Ontario Renal Network

Insomnia

Adapted with permission from the BC Renal Agency's Pharmacy & Formulary Symptom Management Resources – Insomnia, developed by the agency's Pharmacy & Formulary Committee, and the Kidney Supportive Care Research Group (KSCRG), University of Alberta / Northern Alberta Renal Program. To review original source materials, see www.bcrenalagency.ca and www.ualberta.ca/~kscrg.

Ontario

Insomnia Treatment Algorithm for Hemodialysis Patients

Assessment

Sleep symptoms (e.g., latency, total sleep time, early and/or frequent waking, daytime impact), Duration of symptoms, Dialysis impact on insomnia (e.g., napping on dialysis, dialysis interrupting sleep pattern), Detailed medication history (including OTC sleep aids and herbal remedies), Circadian rhythm (e.g., inconsistent sleep schedule, excessive blue spectrum light before bed), Social behaviours – stimulation (e.g., technology, television, worrying/active mind in bed), caffeine, alcohol, nicotine, other recreational drug use†, change in mood/psychological state

Consider Etiology

- Dialysis schedule interrupting usual sleep times
- Medication related – contact pharmacist if uncertain if drug(s) cause insomnia
  - Recreational drugs (alcohol, amphetamines and methamphetamines, caffeine, nicotine, drug withdrawal)
  - Cardiovascular agents (beta blockers, diuretics [if late in the day])
  - Endocrine agents (corticosteroids, thyroid hormone)
  - Stimulants (dextroamphetamine, methylphenidate)
  - Neurologic and psychotropic agent (bupropion, lamotrigine, levodopa, phenytoin, SNRI [e.g., venlafaxine], SSRI [e.g., fluoxetine])
  - Miscellaneous agents (donepezil, interferon, stimulant laxatives, oral contraceptives, pseudoephedrine, salbutamol/salmeterol, theophylline)
- Sleep apnea
- Restless leg syndrome, periodic limb movement disorder
- Pruritus
- Pain
- Depression, anxiety, worry
- Psychosocial problems
- Nocturia (if applicable)
- Heart failure
- COPD
- GERD
- Thyroid abnormality

Non-Pharmacologic Measures

- Treat/eliminate underlying cause(s) (e.g., limit use of alcohol, nicotine and technology [screens such as iPad, iPhones, etc.] before bed)
- Cognitive behavioural therapy
- Relaxation techniques
- Implement good sleep hygiene measures to develop a sleep routine (reassess in 2-4 weeks)
  - Try to wake up at the same time every morning
  - Only go to bed when you feel sleepy
  - Do not "try" to fall asleep
  - Try to avoid napping during the day
  - Avoid caffeine in the evening
  - Consider regular exercise and activity programs
  - Try to save your bedroom for sleep (and sex) only

Refer to the Ontario Renal Network Fatigue Patient Self-Management Guide for more information.

INADEQUATE RELIEF

Pharmacologic Options

- Minimize use after 3-4 weeks
- Avoid OTC sleep aids (e.g., diphenhydramine), short-acting benzodiazepine (e.g., triazolam), long-acting benzodiazepine (e.g., flurazepam or diazepam), chloral hydrate, tricyclic antidepressant or antipsychotic
- Usual sedative dose (give HS PRN), start low dose and titrate up when reassessing every 2 weeks
  - Benzodiazepines **(use with caution)**: Temazepam***** 15-30 mg; Lorazepam***** 0.5-2 mg; Oxazepam***** 10-30 mg
  - Zolpidem **(use with caution)** 5 mg SL (10 mg dose not recommended in elderly)
  - Zopiclone 3.75-7.5 mg
  - Melatonin 3 mg (note: there is limited evidence for efficacy and NO standardization or regulation on health products in Canada)
- Monitor for adverse side effects, especially with daytime sedation and driving (see drug monographs for more information)

