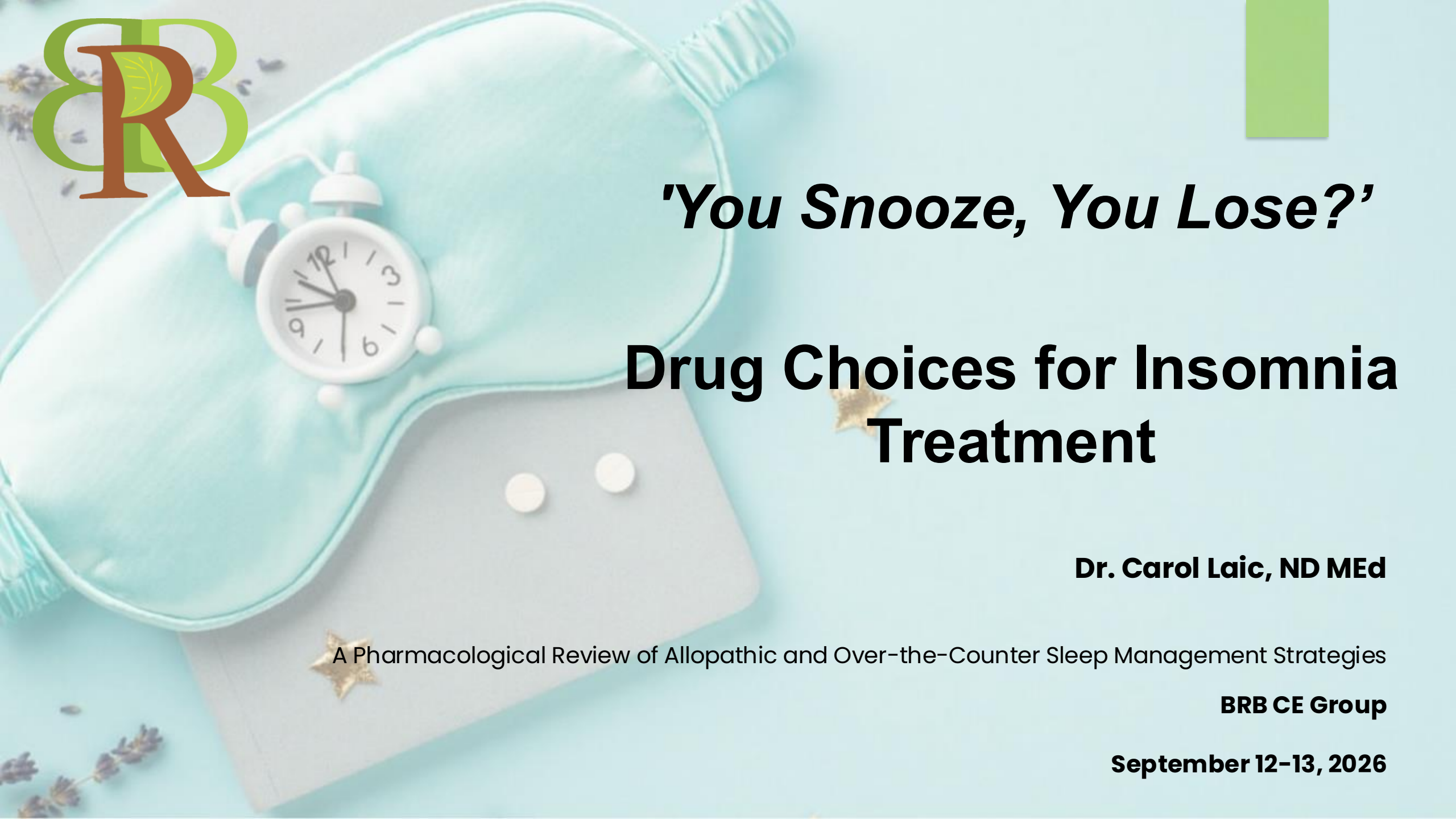


'You Snooze, You Lose?'

Drug Choices for Insomnia Treatment

Dr. Carol Laic, ND MEd

A Pharmacological Review of Allopathic and Over-the-Counter Sleep Management Strategies

BRB CE Group

September 12-13, 2026

Learning Objectives: Enhancing Clinical Competency in Sleep Medicine

1

1. Pharmacological Literacy

Gain confidence in identifying and understanding the primary pharmacological choices used in Canadian primary care for insomnia management.

2

2. Guideline Mastery

Review the most recent updates to Canadian Clinical Guidelines for Insomnia and their implications for long-term health.

3

3. Risk Communication

Improve the ability to communicate clinical pros and cons of pharmaceutical use in both short-term and long-term treatment strategies.

4

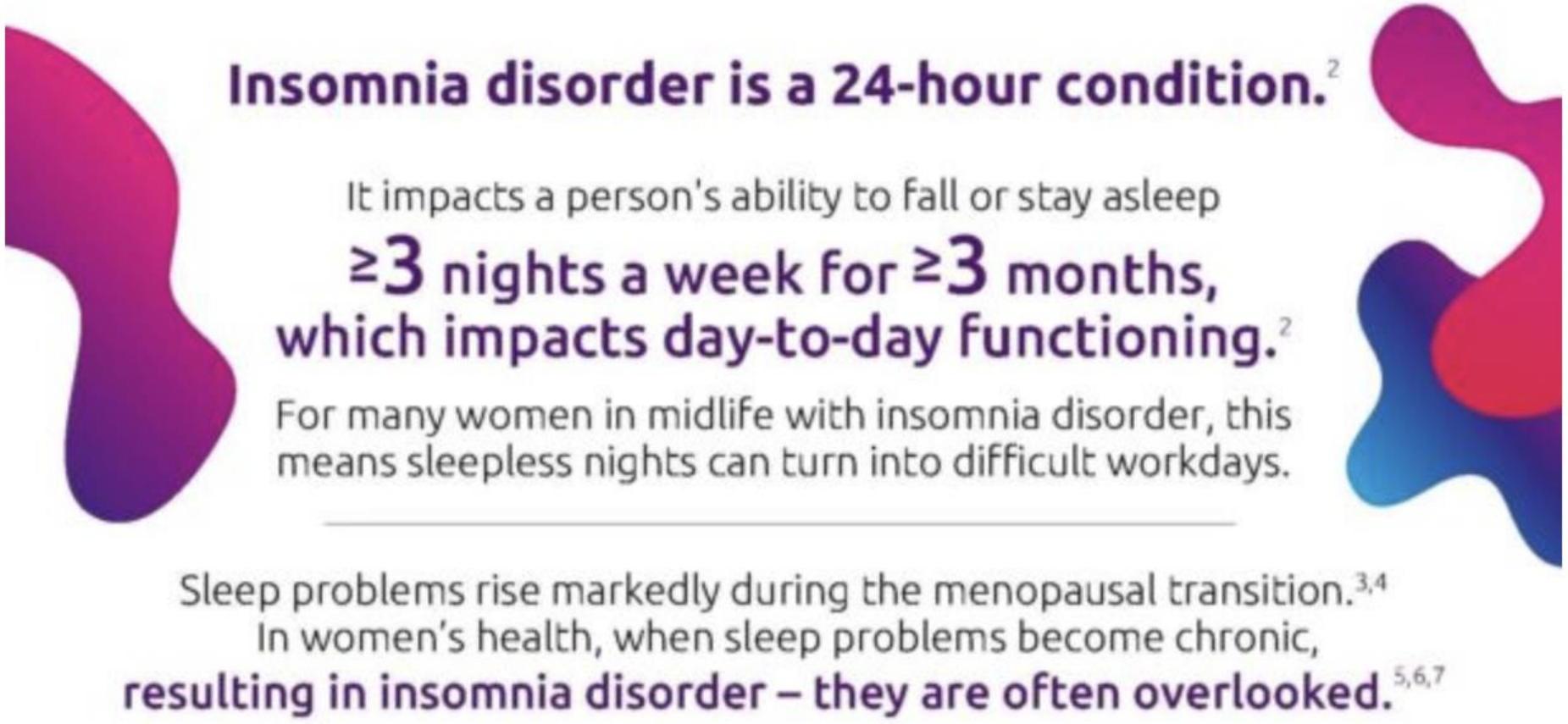
4. Side Effect Identification

Systematically identify symptoms related to drug side effects and toxicity.

5

5. Integrative Safety

Master the identification of potential interactions between allopathic sleep medications and common Naturopathic interventions.



https://worldsleepday.org/usetoolkit/resources/womens-midlife-insomnia

Insomnia in Canada: The Growing Epidemic

Epidemiological Surge

Approximately 25-40% of Canadian adults experience insomnia symptoms, with 10-15% meeting criteria for chronic insomnia disorder.

Economic Impact

Untreated insomnia contributes to reduced workplace productivity, increased absenteeism, and higher motor vehicle accident rates.

Healthcare Burden

Insomnia is frequently comorbid with anxiety, depression, and chronic pain.

Current Access

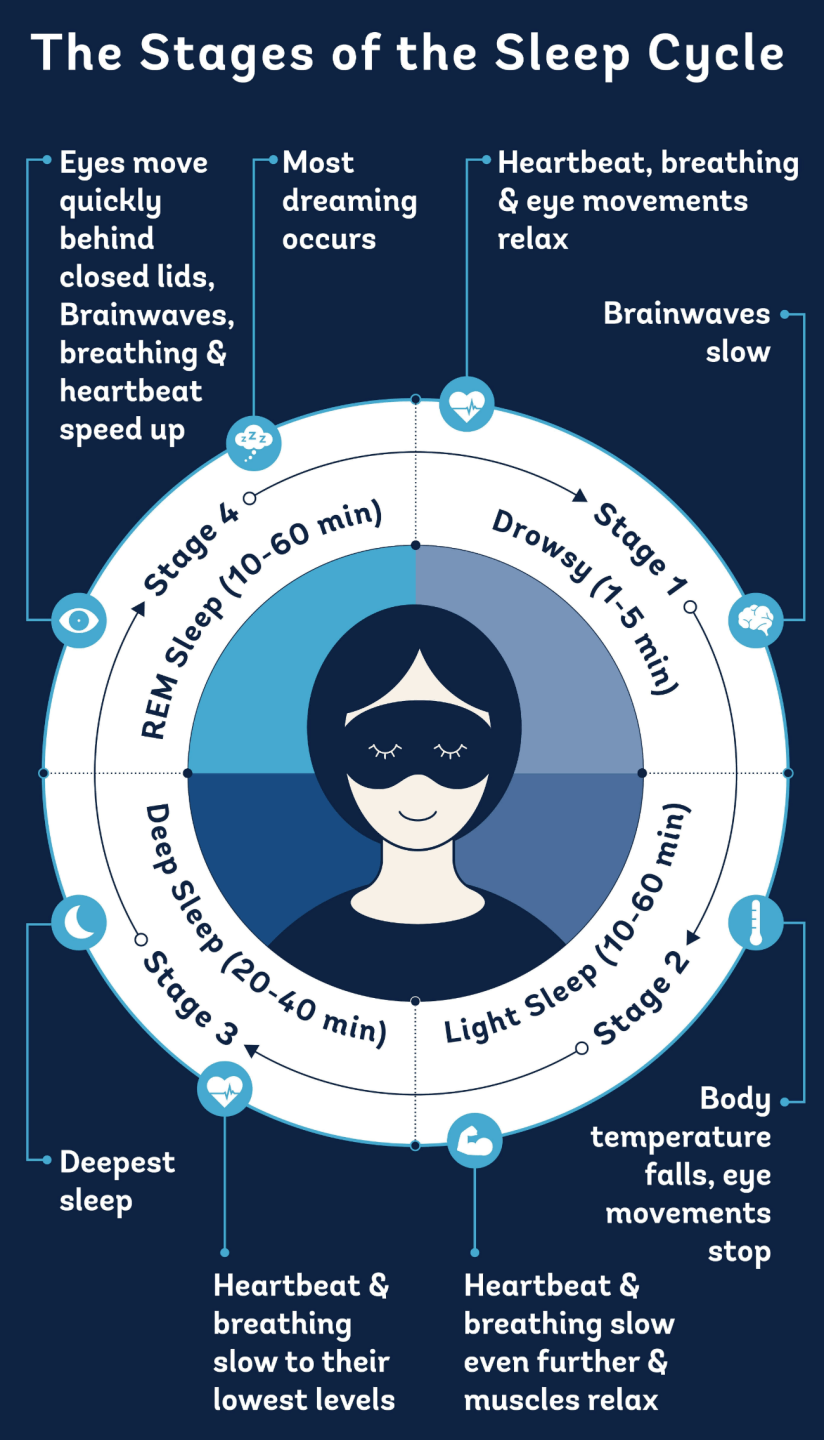
CBT-I remains the gold-standard first-line treatment, but pharmacological interventions remain the most widely utilized secondary strategy.

Sources: CDA-AMC (2025) Insomnia Drugs Protocol; ScienceDirect Prevalence Study (2024)

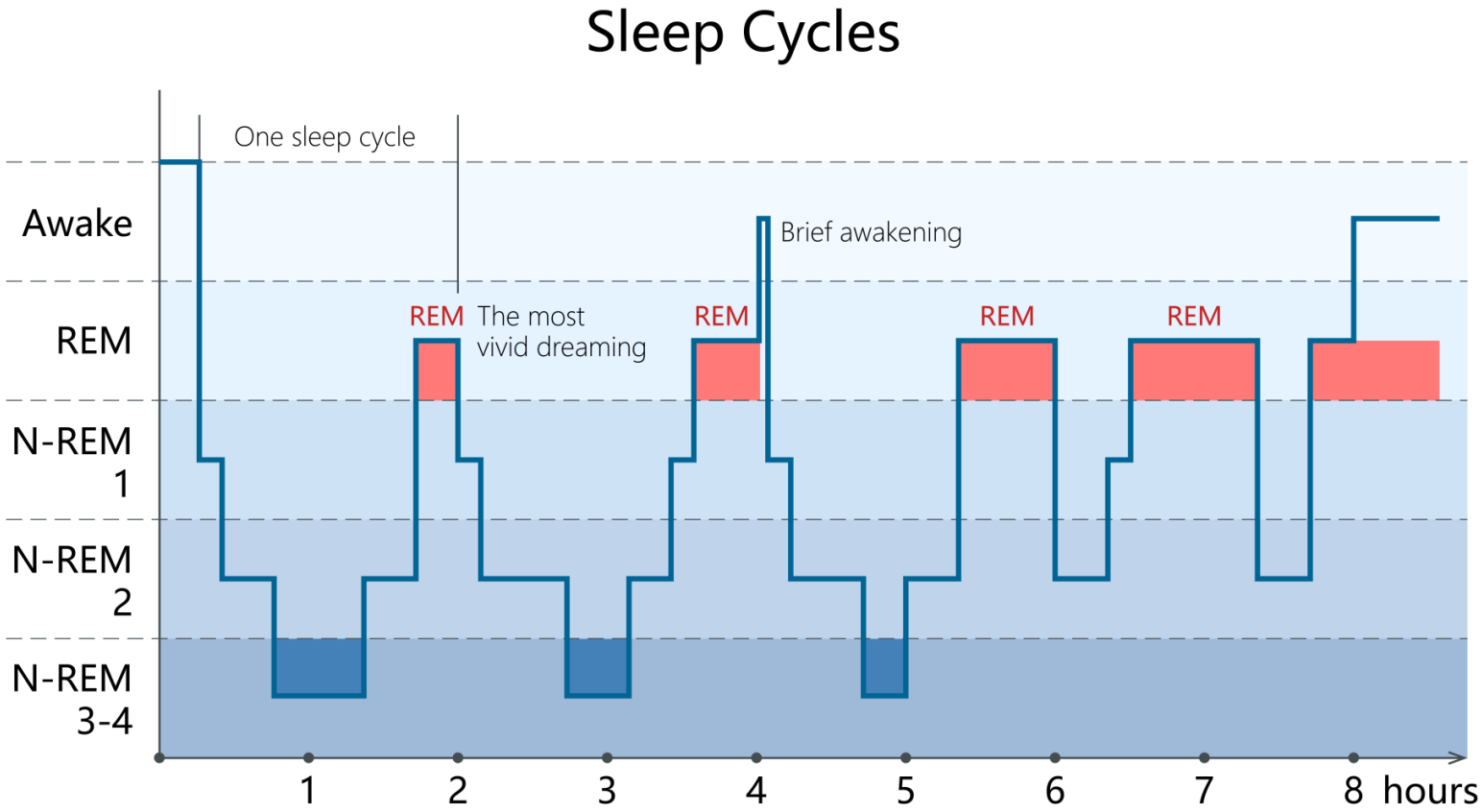
How much sleep do you actually need?

Sleep needs vary by age. These are the ranges recommended by the Canadian Sleep Society and aligned with Health Canada guidance:

INFANT (4–11 MO) **12–15h** Includes naps	TODDLER (1–2 YR) **11–14h** Includes naps	SCHOOL AGE (6–13) **9–11h** Night sleep only	TEEN (14–17) **8–10h** Biology shifts later
YOUNG ADULT (18–25) **7–9h** Brain still developing	ADULT (26–64) **7–9h** Canadian average: 6.9h	OLDER ADULT (65+) **7–8h** Earlier wake common	

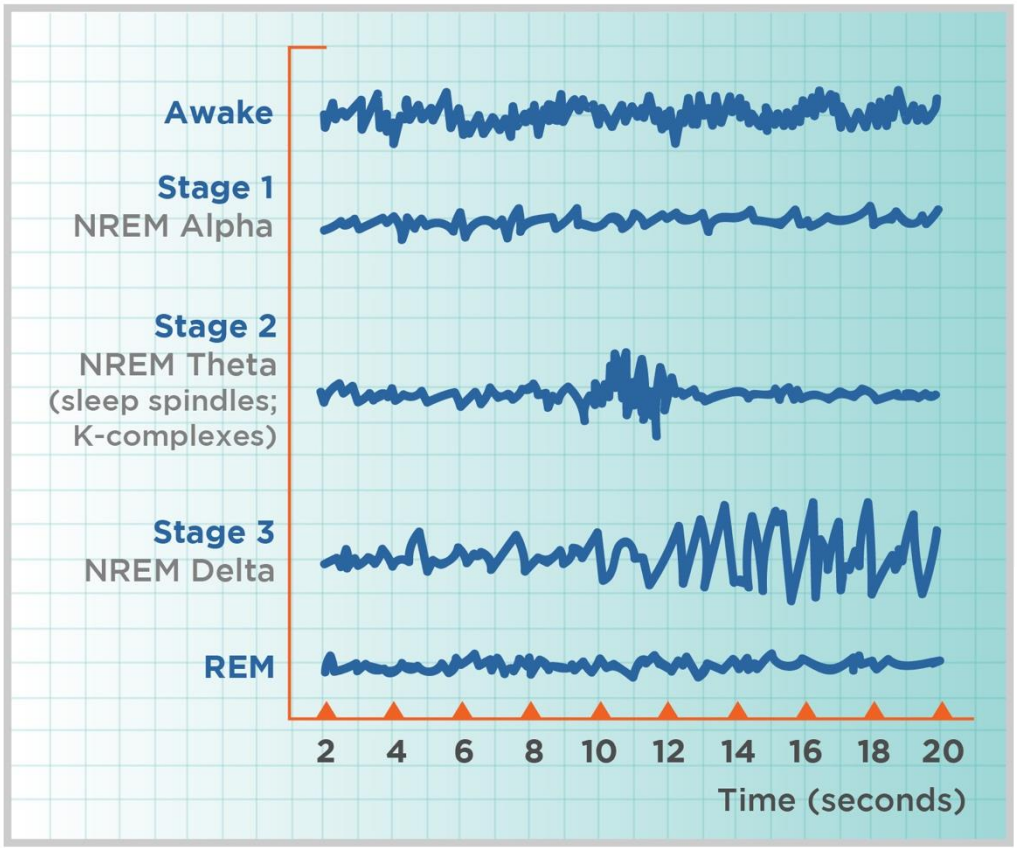


SLEEP CYCLE

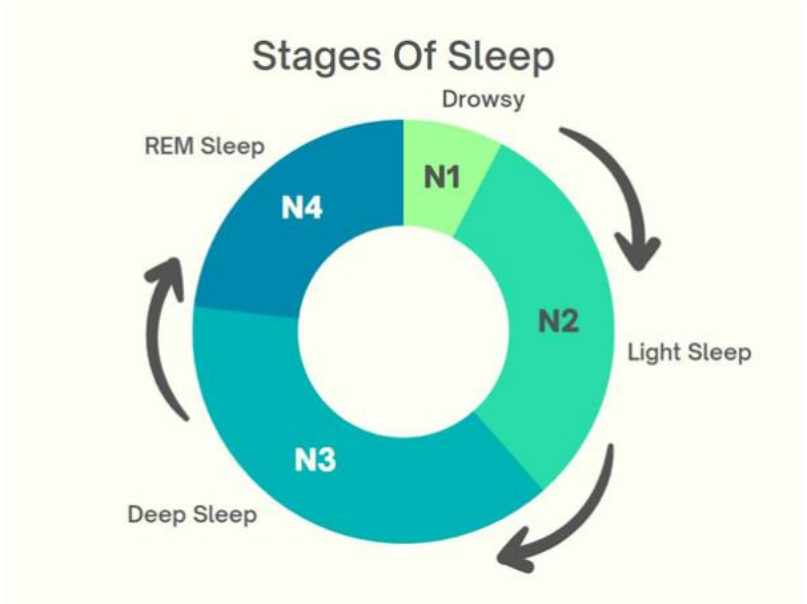


https://www.simplypsychology.org/sleep-stages.html

EEG RECORDINGS DURING SLEEP

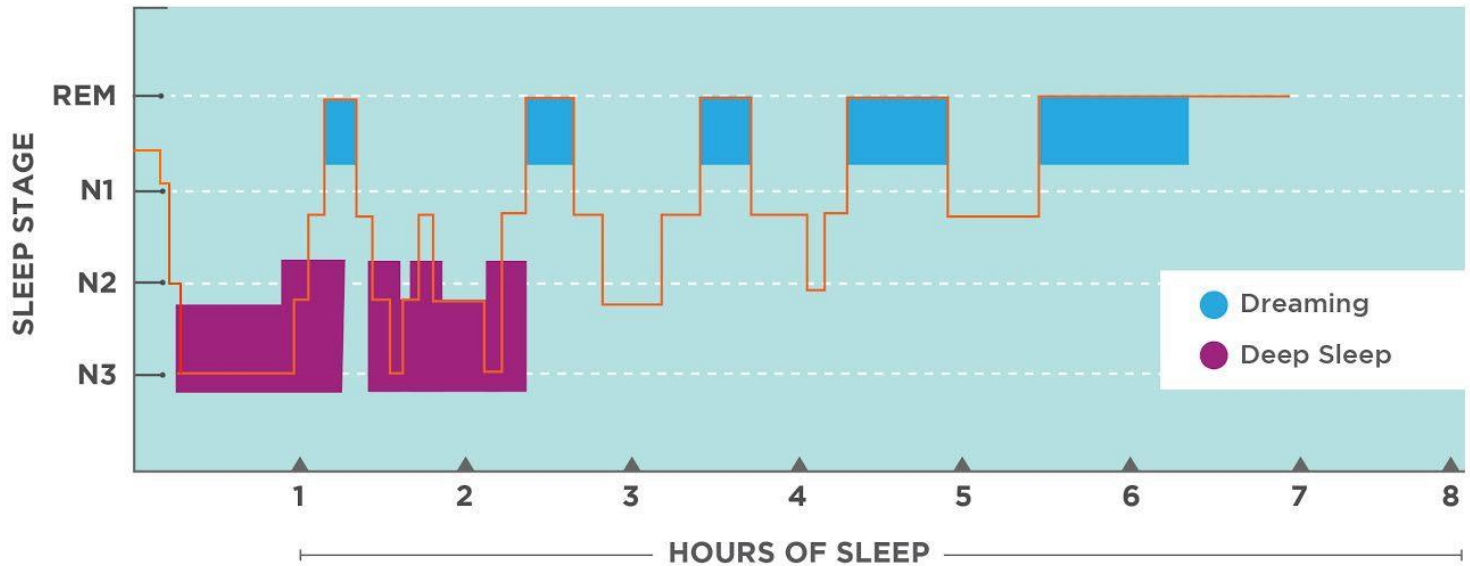


https://courses.lumenlearning.com/waymaker-psychology/chapter/stages-of-sleep/



https://miriqa.com/blogs/educational-articles/learn-about-the-sleep-cycle-stages?srsltid=AfmBOooJcNwicTGawqTG3cdwuLEya41D7YxW1xaZlcP7j-6X6FEDjq8F

SLEEP STAGES



The Evolution of Sleep Pharmacology: From Barbiturates to Targeted Signaling

1

Pre-1950s

Barbiturates and Chloral Hydrate — effective but narrow therapeutic indices and high overdose risk

2

1960s-1980s

Benzodiazepine Era — better safety but concerns of dependency and cognitive decline

3

1990s-2000s

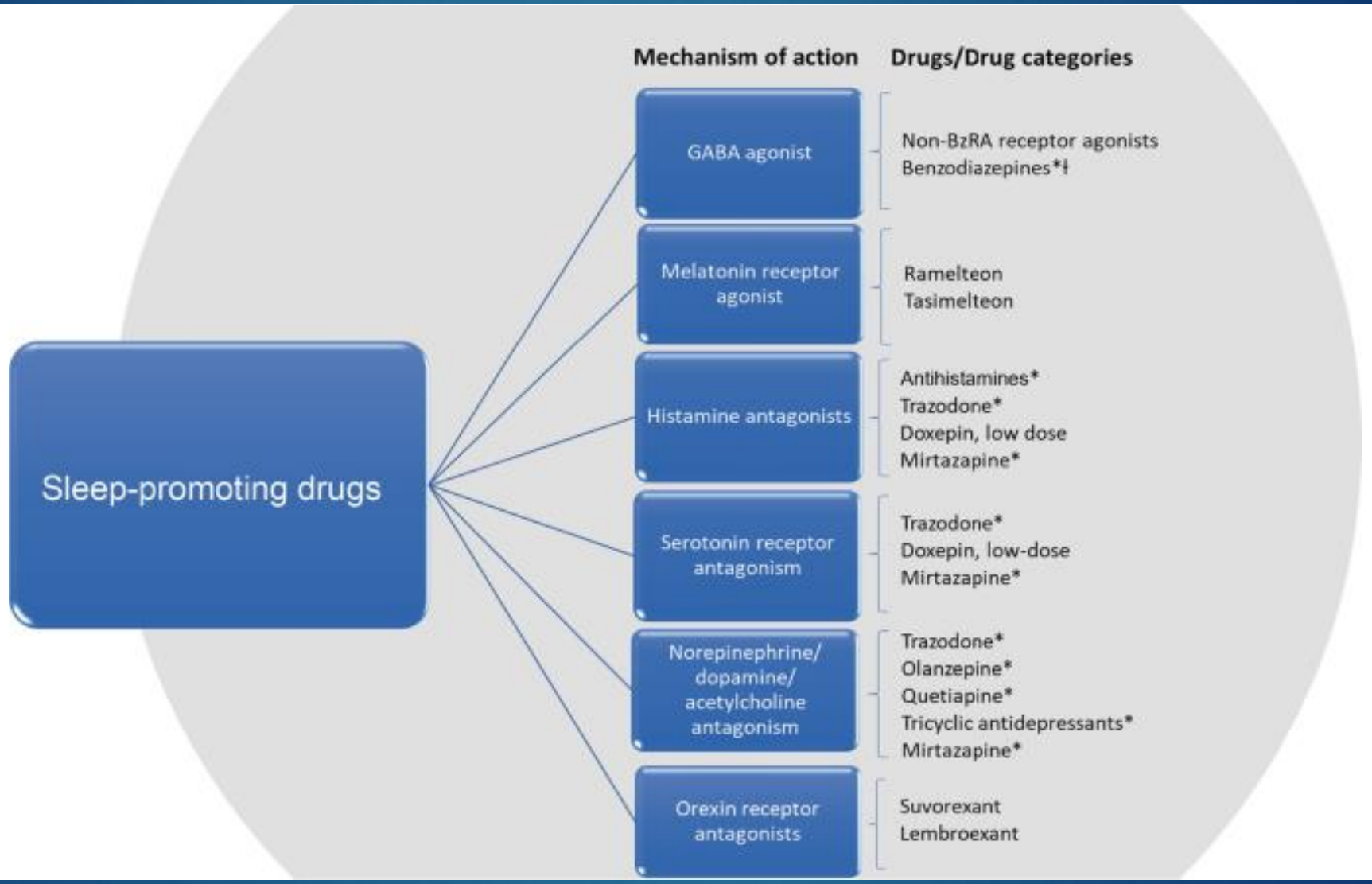
Rise of Z-drugs — targeted GABA-A subunits with reduced side effects

4

2010s-Present

Era of Targeted Modulation — Melatonin agonists and Orexin antagonists (DORAs) offering localized wake-cycle inhibition

Katzung's Basic & Clinical Pharmacology, 16th ed. (2024); Pharmacology Examination & Board Review, 14th ed. (2024)



Physiologic Targets: Mapping the Neurochemical Pathways of Sleep and Wake

Sources: Advance Physiology and Pathophysiology, 2nd ed. (2024); Katzung's Basic & Clinical Pharmacology, 16th ed. (2024)

Canadian clinical practice guidelines

Several Canadian professional bodies have published or endorsed insomnia treatment guidelines:

- **Canadian Sleep Society (CSS):** The CSS endorses CBT-I as first-line treatment and has advocated for better access to trained CBT-I providers across Canada. The CSS also recognises that the therapist shortage requires digital CBT-I as a practical alternative.
- **College of Family Physicians of Canada (CFPC):** The CFPC's **Choosing Wisely Canada** campaign specifically recommends against prescribing sleep medication as first-line treatment for insomnia, and against routinely renewing sleep medication prescriptions without reassessment and discussion of CBT-I.
- **Canadian Psychiatric Association (CPA):** CPA guidelines for insomnia comorbid with anxiety and depression recommend addressing the insomnia directly with CBT-I rather than assuming it will resolve when the mental health condition is treated.
- **Choosing Wisely Canada:** This national initiative — endorsed by 40+ Canadian medical societies — includes specific recommendations against using benzodiazepines or z-drugs for insomnia in older adults, citing fall risk, cognitive impairment, and dependency.

Clinical practice guideline for insomnia in Ontario

Ontario has specific infrastructure for accessing insomnia treatment that differs from other provinces. For Ontarians seeking CBT-I or clinical insomnia care:

- **CAMH (Centre for Addiction and Mental Health):** CAMH in Toronto offers sleep medicine assessment and CBT-I through its Mood and Anxiety Program. Referral through a family physician is typically required.
- **Ontario Sleep Clinics:** Hospital-based sleep clinics at Sunnybrook, Toronto General, and Ottawa Hospital provide polysomnography and CBT-I programs. OHIP covers the assessment; CBT-I delivery varies by clinic.
- **Connex Ontario:** Call 1-866-531-2600 to find provincially funded mental health programs, including those offering CBT for insomnia comorbid with anxiety or depression.
- **Employer extended health:** Ontario's extended health plans frequently cover registered psychologist visits, which can include CBT-I. Confirm "insomnia" or "sleep disorders" is a covered presenting complaint with your insurer.
- **Ontario Drug Benefit (ODB):** For insomnia medication, zopiclone is covered under ODB for eligible Ontarians. However, Ontario pharmacists are encouraged to initiate conversations about CBT-I as an alternative when presenting prescriptions for z-drugs — consistent with the Choosing Wisely Canada guidance endorsed by the Ontario College of Pharmacists.
- There is no single Ontario-specific insomnia clinical practice guideline document separate from the national framework. Ontario clinicians follow CADTH evidence reviews, Canadian Sleep Society recommendations, and the College of Physicians and Surgeons of Ontario's prescribing guidance on benzodiazepines and z-drugs, which limits duration and requires periodic reassessment.

Guiding Principles for Clinical Drug Selection in Insomnia Management

Step 1: Diagnostic Clarification

Step 2: Comorbidity Assessment

Step 3: Safety Profiling

Step 4: Duration Planning

Step 5: Monitoring / Deprescribing

Canadian guidelines for insomnia — what CADTH, Health Canada, and Canadian clinicians recommend

- CADTH (the Canadian Drug and Technologies in Health agency — now part of the broader Canadian health technology assessment framework) has published systematic reviews and rapid evidence reports on insomnia treatment. Key findings from CADTH insomnia reviews:
- **CBT-I produces durable outcomes:** CADTH evidence reviews note that CBT-I benefits persist at 12- and 24-month follow-up, unlike pharmacotherapy whose effects are tied to continued use.
- **Pharmacotherapy is appropriate short-term:** For acute insomnia (less than 4 weeks), short-term use of sleep medication may be appropriate as a bridge while CBT-I is initiated or accessed.
- **Z-drugs carry dependency risk:** CADTH reviews highlight the dependency, tolerance, and rebound insomnia risks of z-drugs (zopiclone, zolpidem) and benzodiazepines, supporting guideline recommendations to limit their duration.
- **Digital CBT-I is effective:** CADTH has reviewed digital health technologies and found app-based and internet-delivered CBT-I programs clinically comparable to therapist-delivered treatment, improving access in underserved regions of Canada.
- **What CADTH means for your treatment:** If your family physician prescribes a sleeping pill as a first response to chronic insomnia without discussing CBT-I, that does not align with current Canadian evidence-based guidelines. You can ask specifically about CBT-I referral or access.

Health Canada approved treatments for insomnia

Health Canada regulates insomnia treatments across two streams:

- **Natural Health Products (NHPs)**
  - Melatonin is the most significant NHP for insomnia in Canada. Unlike the US (where it is an unregulated supplement), Canadian melatonin products must carry an **NPN (Natural Product Number)** issued by Health Canada after pre-market review of safety, efficacy, and quality. Health Canada-approved melatonin indications include: sleep-onset insomnia, jet lag, and shift work sleep disorder. The approved dose range is 0.5–5 mg, with Health Canada guidance noting that lower doses (0.5–1 mg) are as effective as higher doses for most adults. Other NHP sleep aids — valerian, L-theanine, magnesium glycinate — may be sold with NPNs but with more limited efficacy claims.
- **Pharmaceutical : Prescription sleep medications**
  - Zopiclone (a z-drug) is the most commonly prescribed sleep medication in Canada and is only available by prescription. Benzodiazepines (temazepam, triazolam) are also prescribed but carry higher dependency risk. Health Canada has issued warnings on z-drugs regarding next-day impairment, particularly for driving, and recommends limiting use to the shortest effective duration.
- **Pharmaceutical: OTC sleep aids**
  - Diphenhydramine-based OTC sleep aids (Benadryl, ZzzQuil) are approved by Health Canada for occasional sleeplessness. Health Canada does not recommend these for chronic insomnia — tolerance develops within days, and antihistamine effects impair cognitive function the following day. They are not part of evidence-based insomnia treatment guidelines.

