Anxiolytics & Sleep Aids: Advanced Clinical Reference

💊 Comparative Pharmacology and Clinical Applications

This comprehensive reference provides detailed comparisons between anxiolytics and sleep aids for psychiatric prescribers, with evidence-based clinical pearls and monitoring recommendations.

🧠 Mechanism of Action and Receptor Pharmacology

CLASS	PRIMARY MECHANISM	RECEPTOR SPECIFICITY	CLINICAL IMPLICATIONS
🔵 Benzodiazepines (Bounds & Nelson, 2024)	GABA-A positive allosteric modulator	Variable α-subunit selectivity: • α1: sedation, amnesia • α2/α3: anxiolysis • α5: cognitive effects	• Rapid onset of action • Cross-tolerance with alcohol • Dependence/ withdrawal risk
🟣 Z-drugs (Gunja, 2013)	GABA-A positive allosteric modulator	Preferential α1-subunit selectivity	• Less myorelaxation than BZDs • Theoretically less cognitive impact • Still carries dependence risk
🟠 Buspirone (Wilson & Tripp, 2023)	5-HT_{1a} partial agonist	High affinity for 5-HT_{1a} receptors	• Delayed onset (2-4 weeks) • No dependence potential • No cross-tolerance with BZDs
🟢 Hydroxyzine (Entringer, 2022)	H_1 antagonist	• H_1 receptors • Mild anticholinergic • Mild 5-HT_{2a} antagonism	• Rapid onset • No dependence potential • Sedation may diminish over time
🟡 Pregabalin(Pope, 2023)	$\alpha_2\delta$ calcium channel modulator	Binds to $\alpha_2\delta$ subunit of voltage-gated calcium channels	• Anxiolytic and

analgesic effects
• Lower abuse potential than BZDs

CLASS	PRIMARY MECHANISM	RECEPTOR SPECIFICITY	CLINICAL IMPLICATIONS
			• Effective for somatic anxiety
🔴 Gabapentin (Yasaei et al., 2024)	$\alpha_2\delta$ calcium channel modulator	Binds to $\alpha_2\delta$ subunit of voltage-gated calcium channels	• Similar to pregabalin but less potent • Variable absorption • Effective for somatic anxiety
🟤 Melatonin Receptor Agonists (Spadoni et al., 2010)	Melatonin receptor agonism	• MT_1 receptor: sleep onset • MT_2 receptor: circadian phase	• Minimal next-day effects • No dependence potential • Minimal drug interactions
⚪ Orexin Receptor Antagonists (Cecilio Álamo et al., 2024)	Orexin receptor antagonism	• OX_1 and OX_2 receptors • Blocks wake-promoting signals	• Novel mechanism of action • No dependence potential • Minimal impact on sleep architecture

📊 Comparative Efficacy for Anxiety Disorders

MEDICATION	GAD	PANIC DISORDER	SOCIAL ANXIETY	PTSD	SPECIFIC PHOBIA
🔵 Diazepam (Dhaliwal et al., 2023)	★★★★☆ • Rapid onset • Short-term use only • Tolerance develops	★★★☆☆ • Effective for acute attacks • Not ideal for prevention • High-potency BZDs preferred	★★★☆☆ • Effective for performance anxiety • Not first-line for generalized type • PRN use can be appropriate	★★☆☆☆ • May help with hyperarousal • Can worsen emotional processing • Not recommended as monotherapy	★★★★☆ • Effective for situational use • Useful for exposure therapy • PRN for specific situations

🔵 Clonazepam	★★★★☆ • Longer duration than diazepam • Less interdose anxiety • Still for short-term use	★★★★☆ • First-line among BZDs • Longer half-life beneficial • Less rebound anxiety	★★★★☆ • Effective for both types • Less sedation than alprazolam • Still not first line	★★☆☆☆ • Similar limitations to diazepam • May help with sleep • Not recommended as monotherapy	★★★☆☆ • Longer duration may be less ideal • Less "as needed" flexibility • Effective when used