† **contact pharmacist if uncertain if drug(s) cause insomnia**

* **covered by ODB**

Hypnotics

Non-benzodiazepines

Zolpidem (Sublinox®) Oral Disintegrating Tablet			
Mechanism of Action	Selective binding at 1 or more receptor subtype of GABA receptor		
Pharmacokinetics	• Onset: 30 minutes • Peak level: 80 minutes • Half-life: ~2.5 hours • Duration: 6–8 hours • Food delays absorption • Hepatic metabolism mainly via CYP3A4 (~60%)		
Adverse Effects	Drowsiness, dizziness, diarrhea; complex sleep-related behaviour (e.g., sleep driving); headache		
Dosing Guidelines (Normal Renal Function)	• Women = 5mg SL QHS PRN • Men = 5-10mg SL QHS PRN • Elderly = 5mg SL QHS PRN • SL tablets should not be split • Should usually not exceed 7–10 consecutive days • Use for more than 2–3 consecutive weeks requires complete re-evaluation of the patient		
Renal Dosing Guidelines GFR (mL/min)	**>50 (mL/min)**	**10 to 50 (mL/min)**	**<10 (mL/min)**
	100%	100%	100%
Supplemental Dose After	**IHD**	**PD**	
	None	None	
Drug Coverage	No – not covered by ODB		
Estimated Cost (30-day supply) without dispensing fee (Prices as of October 2018)	5 mg PO QHS – $47.40		

<table>
<tr><th colspan="4">Zopiclone (Imovane®)</th></tr>
<tr><td>Mechanism of Action</td><td colspan="3">Selective binding at 1 or more receptor subtype of GABA receptor</td></tr>
<tr><td>Pharmacokinetics</td><td colspan="3">• Onset: 30 minutes
• Peak level: 1–1.5 hours
• Half-life: 5 hours
• Extensive hepatic metabolism via CYP3A4 and CYP2C8</td></tr>
<tr><td>Adverse Effects</td><td colspan="3">Dry mouth, bitter taste, possibly lower incidence of tolerance and withdrawal, complex sleep-related behaviour (e.g., sleep driving), palpitations</td></tr>
<tr><td>Dosing Guidelines (Normal Renal Function)</td><td colspan="3">• 3.75–7.5 mg PO HS PRN; titrate weekly to a maximum of 7.5 mg PO HS PRN
• Should usually not exceed 7–10 consecutive days
• Use for more than 2–3 consecutive weeks requires complete re-evaluation of the patient</td></tr>
<tr><td rowspan="2">Renal Dosing Guidelines GFR (mL/min)</td><td>>50 (mL/min)</td><td>10 to 50 (mL/min)</td><td><10 (mL/min)</td></tr>
<tr><td>100%</td><td>100%</td><td>Maximum suggested dose 5 mg once daily</td></tr>
<tr><td rowspan="2">Supplemental Dose After</td><td colspan="2">IHD</td><td>PD</td></tr>
<tr><td colspan="2">None</td><td>None</td></tr>
<tr><td>Drug Coverage</td><td colspan="3">• No – not covered by ODB
• Can request through EAP if have failed 2 other covered agents</td></tr>
<tr><td>Estimated Cost (30-day supply) without dispensing fee
(Prices as of October 2018)</td><td colspan="3">7.5 mg QHS – $21.88</td></tr>
</table>

Lorazepam (Ativan®), Oxazepam (Serax®), Temazepam (Restoril®)			
Mechanism of Action	Binds to benzodiazepine receptors on the postsynaptic GABA; enhanced inhibitory effect of GABA on neuronal excitability by increased neuronal membrane permeability to chloride ions		

Pharmacokinetics	• Lorazepam
	  • Onset: intermediate (30–60 minutes)
	  • Peak level: 1–4 hours
	  • Half-life: ~15 (8–24) hours
	• Oxazepam
	  • Onset: intermediate to slow
	  • Peak level: 1–4 hours
	  • Half-life: ~8 (3–25) hours
	• Temazepam
	  • Onset: intermediate to slow
	  • Peak level: 2–3 hours
	  • Half-life: ~11 (3–25) hours		

Adverse Effects	• Increased risk of falls/fractures, accidents, especially elderly; dependence, decreased cognition with long-term use, dizziness, incoordination; complex sleep-related behaviour (e.g., sleep driving); daytime drowsiness • Rebound effects (anxiety and tension) when stopping medication		
Dosing Guidelines (Normal Renal Function)	• Lorazepam: 0.5–2 mg PO HS PRN • Oxazepam: 10–30 mg PO HS PRN • Temazepam: 15–30 mg PO HS PRN • Start at minimum dose and titrate up as required		
Renal Dosing Guidelines GFR (mL/min)	**>50 (mL/min)**	**10 to 50 (mL/min)**	**<10 (mL/min)**
	100%	100%	100%
Supplemental Dose After	**IHD**	**PD**	
	None	None	
Drug Coverage	Yes – covered by ODB		
Estimated Cost (30-day supply) without dispensing fee (Prices as of October 2018)	• Lorazepam: 1 mg PO QHS – $5.20 • Oxazepam: 15 mg PO QHS – $5.60 • Temazepam: 15 mg PO QHS – $9.80		

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