Off-Label Sedatives and Classic Pharmacotherapy of Insomnia

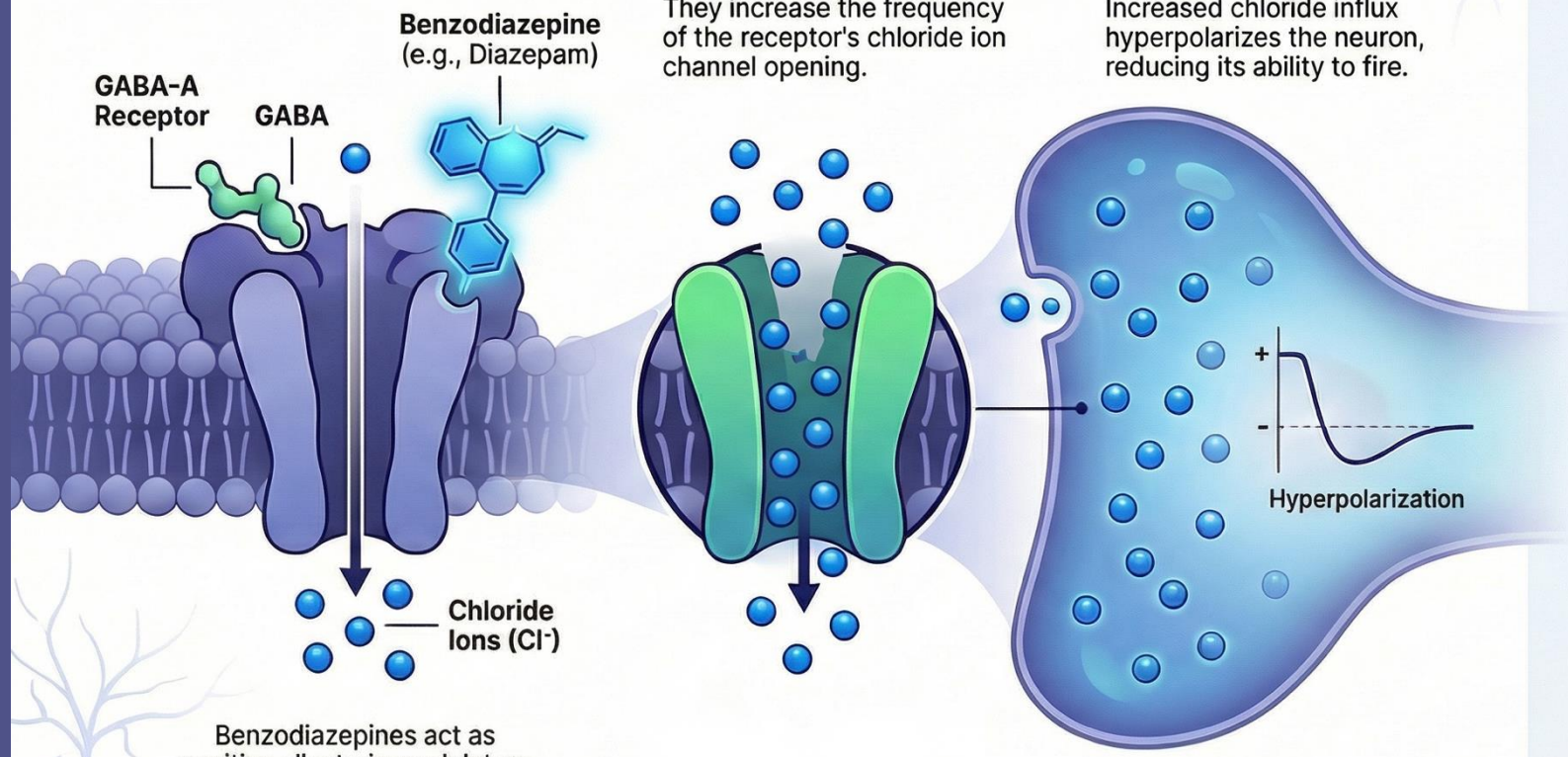
A review of Benzodiazepines and sedating Antidepressants in the management of sleep disorders

Benzodiazepines:
A Closer Look at How Diazepam Works

Enhancing GABA's Natural Effect

Opening the Chloride Channel
They increase the frequency of the receptor's chloride ion channel opening.

Quieting the Neuron
Increased chloride influx hyperpolarizes the neuron, reducing its ability to fire.



Benzodiazepines act as positive allosteric modulators on GABA-A receptors.

https://tmedweb.tulane.edu/pharmwiki/doku.php/benzodiazepines

Clinical Profile: Uses & Side Effects

Key Therapeutic Uses
- Anxiety
- Muscle Relaxation
- Sedation
- Seizures (Status Epilepticus)

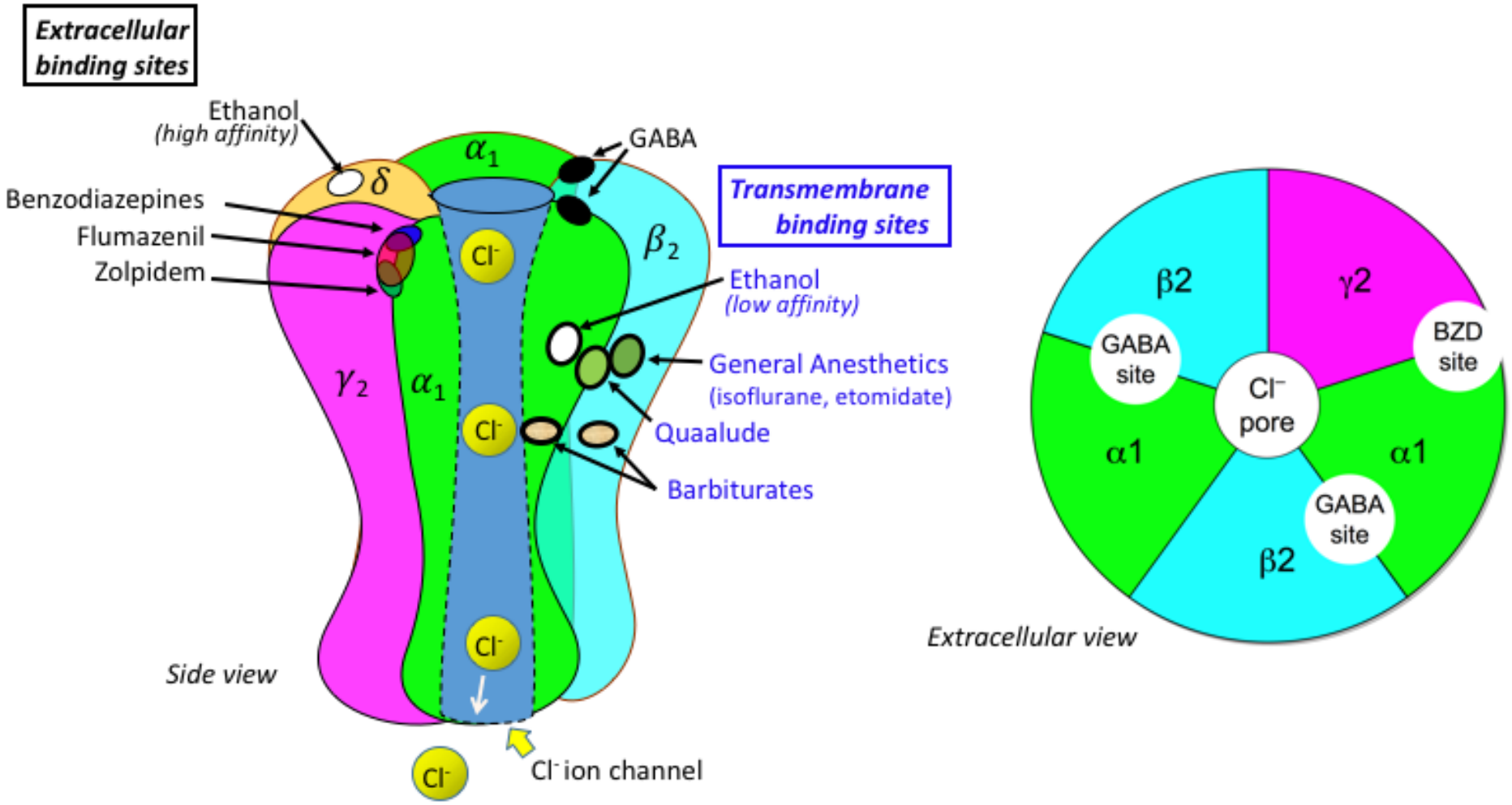
Primarily used for seizures (status epilepticus), anxiety, sedation, and muscle relaxation.

Potential Side Effects
Sedation | Respiratory Depression | Dizziness | Ataxia | Amnesia

Common effects include sedation, respiratory depression, dizziness, ataxia, and amnesia.

Diazepam for Status Epilepticus
Given intravenously (IV), it has a rapid onset but a short duration

Sources: Katzung's Basic & Clinical Pharmacology, 16th ed. (2024); Pharmacology Examination & Board Review, 14th ed. (2024)



THE BENZO BOTTOM LINE

Clinical Pearls for Naturopathic Doctors

Alprazolam is preferred when rapid anxiolysis is required but carries one of the **highest risks for tolerance, dependence, and rebound anxiety**.

Clonazepam provides **longer symptom control** and is commonly selected for patients with anxiety plus seizure disorders or chronic insomnia, though next-day sedation is more common.

Diazepam has the **longest duration of action** and additional **muscle-relaxant** properties, making it useful for muscle spasm, alcohol withdrawal, and acute seizure management, but it is generally **least desirable in older adults** because of metabolite accumulation and increased fall risk.

Lorazepam Undergoes glucuronidation rather than CYP450 metabolism, making it a preferred option in patients with hepatic impairment or those taking multiple CYP-interacting medications. Sedation remains the most common adverse effect.

Temazepam One of the few benzodiazepines specifically approved for the **short-term treatment of insomnia**. Particularly effective for sleep maintenance insomnia but should generally be limited to ≤2–4 weeks because of tolerance, dependence, cognitive impairment, and fall risk. Avoid during pregnancy.

Feature	Alprazolam (Xanax®)	Clonazepam (Klonopin®)	Diazepam (Valium®)
Drug Class	Benzodiazepine anxiolytic	Benzodiazepine; anticonvulsant	Benzodiazepine; anxiolytic, anticonvulsant, muscle relaxant
Primary Indications ; Off-label uses	Generalized anxiety disorder; panic disorder; Anxiety-related insomnia	Seizure disorders (Lennox-Gastaut, absence, myoclonic, akinetic); Anxiety, insomnia, acute psychosis	Anxiety disorders; skeletal muscle spasm; seizure disorders; status epilepticus; preoperative anxiety; tetanus ; Alcohol withdrawal, insomnia (less commonly)
Half-life	Intermediate (approx. 11–16 hrs)	**Long:** 30–40 hrs	**Very long:** 20–50 hrs (active metabolites up to 100 hrs)
Metabolism	CYP3A4	CYP3A4	CYP2C19 and CYP3A4
Clinical Limitations	Shorter duration; higher rebound anxiety and withdrawal risk	Next-day sedation and accumulation, especially in older adults	Accumulation due to active metabolites; prolonged sedation; increased fall risk in older adults
Common Adverse Effects	Sedation, dizziness, impaired coordination, dependence	Sedation, dizziness, cognitive slowing, ataxia	Fatigue, drowsiness, ataxia, confusion

Feature	Alprazolam (Xanax®)	Clonazepam (Klonopin®)	Diazepam (Valium®)
Major Contraindications	Concomitant ketoconazole or itraconazole use	Flumazenil reversal in patients treated for seizure disorders (may precipitate seizures)	Glaucoma; hypersensitivity to diazepam or soy-containing injectable formulation
Pregnancy	Category D – evidence of fetal risk	Generally avoided; benzodiazepines associated with fetal risk	Category D – evidence of fetal risk
Major Drug Interactions	Strong CYP3A4 inhibitors markedly increase serum levels	CYP3A4 inhibitors may increase exposure	CYP3A4/CYP2C19 inhibitors increase exposure; additive CNS depression with alcohol, opioids, sedatives
Dependence / Withdrawal Risk	**High**; abrupt discontinuation may cause severe withdrawal	High; taper gradually	High; withdrawal with abrupt discontinuation despite long half-life
Controlled Substance	Schedule IV	Schedule IV	Schedule IV
Clinical Limitations	Shorter duration; higher rebound anxiety and withdrawal risk	Next-day sedation and accumulation, especially in older adults	Accumulation due to active metabolites; prolonged sedation; increased fall risk in older adults
Naturopathic Clinical Considerations	Avoid combining with valerian, kava, passionflower, hops, cannabinoids, melatonin, or alcohol due to additive CNS depression. Monitor CYP3A4 herb interactions (e.g., grapefruit).	Same CNS depressant precautions; long half-life increases cumulative sedation when combined with sleep-promoting botanicals.	Greater caution with sedative herbs because of prolonged half-life and metabolite accumulation. Increased fall and cognitive impairment risk in geriatric patients.

Remember:

'"LOT" LOVE THE LIVER' :

Lorazepam, **O**xazepam, and **T**emazepam undergo **glucuronidation** instead of CYP450 oxidation, resulting in **fewer drug interactions** and making them the preferred benzodiazepines in patients with liver disease and many older adults.

BZD Risks:

Dependency, Tolerance, and Cognitive Decline

1

Tolerance Development

Chronic use leads to GABA-A receptor downregulation, requiring escalating doses within weeks.

2

Physiological Dependency

Sudden discontinuation can precipitate severe withdrawal including autonomic hyperactivity and seizures.

3

Cognitive Impairment

Correlation between long-term use and increased risk of Alzheimer's disease and dementia.

4

Sleep Architecture Alteration

BZDs suppress deep slow-wave sleep (N3) and REM sleep, making sleep non-restorative despite increased duration.

Sources: Katzung's Basic & Clinical Pharmacology, 16th ed. (2024); CAMH Sleep Disorders Pharmacotherapy Guidelines

Clinical Comparison:

Benzodiazepines vs. Sedating Antidepressants

Parameter	Primary Goal	Abuse Potential	Sleep Architecture	Withdrawal Risk	Best Candidate
Benzodiazepines	Rapid sleep **induction**	High (Schedule IV)	Suppresses REM/SWS	High; requires taper	Short-term/acute situational stress
Sedating Antidepressants (ie Trazodone, Doxepin)	Sleep **duration**/ maintenance	Low (Non-controlled)	Generally preserves REM/SWS	Low; minimal rebound	Patients with **mood** disorders or **substance** use history

Clinical Takeaway : The shift toward *antidepressants for sleep* is driven by

safety and addiction concerns vs**. superior efficacy**

Sources: Compendium of Therapeutic Choices (CTC), 9th ed.; Katzung's Basic & Clinical Pharmacology, 16th ed. (2024)

Clinical Profiles of Sleep-Specific BZDs: Temazepam and Triazolam

Temazepam (Restoril)

- **Intermediate onset** with half-life of 8-15 hours; ideal for sleep maintenance
- Metabolized via **glucuronidation;** safer for mild hepatic impairment
- Associated with **morning 'hangover' effects** and increased fall risk in elderly

Triazolam (Halcion)

- **Ultra-short onset** with half-life of 1.5-5 hours; strictly for sleep-onset insomnia
- Oxidatively metabolized via **CYP3A4;** susceptible to drug interactions
- Higher rates of **rebound insomnia**, anterograde **amnesia**, and paradoxical **agitation**

Sources: Compendium of Therapeutic Choices (CTC), 9th ed.; CPS Drug Monographs (Canadian Pharmacists Association)

Trazodone: The Ubiquitous Off-Label Sleep Aid

Multi-Receptor Profile

Serotonin antagonist and reuptake inhibitor (SARI); sedative properties from potent H1 and alpha-1 adrenergic blockade at low doses (25-100mg).

Off-Label Dominance

Most prescribed sleep aid in North America due to perceived lack of addiction potential.

Clinical Advantage

Useful for patients with comorbid depression or anxiety; does not suppress REM sleep as much as BZDs.

Significant Side Effects

Orthostatic hypotension (alpha-blockade), daytime somnolence, dry mouth, and rare risk of priapism.

Sources: Compendium of Therapeutic Choices (CTC), 9th ed.; Lexi Drug interaction modules (Canadian Pharmacists Association)

Clinical Comparison:

Trazodone vs. Doxepin

Feature	Trazodone	Doxepin
Drug Class	Serotonin Antagonist and Reuptake Inhibitor (SARI)	Tricyclic antidepressant (TCA)
Health Canada Indication	Major depressive disorder **(insomnia use is off-label)**	Low-dose (3–6 mg): insomnia characterized by sleep maintenance difficulty; Higher doses: depression and anxiety
Role in Insomnia	Frequently prescribed **off-label** because of sedative properties	FDA/Health Canada-approved at low doses for chronic insomnia (sleep maintenance)
Mechanism of Action	Antagonizes **5-HT2A**, **H1**, and **a1-adrenergic receptors**; weak serotonin reuptake inhibition	At low doses, highly selective **histamine H1 receptor antagonist**; higher doses also inhibit serotonin and norepinephrine reuptake
Primary Sleep Effect	Improves **sleep onset** and maintenance	Primarily improves **sleep maintenance** (minimal effect on sleep onset)
Typical Insomnia Dose	25–100 mg at bedtime	3–6 mg at bedtime
Antidepressant Dose	150–400 mg/day	75–300 mg/day
Onset of Action	30–60 minutes	Approximately 30 minutes
Half-life	Biphasic; approximately 5–13 hours	Approximately 15 hours

Clinical Comparison:

Trazodone vs. Doxepin

Feature	Trazodone	Doxepin
Metabolism	CYP3A4 → active metabolite (mCPP)	CYP2C19 and CYP2D6
Common Adverse Effects	Daytime sedation, dizziness, dry mouth, orthostatic hypotension	Somnolence, dry mouth (minimal at low doses), headache, nausea
Unique Adverse Effect	**Priapism** (rare but serious); orthostatic hypotension due to a1 blockade	Higher doses produce typical TCA adverse effects (anticholinergic effects, QT prolongation, weight gain); these are uncommon at insomnia doses
Fall Risk	Moderate due to hypotension and sedation	Lower at 3–6 mg; increases with antidepressant doses
Pregnancy	Use only if benefits outweigh risks	Limited human data; generally avoided unless clearly indicated
Major Drug Interactions	CYP3A4 inhibitors (clarithromycin, ketoconazole, grapefruit); additive serotonin syndrome risk; CNS depressants	CYP2D6/CYP2C19 inhibitors; additive CNS depression; avoid MAOIs
Herb/Nutrient Interactions	St. John's wort (serotonin syndrome risk); valerian, kava, melatonin, cannabinoids increase sedation	Similar additive sedation with valerian, kava, hops, melatonin, cannabinoids

POTENTIAL WITHDRAWAL SYMPTOMS:

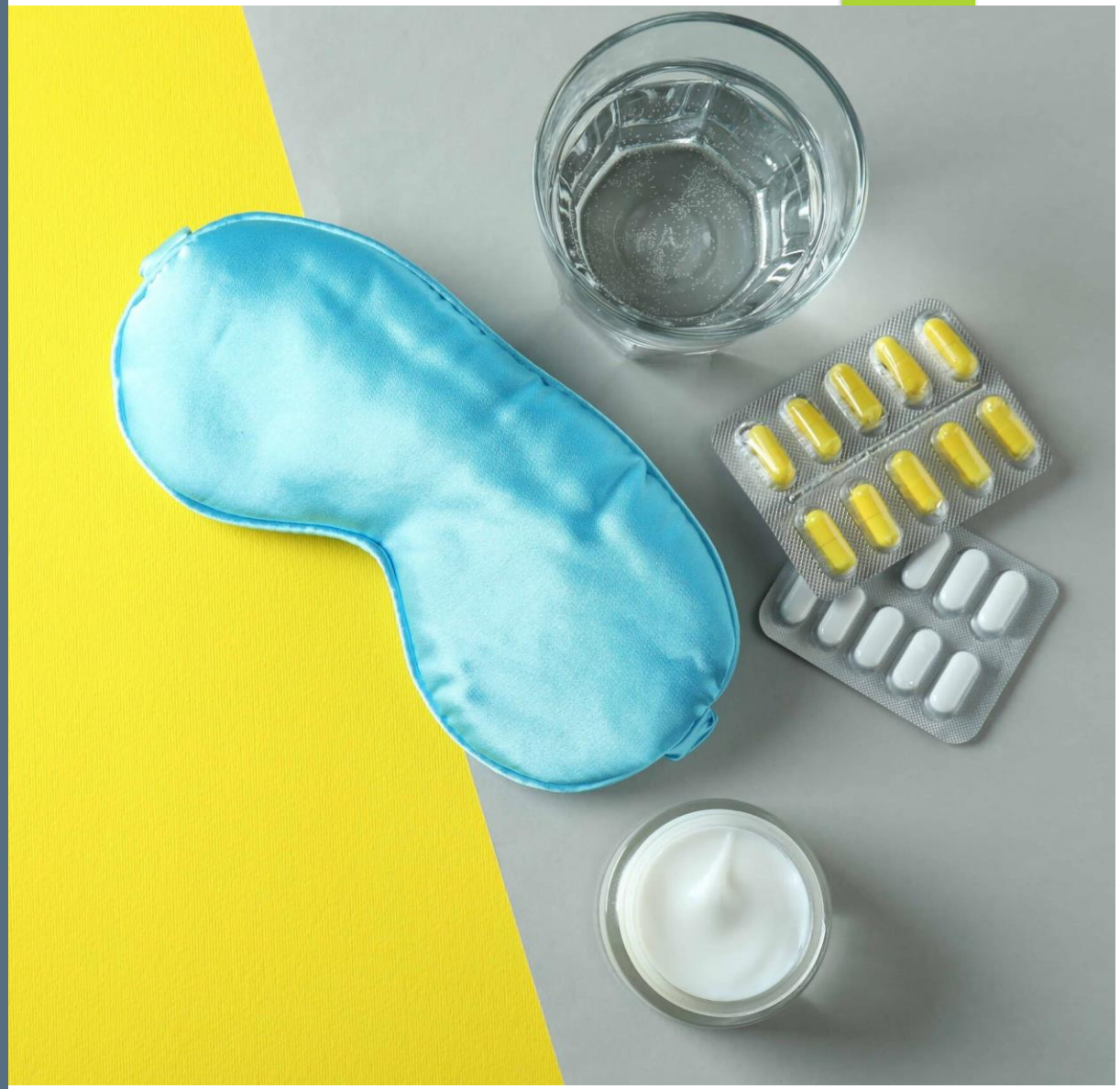
Stopping trazodone abruptly, even at lower doses, can lead to withdrawal symptoms like:

01 **Severe migraines.**

02 **Dizziness or lightheaded-ness.**

03 **Persistent sleeplessness.**

04 **Increased anxiety or agitation.**

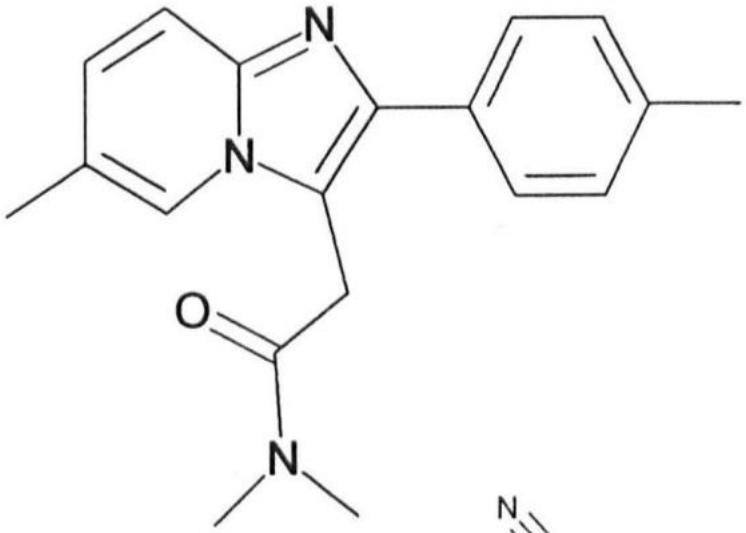


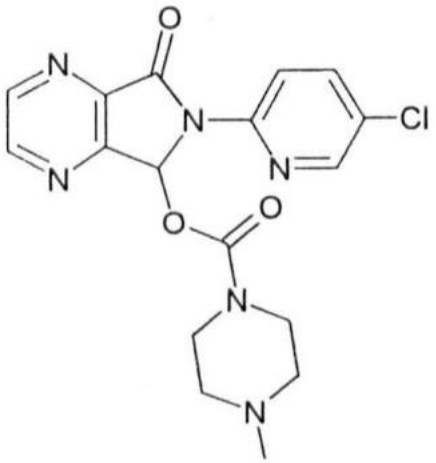
The New Sedative-Hypnotic Sleep Drugs :

“Z-Drugs”

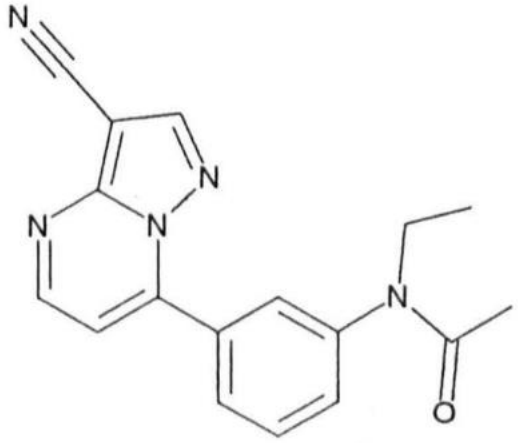
Z's

ZOLPIDEM





ZOPICLONE



ZALEPLON

https://onlinelibrary.wiley.com/doi/pdf/10.1111/j.1527-3458.1998.tb00074.x

Z-Drugs (Sedative-Hypnotics): Selectivity and Clinical Advantages

Selective Binding

Z-drugs preferentially bind to the a1 subunit of GABA-A receptor, associated with sedation rather than muscle relaxation.

Improved Safety Profile

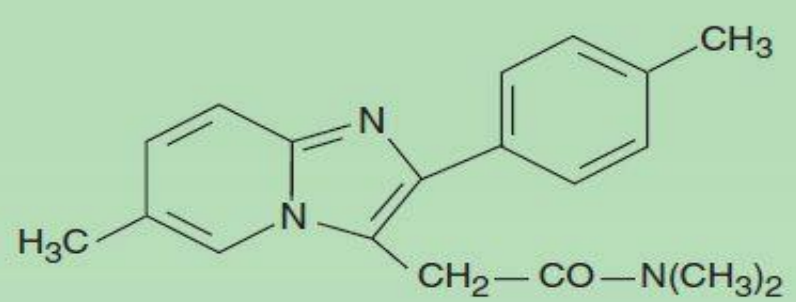
Avoiding a2 and a3 subunits results in lower daytime grogginess and less motor coordination impact than traditional BZDs.

Preserved Sleep Stages

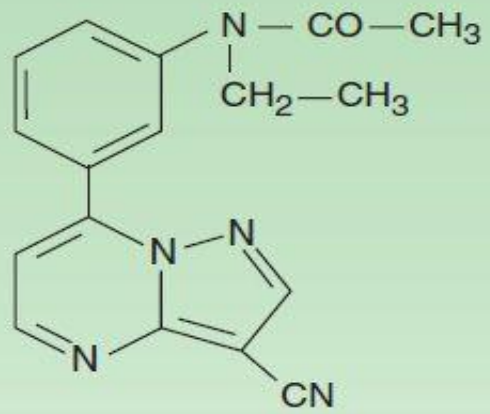
More neutral effect on sleep architecture, allowing natural NREM and REM transitions.

Targeted Usage

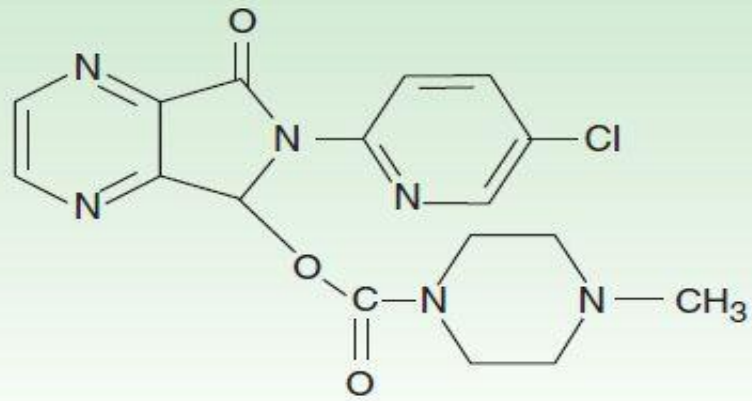
Most common prescription choice for primary insomnia due to rapid onset and reliable efficacy.



Zolpidem



Zaleplon



Eszopiclone

Sources: Compendium of Therapeutic Choices (CTC), 9th ed.; Pharmacology Examination & Board Review, 14th ed. (2024)

Clinical Comparison:

Zolpidem vs Eszopiclone vs Zaleplon

Feature	Zolpidem (Sublinox®)	Eszopiclone (Lunesta®)	Zaleplon (Sonata®)
Drug Class	Non-benzodiazepine hypnotic (Z-drug)	Non-benzodiazepine hypnotic (Z-drug)	Non-benzodiazepine hypnotic (Z-drug)
Mechanism of Action	Selective positive allosteric modulator of the GABA-A receptor (high affinity for a1 subtype)	Positive allosteric modulator of GABA-A receptor (a1, a2, a3 subunits)	Highly selective GABA-A a1 receptor agonist
Primary Clinical Effect	Sleep initiation and moderate sleep maintenance	Sleep initiation **and** sleep maintenance	Sleep initiation only
Best Candidate	Difficulty falling asleep or mild sleep maintenance insomnia	Patients with both sleep-onset and sleep-maintenance insomnia	Patients with isolated sleep-onset insomnia or middle-of-the-night awakening (≥4 hours of sleep remaining)
Typical Dose	5–10 mg (IR); 6.25–12.5 mg (CR)	1–3 mg	5–10 mg
Onset of Action	15–30 minutes	20–30 minutes	10–20 minutes (fastest)
Half-life	~2–3 hours	~6 hours	~1 hour (shortest)
Duration of Action	6–8 hours	7–8 hours	3–4 hours

Clinical Comparison:

Zolpidem vs Eszopiclone vs Zaleplon

Feature	Zolpidem (Sublinox®)	Eszopiclone (Lunesta®)	Zaleplon (Sonata®)
Metabolism	CYP3A4 (minor CYP1A2, CYP2C9)	CYP3A4 and CYP2E1	Aldehyde oxidase (major); CYP3A4 (minor)
Active Metabolites	No	No	No
Controlled Substance	Schedule IV	Schedule IV	Schedule IV
Residual Morning Sedation	Moderate (greater with CR formulation)	Highest among Z-drugs	Minimal
Complex Sleep Behaviors	Highest reported risk	Present	Present but less common
Abuse Potential	Moderate	Moderate	Lower to moderate
Tolerance/Dependence	Possible with prolonged use	Possible	Possible
Major Drug Interactions	CYP3A4 inhibitors, opioids, alcohol, CNS depressants	CYP3A4 inhibitors, CNS depressants	CYP3A4 inhibitors (less clinically significant), CNS depressants
Use in Older Adults	Lower doses recommended; Beers Criteria medication	Use cautiously; prolonged sedation possible	Generally preferred if a Z-drug is required because of very short half-life

Zolpidem (Sublinox®): Versatile Dosing and Release Profiles

Immediate Release (IR)

Targets sleep-onset insomnia within 15-30 minutes; half-life of 2-3 hours; minimal morning residual effects. Lower starting doses for women (5mg) due to slower clearance.

Extended Release (CR/ER)

Bi-layered tablet provides immediate dose plus slow-release for full 8-hour coverage. Recommended 6.25mg for women and elderly to mitigate morning-after driving impairment.

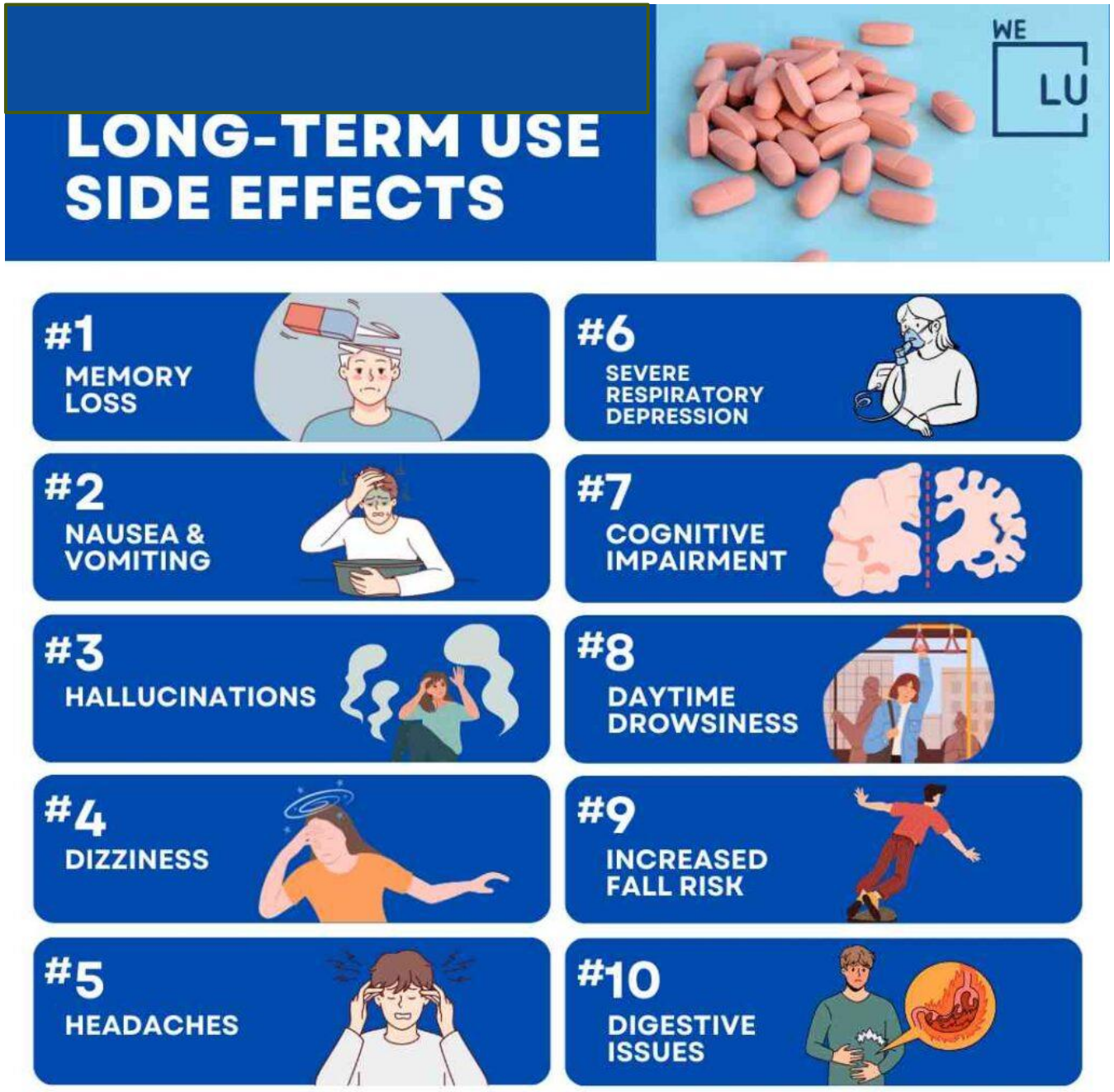
Takeaway

IR for those who can't fall asleep;

CR for those who wake at 2 AM.

Sources: Compendium of Therapeutic Choices (CTC), 9th ed.; CPS Drug Monographs (Canadian Pharmacists Association)

ZOLPIDEM



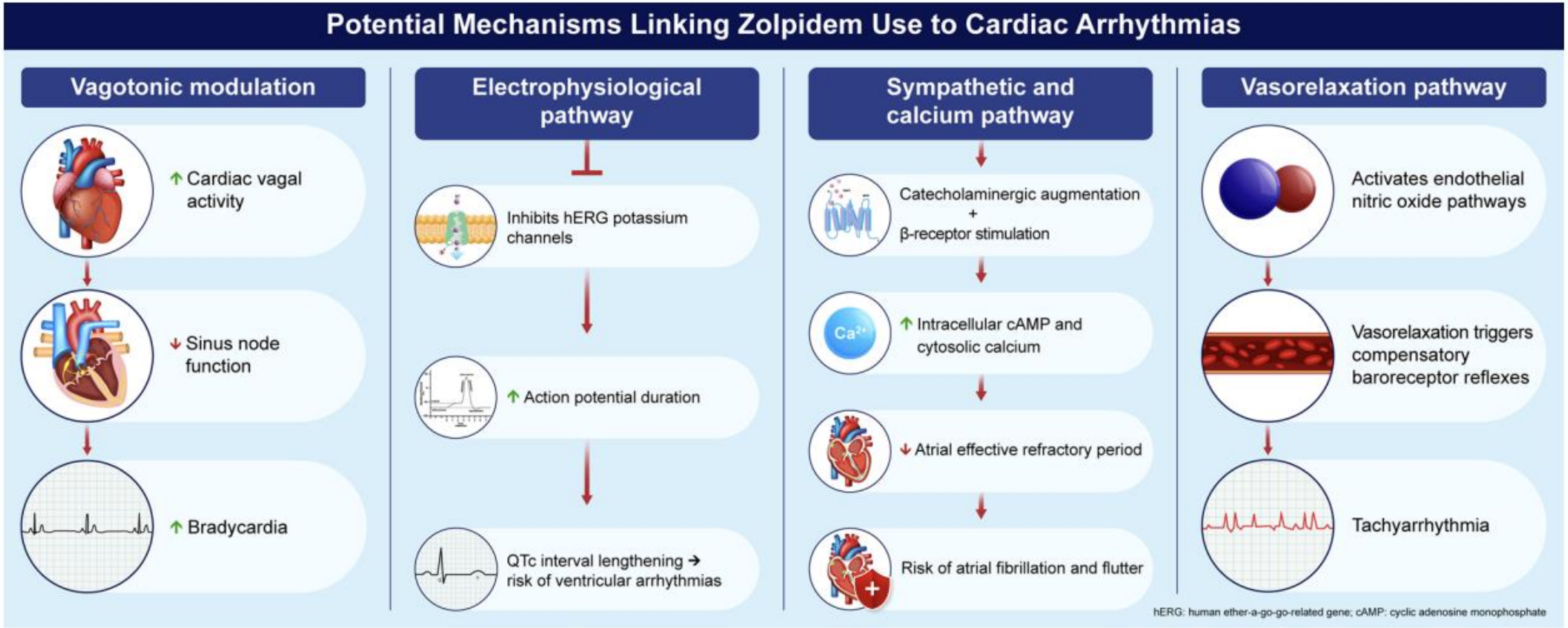


Fig. 2 Schematic representation of potential mechanisms linking zolpidem use [Print] arrhythmias. Zolpidem may induce arrhythmias through multiple pathways: (1) Increased cardiac vagal activity may suppress sinus node function, [illegible]y leading to bradycardia. (2) Inhibition of hERG potassium channels leads to action potential prolongation and QTc interval lengthening, predisposing to ventricular arrhythmias. (3) Modulation of sympathetic tone and intracellular calcium handling can shorten the atrial effective refractory period and enhance automaticity, promoting atrial fibrillation and flutter. (4) Vasorelaxation via nitric oxide (NO) pathways may cause hemodynamic fluctuations and reflex tachycardia.

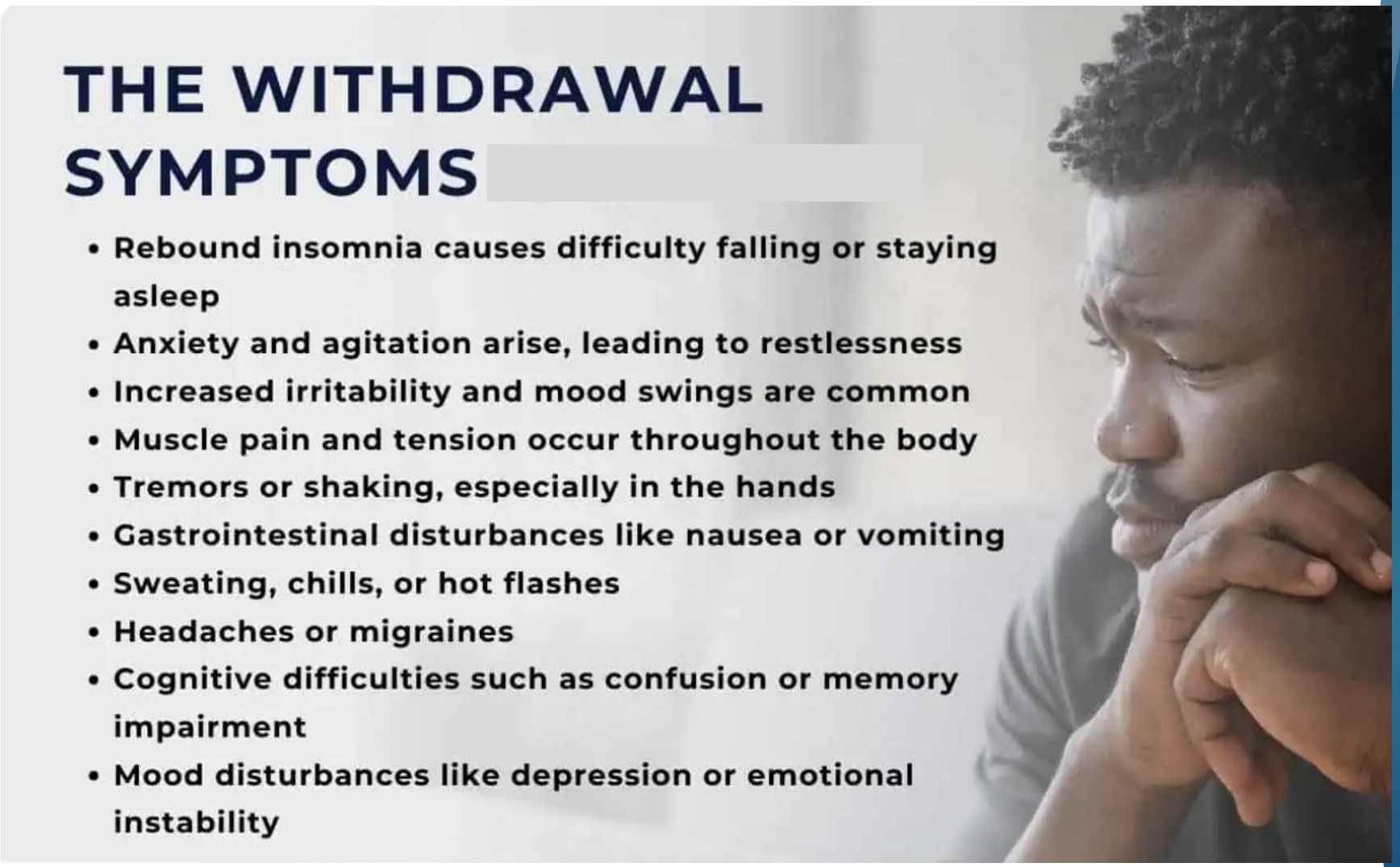
https://www.ovid.com/jnls/jcma/pdf/10.1097/jcma.0000000000001360~zolpidem-use-and-the-risk-of-arrhythmia-a-nationwide

ADDICTION SYMPTOMS

PHYSICAL EFFECTS	MENTAL AND COGNITIVE EFFECTS
• Tolerance • Withdrawal symptoms • Disrupted sleep patterns • Physical health problems	• Cognitive impairment • Mood changes • Increased risk of mental health disorders
BEHAVIORAL AND SOCIAL CONSEQUENCES	**EFFECT ON THE BRAIN**
• Relationship strain • Isolation and withdrawal • Financial difficulties	• Ambien affects the brain by enhancing the effects of a neurotransmitter called gamma-aminobutyric acid (GABA) • Ambien reduces brain activity, induces sedation, and promotes sleep

https://whitelightbh.com/resources/drug-addiction/ambien/

SYMPTOMS OF ZOLPIDEM WITHDRAWL



https://whitelightbh.com/resources/drug-addiction/ambien/

Clinical Trial > J Int Med Res. 2001 May-Jun;29(3):163-77.
doi: 10.1177/147323000102900303.

A double-blind comparative study of zolpidem versus zopiclone in the treatment of chronic primary insomnia

S Tsutsui [1]; Zolipidem Study Group

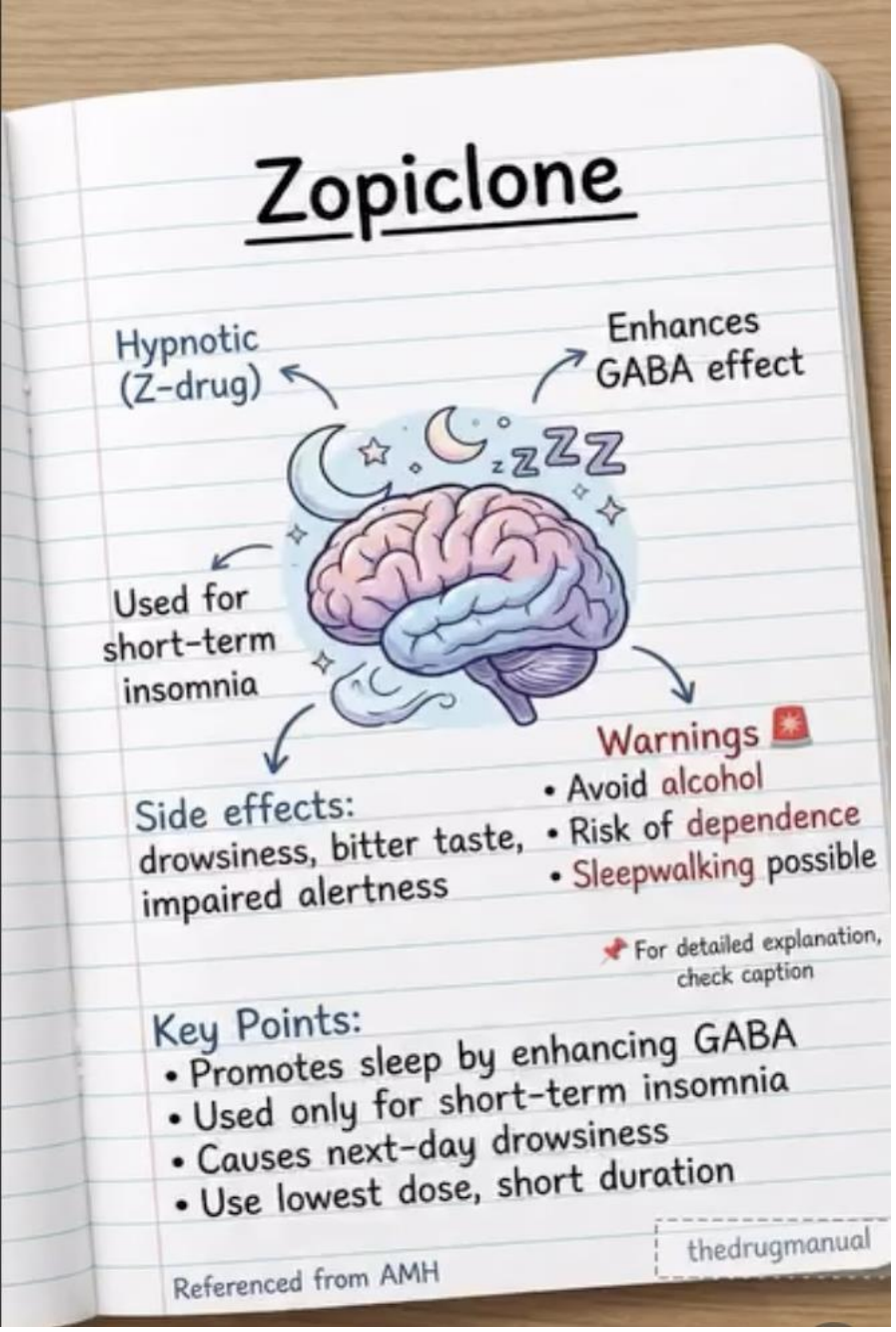
Affiliations + expand

PMID: 11471853 DOI: 10.1177/147323000102900303

Free article

Abstract

Zolpidem (10 mg/day) and zopiclone (7.5 mg/day), administered at night, were compared in a 14-day, double-blind, equivalence trial on 479 chronic primary insomniacs (zolpidem, 231; zopiclone, 248) throughout Japan, with a 1-week follow-up to assess rebound. The primary endpoint was the investigators' rating of global improvement of sleep disorders. A total of 32 patients in the zolpidem group (13.9%) and 45 patients in the zopiclone group (18.1%) withdrew from the study before the end of the treatment. In the zolpidem group, 67.9% (142/209) of patients were rated at least 'moderately improved' versus 61.6% (135/219) with zopiclone, zolpidem being at least as effective as zopiclone (90% confidence interval: -1.7, 14.3). With zolpidem, sleep onset latency improved in significantly more patients (85.8% versus 77.5%) and significantly fewer patients showed aggravated sleep onset latency relative to baseline at follow-up (4.5% versus 15.4%). Significantly fewer patients receiving zolpidem experienced drug-related adverse events (31.3% versus 45.3%), with bitter taste representing 5.8% (six of 104) of such complaints with zolpidem compared with 39.9% (69/173) with zopiclone. In conclusion, zolpidem was at least as effective as zopiclone, showed significantly less rebound on discontinuation and was better tolerated.



Zopiclone (Imovane) vs Eszopiclone (Lunesta)

It is unclear if eszopiclone differs meaningfully from zopiclone for efficacy or safety outcomes but it is costlier. $$$

https://www2.gov.bc.ca/assets/gov/health/practitioner-pro/provincial-academic-detailing-service/pad-refills/pad_refills_oct2021_eszopiclone.pdf

Common Side Effects of Zopiclone

- **Drowsiness and Fatigue**
- **Unpleasant Taste (Bitter / Metallic)**
- **Dry Mouth**
- **Dizziness and Lightheadedness**
- **Headaches**

Less Common But Serious Side Effects

- **Memory Problems and Confusion**
- **Complex Sleep Behaviours**
- **Dependence and Withdrawal:**

Who's Most at Risk?

•**Age**: Older adults tend to be more sensitive to the effects of zopiclone and may be at higher risk for side effects like confusion or memory problems.

•**Dosage**: Higher doses of zopiclone are generally associated with an increased risk of side effects.

•**Other Medications**: Zopiclone can interact with other medications, potentially increasing the risk of side effects. It's essential to inform your doctor about all your medications, including over-the-counter drugs and supplements.

https://addictionhealingcentre.ca/what-are-the-side-effects-of-zopiclone/

https://canadiancentreforaddictions.org/what-are-common-zopiclone-side-effects/

ZOPICLONE SYMPTOMS OF ADDICTION:

PHYSICAL	Daytime drowsiness or grogginess Headaches or nausea, especially in the morning Dry mouth or an unusual metallic taste Shaking hands or racing heart when missing a dose Needing higher doses to fall asleep
PSYCHOLOGICAL	Anxiety about not having Zopiclone nearby Mood swings, especially in the evenings or before taking it Difficulty focusing or remembering things Feeling emotionally numb or low Worrying about sleep constantly, even during the day
BEHAVIOURAL	Taking more than prescribed or using someone else's tablets Hiding tablets or lying about usage Avoiding events or obligations due to fatigue Repeatedly asking for early refills or visiting multiple doctors Feeling unable to sleep without taking Zopiclone, even when exhausted

ZOPICLONE WITHDRAWAL

- Rebound insomnia
- Cravings
- Anxiety
- Depression
- Restlessness
- Intrusive thoughts
- Tremor
- Diarrhoea

TAPERING OFF LONG-TERM ZOPICLONE USE

Phase	Action	Duration
Pre-taper	Medication reconciliation; initiate CBT-I (in-person/digital); set expectations	1–2 weeks
Initial taper	Reduce zopiclone dose by 25%	1–2 weeks per step
Mid-taper	Continue 25% reductions; transition to intermittent dosing (every other night)	2–4 weeks per step
Final taper	Lowest available dose every 2–3 nights → discontinue	2–4 weeks
Post-discontinuation	Continue CBT-I; monitor for rebound insomnia (typically 1–3 days); consider melatonin 2 mg CR for sleep support if desired	Ongoing

https://www.openevidence.com/ask/aa596d01-b195-4921-a3ec-f54e45f6a33e

Eszopiclone and Zaleplon Use: Maintenance and Middle-of-Night Solutions

1	2	3
Eszopiclone (Lunesta)	**Zaleplon (Sonata)**	**Strategic Use**
Longest half-life (6hr) Only Z-drug indicated for long-term use (up to 6 months) Common side effect: metallic taste (dysgeusia) in 15-30% of patients.	Ultra-short half-life of 1 hour (shortest of all sleep medications.) Can be taken mid-night if at least 4 hours of sleep remains.	**Ideal for 'late-night awakeners' without morning sedation risk.**

Compendium of Therapeutic Choices (CTC), 9th ed.; Lexi Drug interaction modules (Canadian Pharmacists Association)

ZOPICLONE HERBAL INTERACTIONS

Supplement	Interaction Type	Mechanism	Clinical Significance
St. John's Wort	Pharmacokinetic	CYP3A4/P-gp induction → ↓ zopiclone levels	High — may cause therapeutic failure
Goldenseal	Pharmacokinetic	CYP3A4 inhibition → ↑ zopiclone levels	Moderate — avoid combination
Valerian	Pharmacodynamic	GABA-A modulation → additive sedation	Moderate — excessive sedation risk
Kava	Both	GABA potentiation + CYP inhibition	High — sedation, hepatotoxicity risk
Passionflower	Pharmacodynamic	GABAergic modulation	Low-moderate — additive sedation
Melatonin	Minimal	Different receptor system (MT1/MT2)	Low — mild additive sleepiness

Z-Drugs and Herb-Drug Interactions

Interactions of Z-drugs (n = 8)

Table 11 shows the adverse interactions between zopiclone, zolpidem and plant preparations. Again, the most common cause was the use of ginseng preparations ($n = 5$, 62.5%).

Table 11. **Zopiclone and zolpidem interactions with medicinal and nutritional supplements containing plant extracts**

Hypnotic taken in monotherapy or in combination with other drugs	Number of cases	Plant active ingredient of a drug or nutritional supplement which is the cause of interaction	Clinical picture of interaction
Zopiclone	2	ginseng	NREM parasomnias
Zopiclone	1	carambola	hallucinations
Zopiclone + mianserin	1	ginseng	headache, sinus tachycardia
Zolpidem	2	ginseng	ventricular arrhythmia
Zolpidem	1	Bacopa	amnesia
Zolpidem	1	Japanese ginkgo biloba	dizziness, somnolence during the day, inability to sleep in the evening

file:///Users/carollaic/Downloads/Unwanted_effects_of_psychotropic_drug_interactions%20(1).pdf

Z-Drug Safety: Complex Sleep Behaviors and FDA Warnings

1

Complex Sleep Behaviors

Sleep-walking, sleep-driving, and preparing food while asleep; patients are typically amnesic to these events.

2

FDA Boxed Warning (2019)

Required for all Z-drugs due to risk of serious injury or death from complex sleep behaviors.

3

Vulnerable Populations

Risks significantly increased when combined with alcohol, opioids, or benzodiazepines.

4

Cognitive Impact

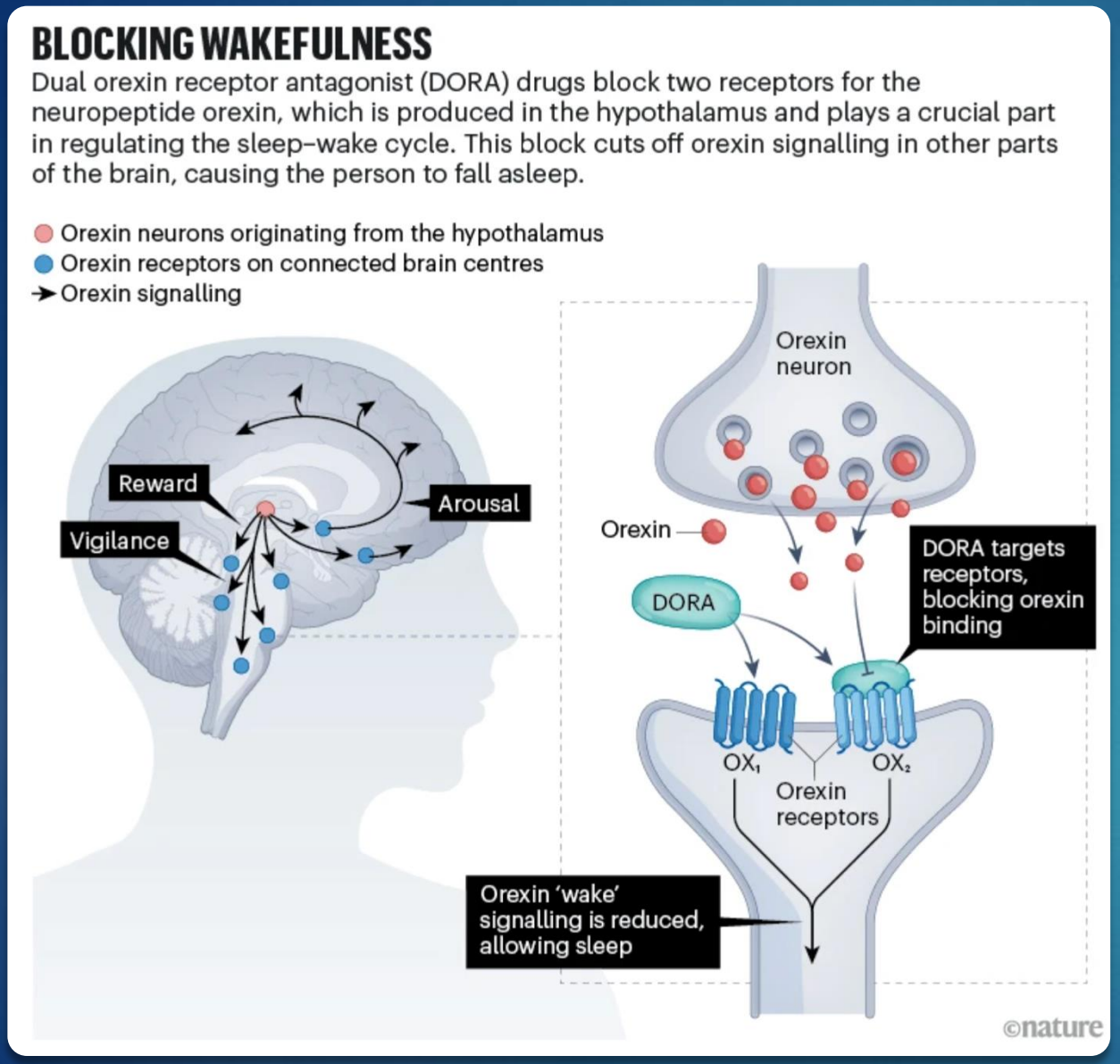
Increased risk of falls and hip fractures in elderly patients; use lowest effective dose.

5

Clinical Precaution

Counsel patients to take medication only when 7-8 hours of uninterrupted sleep is available.

Sources: FDA Boxed Warning (2019) for Z-drugs; Mayo Clinic Sleeping Pills Guide; Compendium of Therapeutic Choices (CTC), 9th ed.



DORAs: The newest sleep drugs

DUAL OREXIN ANTAGONISTS:

- SUVOREXANT
- LEMBOREXANT

https://www.nature.com/articles/d41586-025-00963-x

Dual Orexin Receptor Antagonists (DORAs):

A Paradigm Shift in Sleep Medicine

Understanding the Orexin System

Orexin A and B are neuropeptides from the hypothalamus that promote wakefulness and stabilize arousal.

Mechanism of DORAs

Unlike GABA-ergics that force sleep via sedation, DORAs bind to OX1R and OX2R to block signals that keep us awake.

Clinical Outcome

Results in a more natural transition to sleep with easier awakening if a stimulus occurs.

Next-Day Profile

Less impact on motor coordination and cognition upon waking compared to Z-drugs.

Sources: Katzung's Basic & Clinical Pharmacology, 16th ed. (2024); Advance Physiology and Pathophysiology, 2nd ed. (2024)

Suvorexant (Belsomra): The First-in-Class Orexin Antagonist

Indication

Approved for sleep-onset and sleep-maintenance insomnia; significant data supporting use in Alzheimer's-related insomnia.

Pharmacokinetics

Long half-life of 12 hours; sustained efficacy but increased next-day somnolence risk.

Clinical Studies

Significant reduction in latency to persistent sleep (LPS) and wake after sleep onset (WASO) over 3-month trials.

Metabolic Considerations

Metabolized by CYP3A4; contraindicated with strong inhibitors (ketoconazole, clarithromycin); dose adjustment needed with moderate inhibitors.

Sources: Compendium of Therapeutic Choices (CTC), 9th ed.; CAMH Sleep Disorders Pharmacotherapy Guidelines; Lexi Drug interaction modules

Lemborexant (Dayvigo): Superiority in Sleep Onset and Maintenance

Sleep Onset Latency

20-30 minute faster onset vs placebo and Zolpidem ER in head-to-head trials (SUNRISE-1). Best for patients struggling to fall asleep initially.

Sleep Maintenance

Significant reduction in WASO sustained over 12 months of use. Highly effective for early morning awakenings.

Safety Profile

Lower incidence of postural instability vs Zolpidem; safer for elderly or those prone to nocturia. Common Adverse Effects: Somnolence (10%) and vivid dreams; generally mild and well-tolerated.

Sources: SUNRISE-1 Clinical Trial; Compendium of Therapeutic Choices (CTC), 9th ed.; CAMH Sleep Disorders Pharmacotherapy Guidelines

DORA Side Effects: Somnolence, Vivid Dreams, and Rare Events

Next-Day Somnolence

Most common side effect; caution about driving until patients know their response.

REM-Related Effects

By blocking orexin, DORAs can occasionally trigger sleep paralysis or hypnagogic/hypnopompic hallucinations.

Narcolepsy Paradox

DORA effects can mimic narcolepsy symptoms, though rare at therapeutic doses.

Suicidal Ideation

Small but significant increase noted; requires monitoring in patients with pre-existing depression.

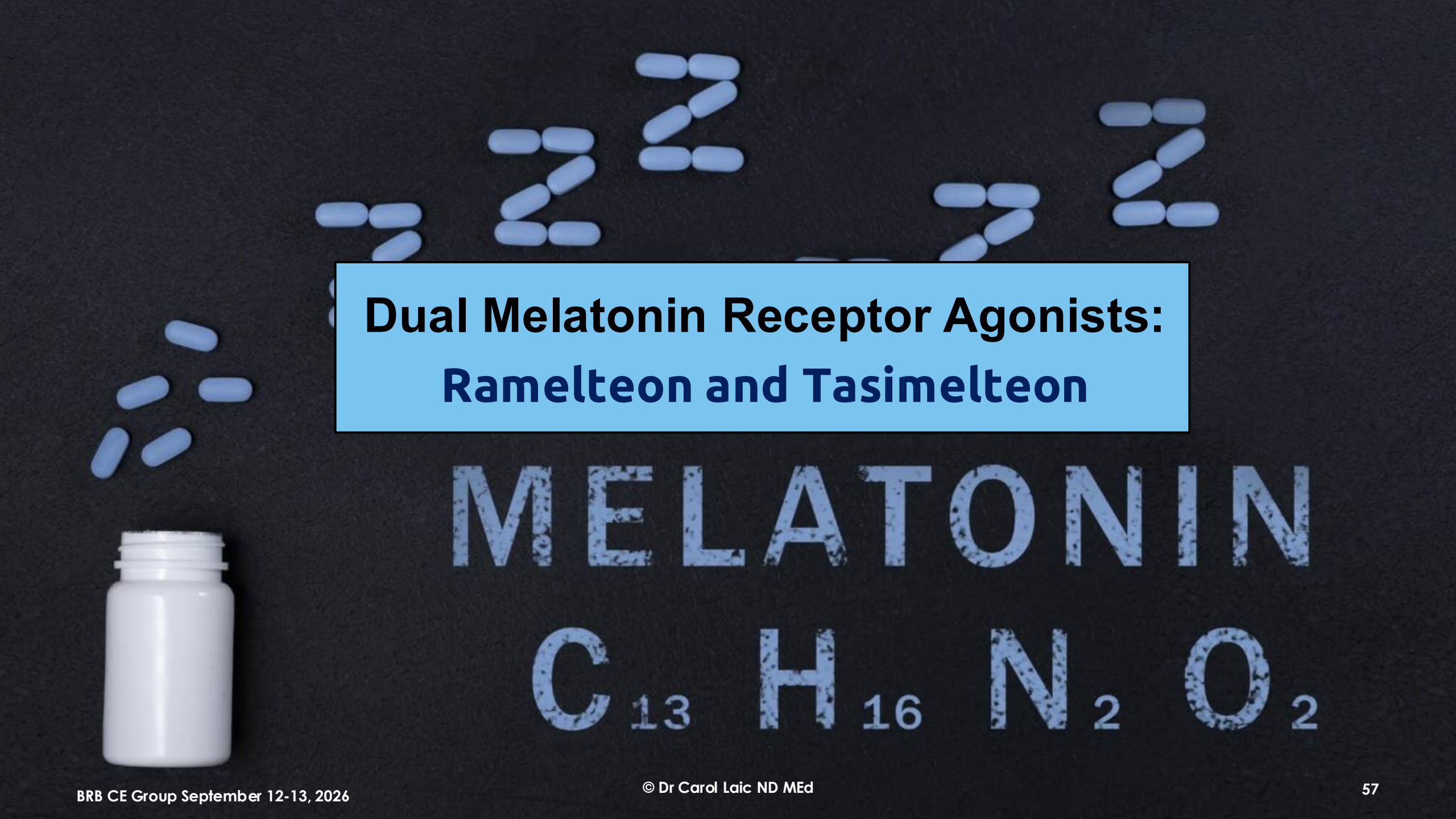
Sources: CAMH Sleep Disorders Pharmacotherapy Guidelines; Compendium of Therapeutic Choices (CTC), 9th ed.; Katzung's Basic & Clinical Pharmacology, 16th ed. (2024)

Comparing DORAs to GABA-ergic Agents: A Strategic Framework

Feature	DORAs (Lemborexant)	GABA-A Modulators (Z-drugs/BZDs)
Primary Action	Inhibits wakefulness signaling	Promotes global CNS inhibition
Dependency/Abuse	Low potential (non-controlled)	High potential (controlled substances)
Respiratory Impact	Negligible (safer for COPD/Sleep Apnea)	Can worsen respiratory depression and apnea
Balance/Coordination	Minimal impact on morning balance	Significant impact on postural stability
Patient Fit	Chronic insomnia, elderly, substance abuse history	Acute insomnia, need for strong sedation
Key Takeaway: DORAs represent a major safety advancement for chronic users and the elderly.		

Sources: Compendium of Therapeutic Choices (CTC), 9th ed.; CAMH Sleep Disorders Pharmacotherapy Guidelines; HQO Insomnia Quality Standard (2025)

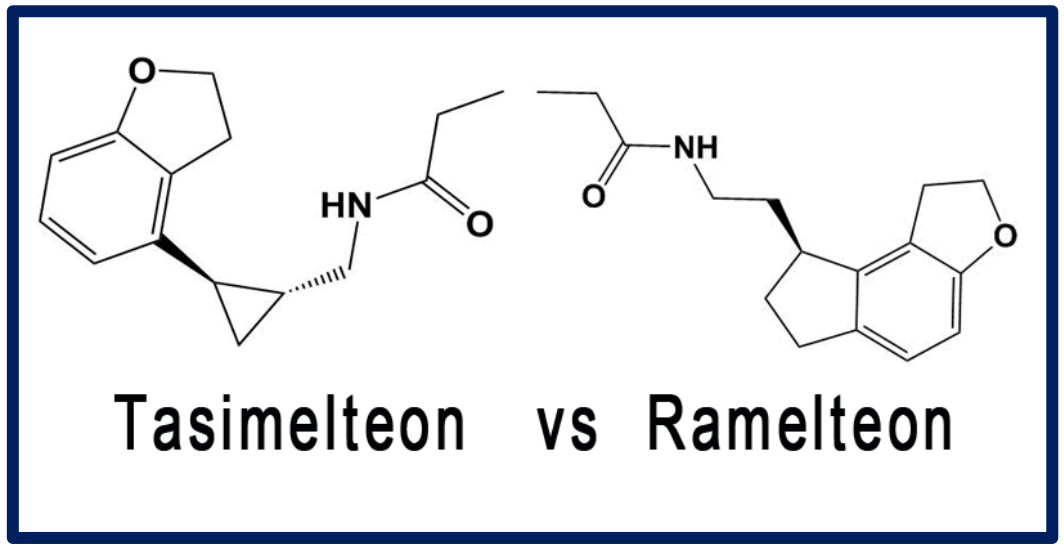
Dual Melatonin Receptor Agonists:
Ramelteon and Tasimelteon



Melatonin Receptor Stimulators: Ramelteon and Tasimelteon

Tasimelteon (Hetlioz)

- Dual MT1/MT2 agonist focusing on entraining the circadian clock
- Indicated for Non-24-Hour Sleep-Wake Disorder in totally blind individuals
- Requires consistent daily dosing at the same time to reset the master clock



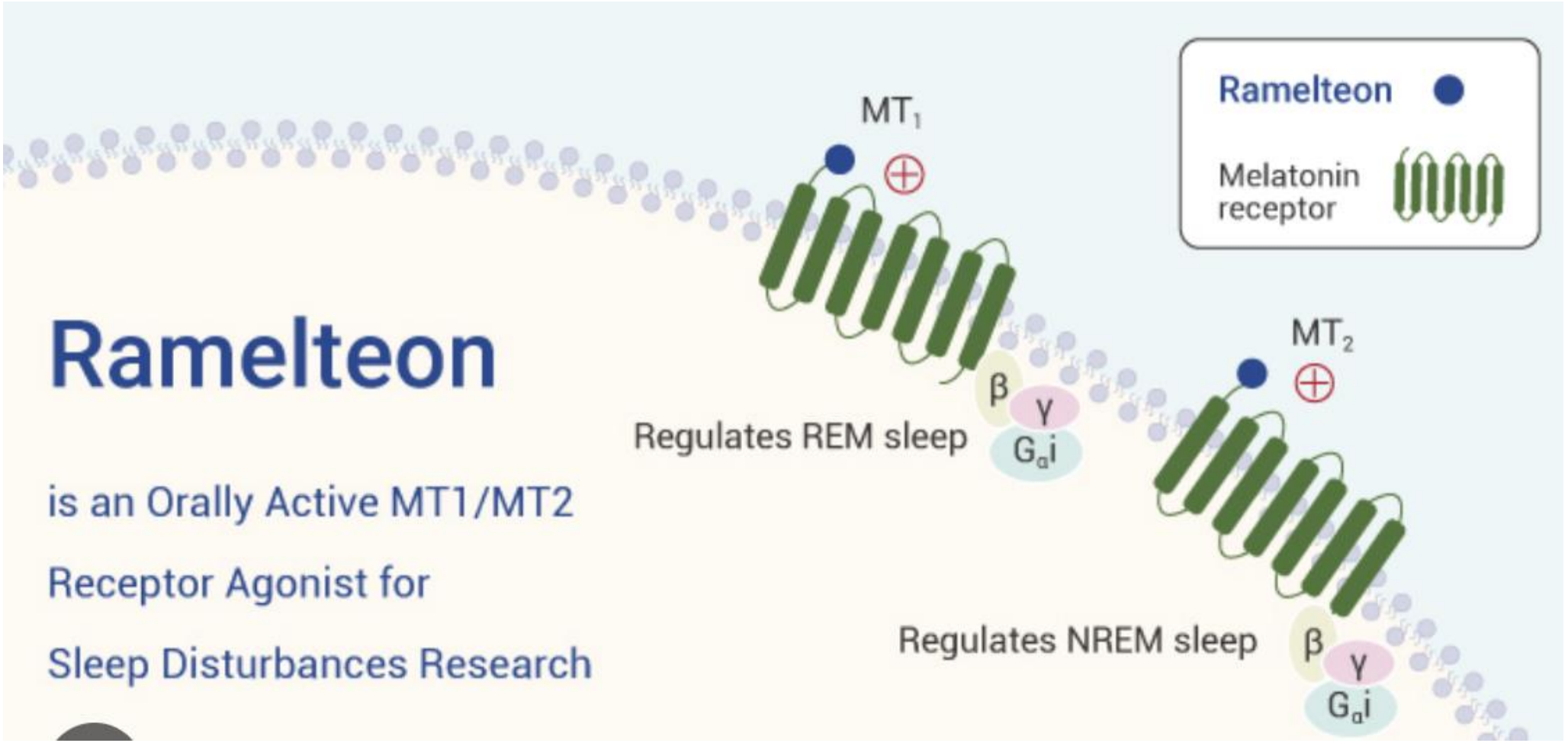
Ramelteon (Rozerem)

- High affinity for MT1 (sleep induction) and MT2 (circadian reset) receptors
- Indicated for primary insomnia with difficulty sleep onset
- No evidence of abuse or dependency
- Effective for 'night owl' tendencies and Delayed Sleep Phase Disorder

Advantage over OTC Melatonin

- Much higher potency and more consistent bioavailability compared to over-the-counter melatonin supplements

Sources: Compendium of Therapeutic Choices (CTC), 9th ed.; CPS Drug Monographs (Canadian Pharmacists Association); CAMH Sleep Disorders Pharmacotherapy Guidelines



https://www.immune-system-research.com/2024/06/27/ramelteon-is-an-orally-active-mt1-mt2-receptor-agonist-for-sleep-disturbances-research/

RAMELTEON

▶https://www.thecarlatreport.com/articles/3321-is-ramelteon-an-effective-hypnotic -

A CARLAT PSYCHIATRY REFERENCE TABLE

Ramelteon: At a Glance	
FDA indications	Primary insomnia
Advantages	Safety in elderly, lack of tolerance or abuse
Other uses	Possible benefits in delirium and bipolar depression
Dosage	8 mg nightly or prn
Side effects	Next-day fatigue, headache, nausea
Interactions	Avoid with CYP1A2 inhibitors, like fluvoxamine, which raise ramelteon levels (inducers, like smoking, lower levels); high-fat meals delay its onset by 1 hour
Contraindications	None
Cost	$2–3/tab (expected to drop over next year)

From the Article:
"Is Ramelteon an Effective Hypnotic?"
by **Randall Moore, MD**
The Carlat Psychiatry Report, Volume 18, Number 11 & 12, November/December 2020
www.thecarlatreport.com

TASIMELTEON

Generic name	Tasimelteon
Trade name	Hetlioz™
Drug class	Melatonin receptor agonist
Formulation, dosing, and administration	Available as 20-mg capsules; recommended dose: 20 mg orally once nightly before bed-time; take without food
Adverse reactions	Headache, increased ALT, nightmares/ abnormal dreams, upper respiratory tract infection, urinary tract infection
Drug interactions	Strong CYP1A2 inhibitors, such as fluvoxamine, strong CYP3A4 inducers such as rifampin, strong CYP3A4 inhibitors such as ketoconazole
Comparable drugs	Ramelteon, agomelatine
Advantage	High affinity for MT2 and entrainment of circadian rhythm. Longer half-life relative to melatonin

Abbreviations: ALT, alanine aminotransferase; CYP, cytochrome P; MT2, melatonin 2.

Table 1. Overview of Tasimelteon.12

Published in Journal of pharmacy and practice 2015

Tasimelteon (Hetlioz™)

▶https://www.semanticscholar.org/paper/Tasimelteon-(Hetlioz%E2%84%A2)-Bonacci-Venci/be1cb8d1ae1a702295b98ec2ed2c01a4af9d15bd/figure/0

DOSING MELATONIN

Population	Rationale for Melatonin	Strength of Evidence	Recommended Formulation
Older adults ≥55	Physiological melatonin deficiency; largest effect sizes on sleep outcomes	Moderate (physiological rationale strong; RCT data mixed)	PR melatonin 2 mg, 1–2 h before bed
Disrupted circadian rhythms	Chronobiotic effect restores interdaily stability	Low (single substudy)	PR melatonin 2–10 mg or IR 1 mg for circadian correction
Severe mental illness	Improved subjective sleep quality during taper	Low (single RCT, small sample)	PR melatonin 2 mg
Patients needing safe adjunct	No abuse potential; minimal interactions; very low toxicity	Expert consensus	PR melatonin 2 mg

Why Use Melatonin Agonists Over OTC Melatonin Supplements?

Receptor Potency

Ramelteon has 3-16x higher binding affinity for MT1 receptors than endogenous melatonin, producing more robust sleep-induction signals.

Metabolic Stability

Synthetic agonists resist rapid first-pass metabolism, providing predictable blood levels vs variable OTC melatonin.

Pharmaceutical Quality

FDA/Health Canada approved drugs ensure 100% purity and dosage accuracy; OTC melatonin often contains 83% to 478% of labeled dose.

No Next-Day Impairment

Generally do not cause daytime somnolence, brain fog, or motor impairment.

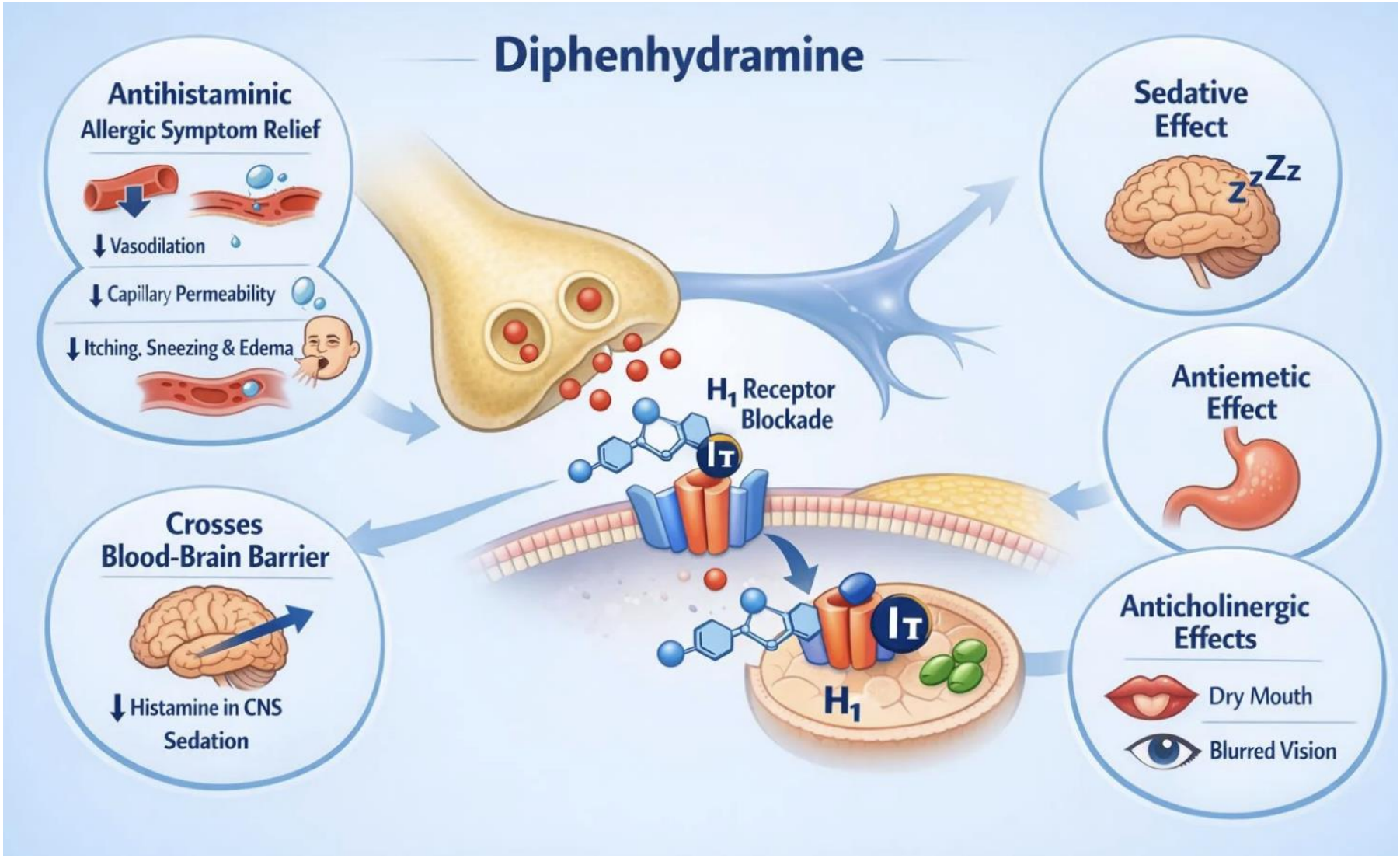
Sources: Compendium of Therapeutic Choices (CTC), 9th ed.; Mayo Clinic Sleeping Pills Guide; ScienceDirect Sleep Medicine Reviews (2024)

DOXYLAMINE 25mg

DIPHENHYDRAMINE 50mg

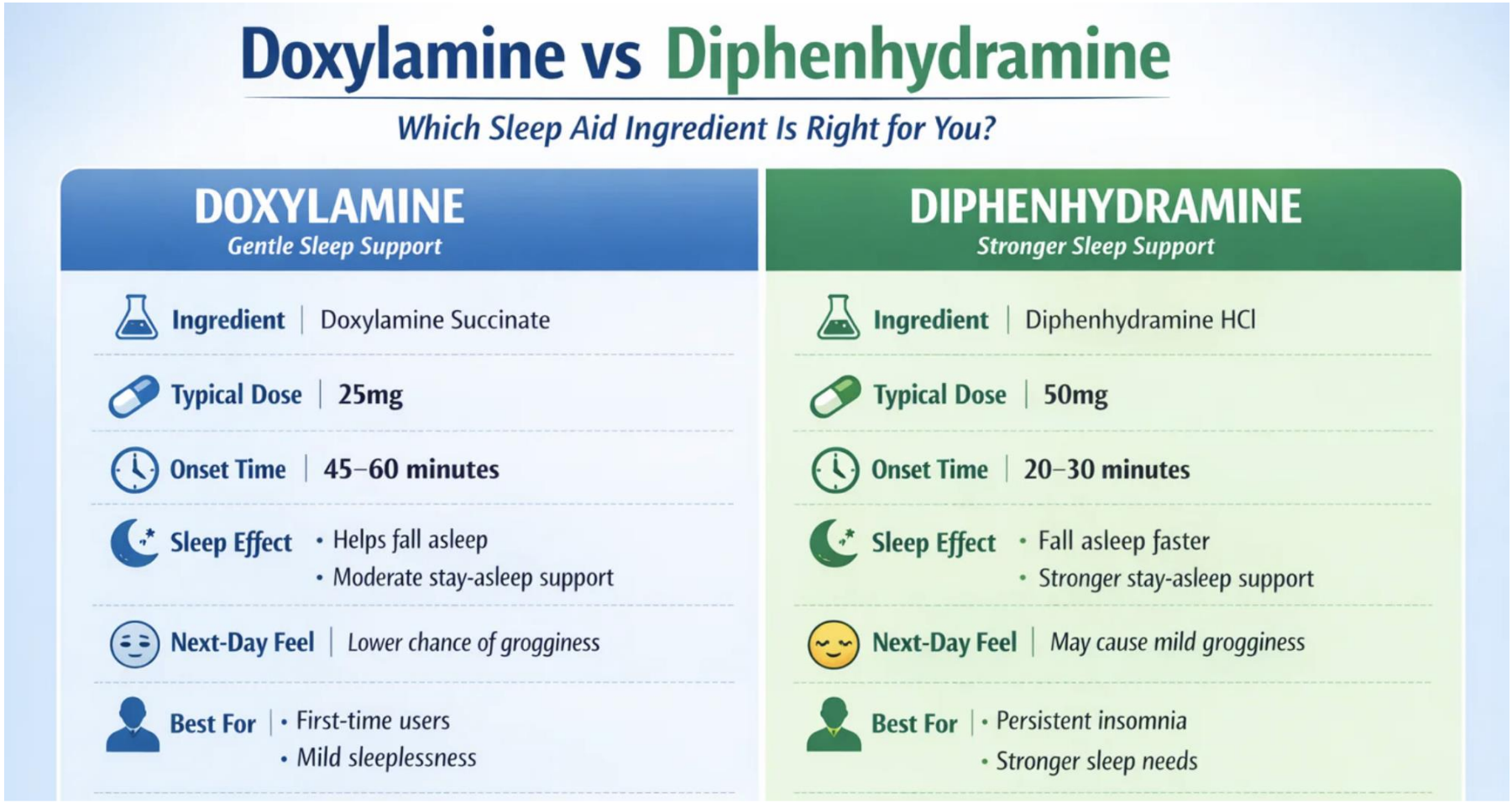
OTC SLEEP AID

MOA



https://pharmacyfreak.com/mechanism-of-action-of-diphenhydramine/

OTC SLEEP AIDS



https://shopycatch.com.au/blogs/news/kirkland-sleep-aid-vs-healtha2z-which-is-better-for-australians-in-2026?srsltid=AfmBOooDjLzybIlJBHkXcnmjRs5fjskFgBsdt5MuyAGcLqlxdkAZj-xf

OTC Sleep Aids: First Generation Antihistamines and Their Risks

Active Ingredients

Diphenhydramine (Benadryl) and Doxylamine Succinate (Unisom) — primary sedating antihistamines in OTC 'PM' products.

Safety Warning

Prolonged use in elderly strongly discouraged due to increased delirium and accelerated cognitive decline risk.

DOXYLAMINE

+

DIPHENHYDRAMINE

Mechanism

Both cross the blood-brain barrier and antagonize H1 receptors in brain arousal centers.

Efficacy Limits

Tolerance develops rapidly (within 3-4 days of nightly use); 'ceiling effect' where increasing dose adds no further benefit.

Anticholinergic Burden

Block muscarinic receptors causing dry mouth, blurred vision, urinary retention, and cognitive 'hangover'.

Sources: Compendium of Therapeutic Choices (CTC), 9th ed.; Mayo Clinic Sleeping Pills Guide; HQO Insomnia Quality Standard (2025)

"Antihistamines make patients sleepy—but not necessarily rested."

While diphenhydramine and doxylamine can facilitate sleep onset, they often impair normal sleep quality, produce next-day cognitive impairment, and rapidly lose effectiveness with repeated use.

Serious Side Effect	Clinical Importance
Falls / fractures	Significant concern over 65years
Delerium	In susceptible ptx
Respiratory depression	Increases with opioids, alcohol, benzodiazepines, cannabinoids
Cardiac arrhythmias	Na+-channel blockade (severe overdose)
Seizures / Hallucinations	With large dose
Acute urinary retention	Especially with BPH
Anticholinergic toxicity	Hyperthermia, agitation, hallucinations, urinary retention, tachycardia, dilated pupils

Clinical Pearls Summary:

H1 antihistamines

- Diphenhydramine and doxylamine are f**irst-generation antihistamines** - their sedative effects are accompanied by significant anticholinergic adverse effects.
- Doxylamine generally produces **longer-lasting sedation** (longer elimination half-life) This increases the likelihood of next-day drowsiness, impaired driving, cognitive slowing, and workplace accidents.
- **Tolerance** to the sedative effects develops rapidly (often within 3–7 days)
- Both medications are listed on the American Geriatrics Society **Beers Criteria** as potentially inappropriate medications for older adults (increase the risk of delirium, cognitive decline, falls, fractures, urinary retention, and constipation)
- **CI:** Patients with benign prostatic hyperplasia (BPH), narrow-angle glaucoma, chronic constipation, dementia, or significant cardiovascular disease
- **Additive CNS depression** may substantially increase the risk of falls, impaired cognition, respiratory depression, and motor vehicle accidents.
- **Minimizing long-term anticholinergic exposure** is considered a prudent clinical strategy, particularly in older adults.
- Current Canadian and international insomnia guidelines do not recommend routine use of OTC antihistamines for chronic insomnia - When pharmacologic therapy is necessary, **other agents** with stronger evidence and lower anticholinergic burden are generally preferred.

DIPHENHYDRAMINE and DOXYLAMINE

Naturopathic Perspectives: Melatonin and Valerian Root Evidence

1

1. Melatonin (Natural)

Most effective for circadian rhythm disruptions (jet lag, shift work) rather than primary chronic insomnia; optimal doses 0.5mg to 3mg.

2

2. Valerian Root (Valeriana officinalis)

Thought to inhibit GABA breakdown and potentially act as weak GABA-A agonist; requires 2-4 weeks of consistent use for maximum effect.

3

3. Clinical Meta-Analysis

Both have small to moderate effect sizes compared to prescription Z-drugs or DORAs in clinical trials.

4

4. Safety Profile

Generally excellent, but caution patients about quality of store-brand products and potential heavy metal contamination.

Sources: ScienceDirect Sleep Medicine Reviews (2024); Psychology Today - Insomnia Treatment Recommendations (2025); CAMH Sleep Disorders Pharmacotherapy Guidelines

SUMMARY: Critical Drug-Herb-Nutrient Interactions

Sleep Drug	Interacting Agent	Mechanism	Clinical Significance
Benzodiazepines/Z-drugs	Kava, Valerian, St. John's Wort	Additive CNS depression / CYP450 inhibition	Increased sedation, respiratory depression risk
Zolpidem	Grapefruit Juice	CYP3A4 inhibition	Increased zolpidem levels, enhanced effects
Trazodone	5-HTP, SAMe, Tryptophan	Serotonin syndrome risk	Agitation, hyperthermia, reflex hyperactivity
DORAs	Strong CYP3A4 inhibitors	Reduced DORA metabolism	Dose adjustment required
All sedatives	Magnesium, GABA supplements	Additive CNS depression	Enhanced sedation, cognitive impairment

Sources: Lexi Drug interaction modules (Canadian Pharmacists Association); Compendium of Therapeutic Choices (CTC), 9th ed.; ScienceDirect Clinical Pharmacology Studies (2024)

Identifying Best Candidates: Matching Drug to Patient Profile

Profile 1 — Acute Stress Insomnia

Profile 2 — Chronic Insomnia with Depression

Profile 3 — Elderly Patient with Fall Risk

Profile 4 — Shift Worker/ Jet Lag

Profile 5 – Frequent Waking

Sources: Compendium of Therapeutic Choices (CTC), 9th ed.; HQO Insomnia Quality Standard (2025); CDA-AMC Insomnia Drugs Protocol (2025)

Short-Term Strategy (1-4 Weeks)

Acute situational insomnia treatment using BZDs or Z-drugs with CBT-I referral; taper plan established upfront to prevent dependence

Deprescribing Protocol

Reduce dose by 25% every 2 weeks; substitute long-acting with short-acting if rebound occurs; melatonin support during taper

Long-Term Strategy (3+ Months)

Chronic insomnia management with DORAs or Ramelteon; address root causes (pain, mood, hormones) and integrate Naturopathic interventions

Sources: HQO Insomnia Quality Standard (2025); CDA-AMC Insomnia Drugs Protocol (2025); Psychology Today - Insomnia Treatment Restructured (2025)

Red Flags: When to Refer or Escalate Care

Sleep-Related Breathing Disorders

Snoring, gasping, witnessed apneas; sedatives can worsen OSA

Parasomnias

Sleepwalking, sleep terrors, REM behavior disorder

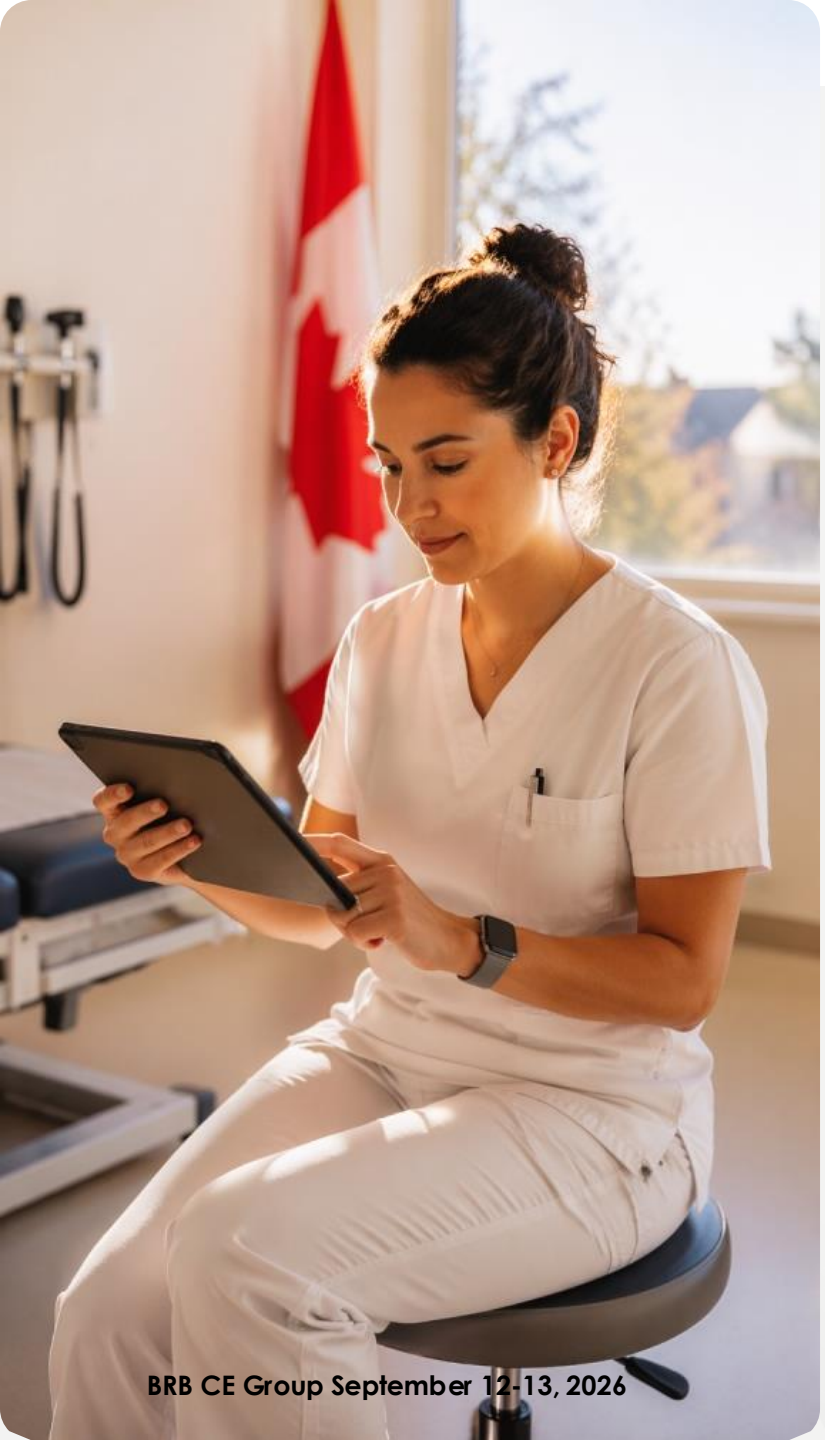
Psychiatric Emergencies

Suicidal ideation, severe depression, psychosis

Shift Work Disorder

Requires circadian rhythm interventions

Sources: CDA-AMC Insomnia Drugs Protocol (2025); Canadian Primary Care Today - Sleep Management Guidelines; CFP (Canadian Family Physician) Sleep Article



Canadian Guidelines Update: Key Recommendations for 2026

CBT-I as First-Line

All guidelines now prioritize Cognitive Behavioral Therapy for Insomnia as the initial treatment before pharmacological intervention.

Deprescribing Protocols

New frameworks for tapering BZDs and Z-drugs in long-term users; emphasis on patient-centered approaches.

DORA Recommendations

DORAs now recommended for elderly patients and those with fall risk history.

Pregnancy Considerations

New safety data on Trazosin and BZDs during pregnancy; melatonin remains preferred natural option.

Sources: HQO Insomnia Disorder Quality Standard (2025); CDA-AMC Insomnia Drugs Proposed Protocol (2025); Canadian Primary Care Today - Chow et al.

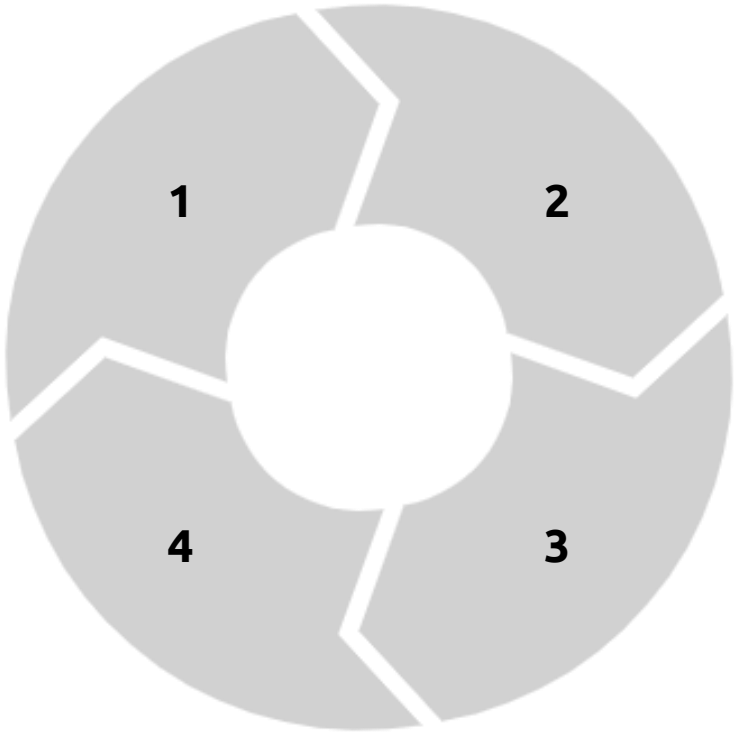
Integrating Naturopathic Approaches with Pharmacological Treatment

Stage 1 — Foundation

Address sleep hygiene, circadian light exposure, and nutritional timing before medication.

Stage 2 — Complementary

Layer herbal supports (ashwagandha, passionflower) with low-dose medication for synergistic effect.



Stage 4 — Maintenance

Transition to evidence-based natural supplements once pharmaceutical support is reduced; monitor sleep logs.

Stage 3 — Weaning Support

Use adaptogens and nervines during medication taper to reduce rebound insomnia.

Sources: CAMH Sleep Disorders Pharmacotherapy Guidelines; Psychology Today - Insomnia Treatment Recommendations (2025); ScienceDirect Sleep Medicine Reviews (2024)

Key Takeaways: Essential Points for Clinical Practice

1

1. Match Drug Half-Life to Symptom Pattern

Sleep-onset insomnia requires short-acting agents; maintenance needs intermediate or long-acting medications.

2

2. DORAs Offer Superior Safety Profile

Preferred for elderly patients, chronic use, and individuals at fall-risk.

3

3. Always Check CYP Interactions

Even 'natural' supplements can significantly alter drug metabolism pathways.

4

4. Combine with CBT-I

Pharmacotherapy should be adjunctive to cognitive behavioral therapy, not a standalone treatment.

5

5. Plan Deprescribing from Day One

Establish taper protocol before initiating any treatment regimen.

Sources: HQO Insomnia Quality Standard (2025); CDA-AMC Insomnia Drugs Protocol (2025); Compendium of Therapeutic Choices (CTC), 9th ed.

Canadian guidelines for insomnia — what CADTH, Health Canada, and Canadian clinicians recommend

CADTH (the Canadian Drug and Technologies in Health agency — now part of the broader Canadian health technology assessment framework) has published systematic reviews and rapid evidence reports on insomnia treatment. Key findings from CADTH insomnia reviews:

- **CBT-I produces durable outcomes:** CADTH evidence reviews note that CBT-I benefits persist at 12- and 24-month follow-up, unlike pharmacotherapy whose effects are tied to continued use.
- **Pharmacotherapy is appropriate short-term:** For acute insomnia (less than 4 weeks), short-term use of sleep medication may be appropriate as a bridge while CBT-I is initiated or accessed.
- **Z-drugs carry dependency risk:** CADTH reviews highlight the dependency, tolerance, and rebound insomnia risks of z-drugs (zopiclone, zolpidem) and benzodiazepines, supporting guideline recommendations to limit their duration.
- **Digital CBT-I is effective:** CADTH has reviewed digital health technologies and found app-based and internet-delivered CBT-I programs clinically comparable to therapist-delivered treatment, improving access in underserved regions of Canada.
- **What CADTH means for your treatment:** If your family physician prescribes a sleeping pill as a first response to chronic insomnia without discussing CBT-I, that does not align with current Canadian evidence-based guidelines. You can ask specifically about CBT-I referral or access.

https://worldsleepday.org/usetoolkit/resources

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March 13, 2026

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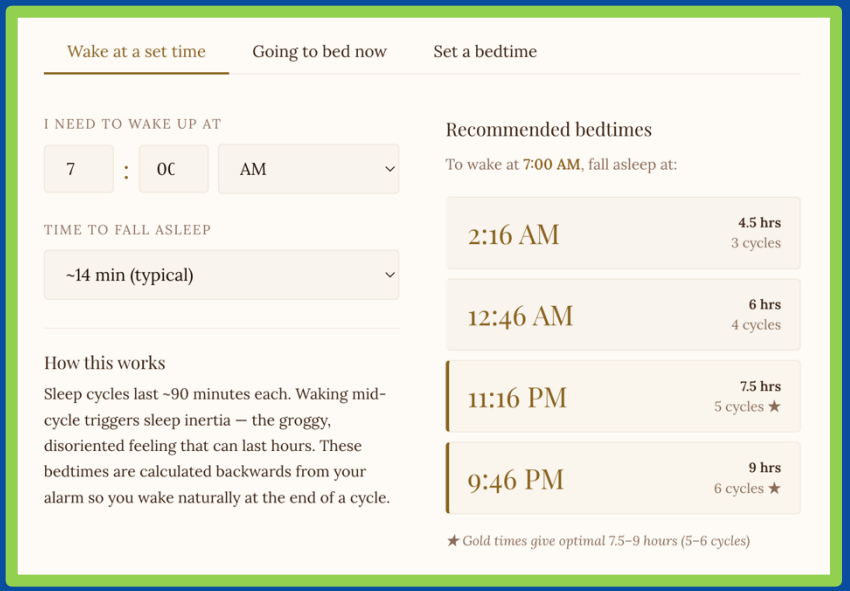
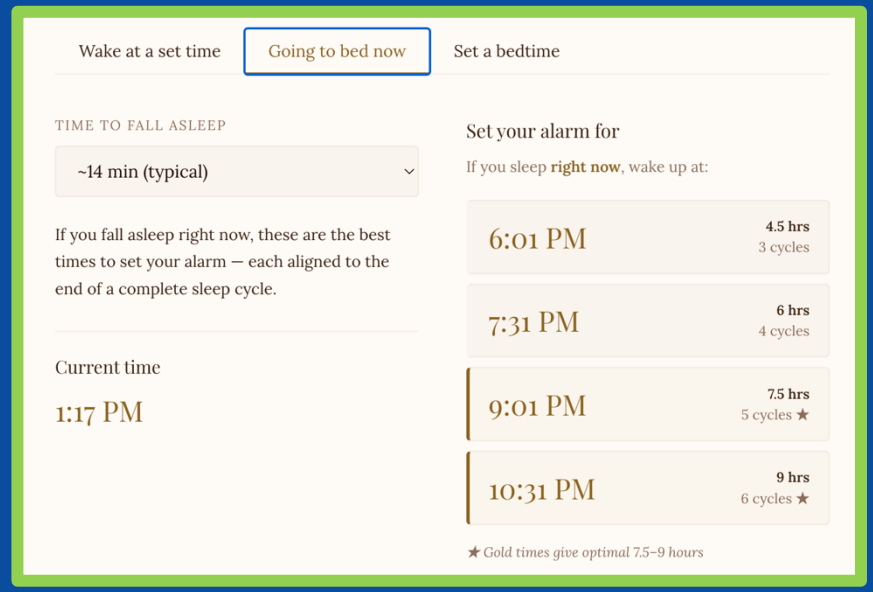
New Frontier's

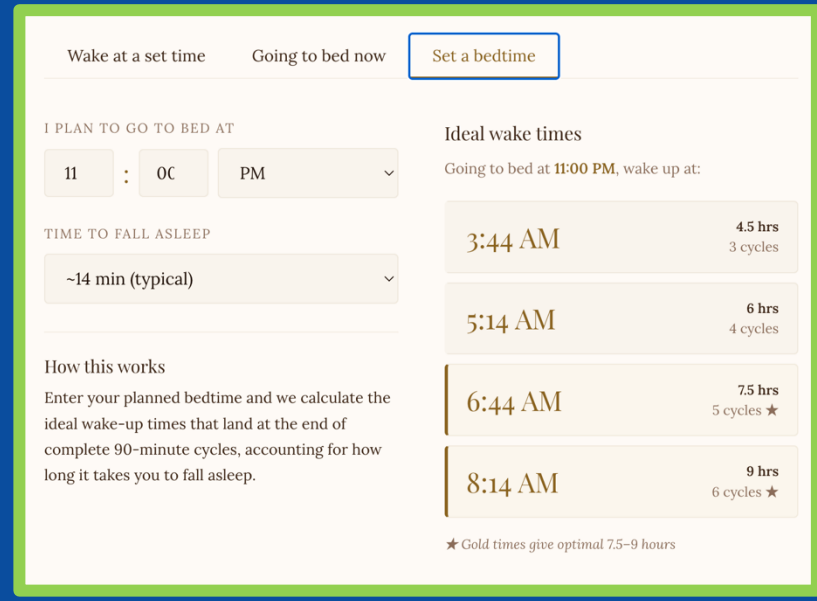
- Digital CBT-1 (app) – auditory tones, mild electrical stimulation,etc
- Smart-phone based tracking
- Other Orexin drugs (single orexin targets)
- Cannabinol
- Precision medicine: Personalized therapies based on demographics, genetics, co-morbidities
- Non-invasive neuromodulation

https://www.nature.com/articles/d41586-025-00963-x

FREE SLEEP TOOL







https://www.gotosleep.ca/tools/sleep-calculator

Questions?