MEDICATION	GAD	PANIC DISORDER	SOCIAL ANXIETY	PTSD	SPECIFIC PHOBIA
🔵 Alprazolam	★★★★☆ • Rapid onset • Short half life problematic • High dependence risk	★★★★☆ • Extensively studied • Effective for acute attacks • Interdose anxiety common	★★★☆☆ • Effective for performance anxiety • Short duration beneficial for PRN • High dependence risk	★★☆☆☆ • Not recommended • Rebound anxiety problematic • May worsen trauma processing	★★★☆☆ • Short duration good for PRN • Rapid onset beneficial • High potency effective
🟣 Buspirone (Wilson & Tripp, 2023)	★★★☆☆ • Delayed onset (2-4 weeks) • No dependence potential • Less effective than SSRIs	★☆☆☆☆ • Not effective • No benefit for acute attacks • Not recommended	★★☆☆☆ • Limited efficacy • Delayed onset problematic • Not first-line	★☆☆☆☆ • Not effective • No significant benefit shown • Not recommended	★☆☆☆☆ • Not effective • Delayed onset impractical • Not recommended
⬜ Hydroxyzine (Entringer, 2022)	★★★☆☆ • Moderate efficacy • No dependence potential • Sedation may limit use	★★☆☆☆ • Limited efficacy • May help with acute symptoms • Not first-line	★★☆☆☆ • Limited efficacy • May help with somatic symptoms • Not first-line	★★☆☆☆ • May help with insomnia • Limited efficacy for core symptoms • Adjunctive role only	★★☆☆☆ • May help with anticipatory anxiety • Sedation can be beneficial • Limited evidence

Pregabalin	★★★★☆ • Effective • Rapid onset (days vs weeks) • Approved in Europe for GAD	★★☆☆☆ • Limited evidence • May help with somatic symptoms • Not first-line	★★★☆☆ • Effective • Helps with somatic symptoms • Less studied than SSRIs	★★☆☆☆ • Limited evidence • May help with hyperarousal • Not first-line	★☆☆☆☆ • Not studied • Not recommended • Other options preferred

Comparative Efficacy for Insomnia

MEDICATION	SLEEP ONSET	SLEEP MAINTENANCE	NEXT-DAY EFFECTS	LONG-TERM EFFICACY
Temazepam	★★★★☆ • Effective • Intermediate	★★★★☆ • Effective • Intermediate half-	★★☆☆☆ • Moderate risk • Dose-dependent • Worse in elderly	★☆☆☆☆ • Tolerance develops • Efficacy wanes over time • Not recommended beyond 2-4 weeks
	onset (20-30 min) • Intermediate half-life	life beneficial • Less early morning awakening		
Triazolam	★★★★★ • Very effective • Rapid onset (15-30 min) • Ultra-short half life	★★☆☆☆ • Limited efficacy • Early morning awakening common • Rebound insomnia risk	★★★☆☆ • Less than longer acting BZDs • Anterograde amnesia risk • Rebound anxiety possible	★☆☆☆☆ • Tolerance develops rapidly • Rebound insomnia common • High dependence potential

☐ Zolpidem (Gunja, 2013)	★★★★★ • Very effective • Rapid onset (15-30 min) • Selective for sleep induction	★★☆☆☆ • Limited efficacy • Early morning awakening common • Extended release improves	★★★☆☆ • Less than BZDs • Dose-dependent • Complex sleep behaviors possible	★★☆☆☆ • Tolerance develops • Less than BZDs • Still not recommended beyond 4 weeks
☐ Eszopiclone	★★★★☆ • Effective • Rapid onset (15-30 min) • Longer half-life than zolpidem	★★★★☆ • Better than zolpidem • Longer half-life beneficial • Less early morning awakening	★★☆☆☆ • Metallic taste most common • Dose-dependent sedation • Less than longer acting BZDs	★★★☆☆ • Studied for up to 6 months • Less tolerance than BZDs • Still develops over time
☐ Ramelteon	★★★☆☆ • Moderate efficacy • Slower onset (30-45 min) • Minimal side effects	★☆☆☆☆ • Not effective • No impact on WASO • Not recommended	★★★★★ • Minimal next-day effects • No psychomotor impairment • No cognitive effects	★★★☆☆ • Maintains efficacy • No tolerance development • Limited overall efficacy
☐ Suvorexant (Cecilio Álamo et al., 2024)	★★★☆☆ • Moderate efficacy • Slower onset (30-45 min) • Dose dependent effects	★★★★☆ • Effective • Reduces WASO • Maintains efficacy	★★★☆☆ • Dose-dependent somnolence • Less than BZDs • Minimal cognitive effects	★★★★☆ • Maintains efficacy • No significant tolerance • Studied for up to 1 year
☐ Doxepin (low-dose) ★★☆☆☆ • Limited efficacy • Slower onset (30-45 min)	• Very effective • Reduces WASO • Reduces early morning awakening	★★★★☆ • Minimal at low doses (3-6mg) • Less anticholinergic than at antidepressant doses	No significant tolerance	
★★★★☆		★★★★☆ • Maintains efficacy •		

MEDICATION	SLEEP ONSET	SLEEP MAINTENANCE	NEXT-DAY EFFECTS	LONG-TERM EFFICACY
	• Not primary indication		• Minimal cognitive effects	• Studied for up to 12 weeks

Trazodone	★★★☆☆ • Moderate efficacy • Intermediate onset (30-60 min) • Sedation primary effect	★★★☆☆ • Moderate efficacy • May reduce awakenings • Variable response	★★☆☆☆ • Residual sedation common • Orthostatic hypotension risk • Cognitive effects possible	★★★☆☆ • Maintains efficacy • No significant tolerance • Limited long-term data

Pharmacokinetics and Dosing Considerations

MEDICATION	HALF-LIFE	ONSET/ DURATION	METABOLISM	DOSING PEARLS
Diazepam (Dhaliwal et al., 2023)	• 20-80 hours • Active metabolites: 50-100 hours • Significant accumulation	• Onset: 15-30 min • Duration: 6-24 hours • Longer with repeated dosing	• CYP3A4, CYP2C19 • Active metabolites: nordazepam, oxazepam, temazepam • Significant drug interactions	• Start: 2-5mg BID/ TID • Elderly: 2mg daily BID • Reduce dose in hepatic impairment • Longer interval in elderly
Clonazepam	• 30-40 hours • No active metabolites • Less accumulation than diazepam	• Onset: 30-60 min • Duration: 8-12 hours • Less interdose anxiety	• CYP3A4 • Nitro-reduction • Fewer drug interactions than diazepam	• Start: 0.25-0.5mg BID • Elderly: 0.125-0.25mg daily BID • Gradual titration reduces sedation • BID dosing preferred
Alprazolam	• 11-16 hours • Minor active metabolites • Minimal accumulation	• Onset: 15-30 min • Duration: 4-6 hours • Interdose anxiety common	• CYP3A4 • Significant drug interactions • Grapefruit juice increases levels	• Start: 0.25-0.5mg TID • Elderly: 0.125-0.25mg BID • TID-QID dosing often needed • XR formulation reduces interdose anxiety
	• 2-3 hours • Active metabolite: 1-	• Onset: 2-4	• CYP3A4	• Start: 5mg BID-TID

		weeks		
Buspirone (Wilson & Tripp, 2023)		• Duration: 4-6	• Significant first-pass metabolism	• Target: 15-30mg daily in divided

MEDICATION	HALF-LIFE	ONSET/ DURATION	METABOLISM	DOSING PEARLS
	pyrimidinylpiperazine • No accumulation	hours per dose • Requires consistent dosing	• Food increases absorption	doses • TID dosing preferred • Take consistently with/without food
☐ Hydroxyzine (Entringer, 2022)	• 20-25 hours • Active metabolite: cetirizine • Moderate accumulation	• Onset: 15-30 min • Duration: 6-8 hours • Sedation may diminish over time	• CYP2D6 • Minimal drug interactions • Renal elimination of metabolites	• Anxiety: 25-50mg TID-QID • Insomnia: 25-100mg at bedtime • Elderly: reduce dose by 50% • Anticholinergic burden in elderly
☐ Pregabalin (Pope, 2023)	• 6-7 hours • No active metabolites • Minimal accumulation	• Onset: 1-2 days • Duration: 8-12 hours per dose • Requires BID TID dosing	• Not metabolized by CYP enzymes • Renal elimination (unchanged) • Minimal drug interactions	• Start: 75mg BID • Target: 300-600mg daily in divided doses • Reduce dose in renal impairment • Take with/without food consistently
☐ Gabapentin (Yasaei et al., 2024)	• 5-7 hours • No active metabolites • Minimal accumulation	• Onset: 1-2 days • Duration: 6-8 hours per dose • Requires TID dosing	• Not metabolized by CYP enzymes • Renal elimination (unchanged) • Saturable absorption	• Start: 300mg at bedtime • Titrate: add 300mg every 1-3 days • Target: 900-3600mg daily in divided doses • Take with food to increase absorption

Ramelteon	• 1-2.6 hours • Active metabolite: M-II (2-5 hours) • No accumulation	• Onset: 30-45 min • Duration: 6-8 hours • Take 30 min before bedtime	• CYP1A2 • Significant first-pass metabolism • Fluvoxamine contraindicated	• Fixed dose: 8mg at bedtime • No dose adjustment needed in elderly • Take 30 min before bedtime • Avoid high-fat meals before dosing
Suvorexant (Cecilio Álamo et al., 2024)	• 12 hours • No significant active metabolites • Moderate accumulation	• Onset: 30-45 min • Duration: 8 hours • Take 30 min before bedtime	• CYP3A4 (major) • CYP2C19 (minor) • Significant drug interactions	• Start: 10mg at bedtime • Maximum: 20mg at bedtime • Elderly: 5-10mg at bedtime • Take 30 min before bedtime

Adverse Effects and Management Strategies

MEDICATION	COMMON ADVERSE EFFECTS	SERIOUS ADVERSE EFFECTS	MANAGEMENT STRATEGIES	CONTRAINDICATIONS

Benzodiazepines (Bounds & Nelson, 2024)	• Sedation/ somnolence • Cognitive impairment • Ataxia/dizziness • Anterograde amnesia • Muscle relaxation	• Respiratory depression • Paradoxical reactions • Physical dependence • Withdrawal seizures • Falls/fractures in elderly	• Use lowest effective dose • Limit duration (2-4 weeks ideally) • Gradual tapering (10-25% every 1-2 weeks) • Cognitive behavioral therapy for insomnia • Avoid alcohol and other CNS depressants	• Sleep apnea • Severe respiratory insufficiency • Myasthenia gravis • Acute narrow-angle glaucoma • Pregnancy/ breastfeeding (relative)
Z-drugs (Gunja, 2013)	• Sedation/ somnolence • Dizziness • Headache • Metallic taste (eszopiclone) • GI disturbances	• Complex sleep behaviors • Physical dependence • Withdrawal insomnia • Falls/fractures in elderly • Rare anaphylaxis	• Use lowest effective dose • Limit duration (2-4 weeks ideally) • Take immediately before bedtime • Ensure 8 hours available for sleep • Avoid alcohol and other CNS depressants	• Sleep apnea • Severe hepatic impairment • History of complex sleep behaviors • Pregnancy/ breastfeeding • Alcohol consumption

Buspirone
• Dizziness
• Headache
• Nausea
• Nervousness • Lightheadedness
• Serotonin syndrome (with SSRIs/SNRIs)
• Rare movement disorders
• Rare elevation of 7

• Divided dosing reduces side effects
• Take with food consistently
• Allow 2-4 weeks
• MAOIs within 14 days • Severe hepatic or renal impairment
• Hypersensitivity
• Caution with CYP3A4 inhibitors

MEDICATION	COMMON ADVERSE EFFECTS	SERIOUS ADVERSE EFFECTS	MANAGEMENT STRATEGIES	CONTRAINDICATIONS
		blood pressure • Rare chest pain	for full effect • Avoid abrupt discontinuation • Monitor for serotonin syndrome with SSRIs	
☐ Hydroxyzine (Entringer, 2022)	• Sedation/ somnolence • Dry mouth • Blurred vision • Constipation • Urinary retention	• QT prolongation • Anticholinergic toxicity in elderly • Rare blood dyscrasias • Rare hypersensitivity reactions	• Divided dosing reduces side effects • Anticholinergic management (hydration, etc.) • Avoid in elderly when possible • Monitor ECG with high doses or risk factors • Tolerance to sedation may develop	• QT prolongation • History of torsades de pointes • Hypokalemia/ hypomagnesemia • Concurrent QT prolonging drugs • Elderly with significant comorbidities
☐ Pregabalin (Pope, 2023)	• Dizziness • Somnolence • Peripheral edema • Weight gain • Blurred vision	• Angioedema • Hypersensitivity reactions • Suicidal ideation (rare) • Physical dependence • Withdrawal symptoms	• Gradual titration reduces side effects • Divided dosing reduces side effects • Monitor weight and edema • Gradual discontinuation (over 1+ week) • Monitor mood changes	• Hypersensitivity • Significant renal impairment without dose adjustment • History of substance abuse (relative) • Caution in heart failure (edema)

☐ Gabapentin (Yasaei et al., 2024)

	symptoms • DRESS syndrome (rare)		effects • Take with food to increase absorption • Divided dosing reduces side effects • Gradual discontinuation	• History of substance abuse (relative) • Caution in elderly (falls risk)
• Dizziness • Somnolence • Ataxia • Fatigue • Peripheral edema • Respiratory depression (with opioids) • Suicidal ideation (rare) • Physical dependence • Withdrawal		8 • Gradual titration reduces side	• Hypersensitivity • Significant renal impairment without dose adjustment	

MEDICATION	COMMON ADVERSE EFFECTS	SERIOUS ADVERSE EFFECTS	MANAGEMENT STRATEGIES	CONTRAINDICATIONS
			(over 1+ week) • Monitor respiratory status with opioids	
☐ Ramelteon	• Dizziness • Somnolence • Fatigue • Nausea • Exacerbated insomnia	• Angioedema • Hypersensitivity reactions • Rare behavioral changes • Rare hormonal effects (↓ testosterone, ↑ prolactin)	• Take 30 minutes before bedtime • Avoid high-fat meals before dosing • Avoid activities after taking • No dose adjustment needed in elderly • No tapering needed for discontinuation	• Severe hepatic impairment • Concurrent fluvoxamine use • History of angioedema with ramelteon • Concurrent strong CYP1A2 inhibitors
☐ Suvorexant (Cecilio Álamo et al., 2024)	• Somnolence • Headache • Dizziness • Abnormal dreams • Dry mouth	• Complex sleep behaviors • Sleep paralysis • Hypnagogic/ hypnopompic hallucinations • Suicidal ideation (rare) • Worsening depression	• Take 30 minutes before bedtime • Ensure 8 hours available for sleep • Avoid activities after taking • Lower dose in elderly • Avoid with strong CYP3A4	• Narcolepsy • Severe hepatic impairment • Concurrent strong CYP3A4 inhibitors • History of complex sleep behaviors

			inhibitors	

Drug Interactions and Combination Strategies

MEDICATION	SIGNIFICANT INTERACTIONS	EFFECT ON OTHER DRUGS	COMBINATION STRATEGIES	SPECIAL POPULATIONS
Benzodiazepines (Bounds & Nelson, 2024) • CNS depressants: additive effects • CYP3A4 inhibitors: ↑ levels	• CYP3A4 inducers: ↓ levels • Opioids: respiratory depression • Alcohol: enhanced sedation • Minimal effect on other drugs • No significant	enzyme induction • No significant enzyme inhibition • Protein binding displacement possible • With antidepressants:	monitor for sedation • With antipsychotics: monitor for sedation, falls • Avoid with opioids when possible • With Z-drugs: avoid combination • With	• Elderly: ↓ dose by 50%, prefer short acting • Hepatic impairment: ↓ dose, prefer oxazepam/ lorazepam • Pregnancy: potential teratogenicity,

MEDICATION	SIGNIFICANT INTERACTIONS	EFFECT ON OTHER DRUGS	COMBINATION STRATEGIES	SPECIAL POPULATIONS
			anticonvulsants: monitor for sedation	neonatal withdrawal • Respiratory disorders: caution, monitor closely
Z-drugs (Gunja, 2013)	• CNS depressants: additive effects • CYP3A4 inhibitors: ↑ levels (zolpidem, eszopiclone) • CYP3A4 inducers: ↓ levels • Food: delayed absorption (zolpidem) • Alcohol: enhanced sedation	• Minimal effect on other drugs • No significant enzyme induction • No significant enzyme inhibition • Less protein binding issues than BZDs	• With antidepressants: monitor for sedation • With antipsychotics: monitor for sedation, falls • Avoid with opioids when possible • With BZDs: avoid combination • Take on empty stomach for faster onset	• Elderly: ↓ dose by 50% • Women: lower doses (especially zolpidem) • Hepatic impairment: ↓ dose • Pregnancy: limited data, avoid if possible • Asian patients: lower metabolism, ↓ dose

☐ Buspirone (Wilson & Tripp, 2023)	• MAOIs: hypertensive crisis • SSRIs/SNRIs: serotonin syndrome risk • CYP3A4 inhibitors: ↑ levels significantly • CYP3A4 inducers: ