MONTH
Zaleplon -STARNOC (5,10mg cap) ✗ ✆ ❋	5mg pyrazolopyrimidine Gaba $A_{1\ \alpha1}$	0.9-1.5hr Rapid(15-30min)	1 hr None	**Duration of action of ~4 hrs**; little tolerance **SE**: headache, somnolence, dizziness **Least hangover** effect;**DI**:cimetidine & rifampin	C 5mg (20mg)	5mg po hs 10mg po hs	25 34
Zopiclone -IMOVANE / RHOVANE (5, 7.5ς mg tab) ✗ ✆ ❋	5mg cyclopyrrolone Gaba A_1	1-1.5hr Rapid (30min)	5 hr Yes	√**Sedative**/hypnotic-**Good Choice**,↓ tolerance **SE**:dry mouth, **bitter taste**, residual sedation **DI's**: erythromycin, ketoconazole, rifampin	Pregnancy category ↕ U **3.75mg** (15mg)	5mg po hs 7.5mg po hs (Rhovane less money)	15 16
Clonazepam -RIVOTRIL (0.25✗▼; 0.5ς,1,2ς mg tab)	0.25mg Nitro **BENZODIAZEPINE**	1-4hr Intermed. (20-60min)	34 (19-60) hr None	**CAUTION:** ↑ **falls** & vehicle **accidents** in elderly, **dependence**, may ↓ **cognition** (esp. long-term use) √**Sedatives/hypnotic-Good BZ choices:** **temazepam;** possibly oxazepam, lorazepam **Clonazepam** good sedative if daytime anxiety; √Anticonvulsant, Panic; (Also used: Social phobia, BPAD Manic phase or for akathisia) **Flurazepam** (**not recommended,** **Accumulation/hangover**→confusion) **Triazolam** (**not recommended,** **Behavioral** changes/anterograde amnesia, **DI's** & **withdrawal** effects) **Less DI'S:** temazepam, oxazepam & lorazepam	D 0.25mg (10mg)	0.5mg po hs 1mg po hs	10 15
Flurazepam -DALMANE (15,30mg cap)	15mg 2-Keto	0.5-1hr Intermed.(30-60min)	100 (40-250) hr Yes- Desalkyl		X 15mg (60mg)	15mg po hs 30mg po hs	10 11
Lorazepam -ATIVAN (0.5,1ς,2ς mg tab); (0.5,1,2mg sl▼tab;4mg/ml amp⊗) ˣ	1mg 3- Hydroxy	PO 1-4hr, SL/IM 1hr, IV 5 min Intermed.(30-60min)	15 (8-24) hr None		D 0.5mg (10mg)	0.5mg po hs 1mg po hs	8 9
Oxazepam -SERAX (10ς,15ς,30ς mg tab)	15 3-Hydroxy	1-4 hr Intermediate→**slow**	8 (3-25) hr None		D 10mg (120mg)	15mg po hs 30mg po hs	10 11
Temazepam -RESTORIL (15,30mg cap)	10mg 3- Hydroxy	2-3 hr Intermediate→slow	11 (3-25) hr None		X 15mg (60mg)	15mg po hs 30mg po hs	12 13
Triazolam -HALCION (0.125ς,0.25ς mg tab)	0.25mg Triazolo	1-2hr Rapid (15-30min)	2 (1.5-5) hr None		X 0.125mg (0.5mg)	0.125mg po hs 0.25mg po hs	9 10
Chloral hydrate - NOCTEC (500mg/5ml syrup) ⊗	500mg	30-60min Rapid (30min)	4 - 8 hr Yes	√Sedative; (**not recommended**: Fatal 4-5gm; DI's; **SE**: gastric irritation, arrhythmias, rash)	C 500mg (2gm)	500mg po hs 1gm po hs	15 23
Diphenhydramine OTC✗▼ -Benadryl, Nytol, Simply Sleep, Sleep aid, Sleepeze D, Sominex, Unisom (12.5mg chew®; 25,50mg cap/tab, 1.25mg/ml liquid, 2.5mg/ml elix, 50mg/ml inj)	50mg **Antihistamine**	1-4 hrs Slow(60-180min)	4 - 8hr None	√ Allergic reactions, sleep aid -but residual sedation **SE**: **anticholinergic** (dry mouth, urinary retention etc.), cognitive impairment	B 25mg (200-300mg)	25mg po hs 50mg po hs	11 11
Doxylamine OTC -UNISOM-2 (25 mg tab) ✗ ⊗	25mg **Antihistamine**	2-4hr Slow(60-120min)	10 hr Yes-? Active	√ Sedative/hypnotic -but residual daytime sedation **SE**: **anticholinergic**,cognitive impairment	A 25mg (75-150mg)	25mg po hs 50mg po hs	10 20
Methotrimeprazine (NOZINAN) (2,5,25,50 mg tab, 5mg/ml& 40mg/ml soln); (25mg/ml amp✗⊗)	**Phenothiazine Neuroleptic**	1-3hr Slow	15-30 hr None	√Antipsychotic,sedative(**non addictive**),analgesia **SE**: hypotension, **extrapyramidal reactions**, anticholinergic,cognitive impairment	C 5mg (1000mg)	5-10mg po hs 25-50mg po hs	10 13
Trazodone -DESYREL (50ς,100ς mg tab); (75mg, Dividose 150mg) ✗▼ ❋	50mg **Antidepressant**	0.5-2 hr Intermediate	4 - 7.5hr Yes	√ Antidepressant, **Agitated dementia**, √Sedative-**antidepressant induced** insomnia **SE**: orthostatic hypotension, priapism	C 25mg (600mg)	50mg po hs 100mg po hs	14 18
Amitriptyline ELAVIL (10,25,50); (75mg✗▼)	**Antidepressant** Or less SE's - **Nortriptyline** 10-25mg po hs ≤$15	<4 hr Slow	15hr Yes- nortriptyline -26hr	√ Antidepressant, Sedative-but performance impairment **SE:** hypotension, anticholinergic,cognitive impairment	C 10mg (300mg) ~2hr pre hs	10-25mg po hs 50mg po hs	**9**-11 15
L-Tryptophan -TRYPTAN (250,500,750mg,1gm tab, 500mg cap)✗⊗ ❋	Watch for serotonin syndrome esp. if used with SSRI or MAOI's. Eosinophilia-myalgia syndrome before due to impurities.			√Adjunct in BPAD/may potentiate lithium √ Sedative- no tolerance reported **SE**: GI upset, dry mouth, dizzy, headache	U 500mg (5gm)	500mg po hs 1g po hs	23 46
Melatonin (By Special Access) (1,3mg cap, 2mg CR cap)✗⊗ ❋?	mfg synthetic metabolite of 5HT	0.5-2hr Slow(60-120min)	1 hr None	**Limited studies**-?dose/sedative/jet lag **SE**: h/a,↑ heart rate, pruritis, nightmares	U 1mg (10mg) give 2hr before hs	1mg po hs 2mg CR po hs	3 5
Valerian Root OTC-VALERIAN, NYTOL & UNISOM NATURAL SOURCE (400 mg tab)✗⊗ ❋?	? valepotriates ? valerenic acid ? pyridine alkaloids	Not known (mild effect)	Not known	**Limited studies**-? dose/sleep aid; **Purity** concerns **SE**: nausea,headache,morning hangover	U 400mg (800mg)	400mg po hs 800mg po hs	6 10

Guidelines:Use lowest dose,use agents with short/intermediate half lives to avoid daytime sedation,use intermittent dosing (2-4 x/wk),use for no more than 3-4 weeks,D/C gradually,& be aware of rebound insomnia.
Consider/Rule Out: Depressive symptom, Mania/hypomania, primary sleep disorder (eg sleep apnea) altered sleep cycle & other drug use (Decrease total daily dose/change timing of other meds/agents as in Table 1).
Misc products: ***Herbal Sleep Aid***: valerian,hops flower,passion flower; ***Naturarest:*** valerian, St. Johns wort, catnip herb; ***Nighty Night Herbal tea***: passion flower, chamomile, catnip, hops. ❋ little effect on sleep structure
√ official indication (TPP/FDA) or use **BZ**=benzodiazepines **DI**=drug interaction **SE**=side effect * **t ½ average(range)** half-life:↑ in geriatric pts & altered by drug interactions ✗ =non-formulary Sask.=↓ dose for renal dysfx ς =scored ⊗=not covered NIHB ▼=covered NIHB

SEDATIVES: A CONCISE OVERVIEW

GOALS OF THERAPY FOR INSOMNIA:

- to improve sleep (ie. decrease time it takes to fall asleep, decrease the frequency of nighttime awakenings & increase the duration of sleep) without dependence on drug therapy
- to improve daytime functioning
- to avoid daytime drowsiness & psychomotor impairment

GENERAL APPROACH TO INSOMNIA:

Non-pharmacologic

- Resolve any **underlying medical, psychiatric or environmental** causes first
- Consider / rule out **drug causes** (See Table 1); note common social drug causes such as (caffeine, alcohol & nicotine)
- Changing sleep habits, relaxation techniques and cognitive therapy are preferred & often more effective than drugs
- Consider restricting/avoiding daytime naps
- Provide counseling, encouragement, and reinforcement

Pharmacologic

- Sedatives should be used in combination with non-drug measures to promote sleep (see Table 2 - Sleep Hygiene)
- Ideally, sedatives should be taken only for short periods depending on the medication (2-4 weeks)
- Prescription sedatives are all equally effective and all, to varying degrees, may cause daytime drowsiness & confusion
- Low doses of short-acting sedatives have a lower risk for side effects when taken on a short-term basis
- Sedatives can be "habit forming." Expect **2-3 nights** of **poor sleep** when stopped. One suggestion is to decrease sleep time by 20mins 2 nights before stopping the medication. Consider stopping at a low stress time such as on a weekend.
- Use the lowest dose possible & only when required; intermittent use (e.g. up to 4 nights/week) sometimes recommended to minimize tolerance & dependence
- Generally, begin with mild agents, and gradually move to more potent medications as necessary
- **Restless Leg Syndrome** Early NEJM 03 –assess/replace iron stores; dopaminergics (levodopa, pergolide, pramipexole, ropinirole); clonazepam. If painful, may consider gabapentin or opiates.

Table 1: Drug Causes of Insomnia

alcohol	interferon	propranolol
amantadine	ipratropium	pseudoephedrine
atenolol	lamotrigine	quinidine
bupropion	leuprolide	salbutamol
caffeine e.g. coffee, tea, soft drinks	levodopa	salmeterol
clonidine	medroxyprogesterone	selegiline
corticosteroids	methyldopa	SSRI's* (eg. fluoxetine, paroxetine, sertraline)
daunorubicin	methylphenidate	terbutaline
decongestants	nicotine	theophylline
dextroamphetamine	oral contraceptives	thyroid hormones
diuretics	pemoline	venlafaxine
donepezil	phenylephrine	
fluoxetine	phenytoin	
flutamide	pindolol	
	progesterone	

* consider dosing in AM

Table 2: Good Sleep Hygiene Measures

- Maintain a regular schedule for bedtime and awakening
- Go to bed only when sleepy
- Avoid daytime naps or going to bed too early in evening.
- Reserve the bedroom for sleep & sexual activity (no TV)
- Avoid caffeine & nicotine especially within 4-6hrs of bedtime
- Do not drink alcohol (especially within 4hrs of bedtime), since it causes fragmented sleep
- Avoid heavy meals before going to bed, but a light carbohydrate snack before bedtime is acceptable
- Do not eat chocolate or large amounts of sugar before bedtime
- Avoid drinking excessive amounts of fluid in the evening
- Take "water pills" in the morning or early afternoon
- Minimize noise, light & extreme temperature in the bedroom
- Exercise regularly during the day, but avoid vigorous exercise within 3 hrs of retiring
- Develop relaxing bedtime rituals (e.g. reading, listening to music)
- Get the clock out of visible range to avoid watching!
- Get out of bed & go to another room if unable to sleep within 20 minutes. Return when sleepy.

Table 3: Sedatives – General Classification & Comments

Classification	Examples		Comments (see also detailed comparison chart)
Non-BZ but BZ-Like MOA (mechanism of action)	Zaleplon Zopiclone	Starnoc Imovane	• little effect on sleep structure • **less problem with tolerance** than BZ; still have problem with dependence • zaleplon lasts ≤4hr & has **least hangover effect**; however limited studies
Benzodiazepines (BZ)	Temazepam Oxazepam Lorazepam	Restoril Serax Ativan	• significant adverse effects on sleep structure (e.g. ↓ REM & Delta sleep) • option for transient, short-term insomnia; clonazepam if long-term/anxiety • problems: **tolerance**, **dependence**, withdrawal, poor cognition/coordination, increased risk of accidents & falls; "hangover effect" = residual sedation
Antidepressants - Non-TCA	Trazodone	Desyrel	• trazodone preserves **normal sleep structure**; REM/ Delta effect neutral • useful at **low-doses** (≤50-100mg) for longer-term sedation in agitated dementia & antidepressant induced insomnia
Antidepressants - TCAs	Amitriptyline(3°) trimipramine (3°) nortriptyline (2°)	Elavil Surmontil Aventyl	• some effect on sleep structure which may be corrective in some patients • low-doses of 3° TCAs (e.g. amitriptyline/trimipramine 10-50mg) useful for sleep disorders especially in patients with **chronic pain,** depression, etc. • 2° TCAs such as **nortriptyline** are an alternative for patients intolerant of amitriptyline, especially if concomitant pain & in elderly
Antipsychotics Highly sedating SE profile	methotrimeprazine	Nozinan	• potent/useful in **severe cases of insomnia**; non-addictive • atypical antispychotics also options; e.g. **low-dose quetiapine** (Seroquel)
Miscellaneous	see chart		• most other sedatives have limited evidence / usefulness; see chart

Prepared by Brent Jensen & Loren Regier in consultation with RxFiles advisors & reviewers.
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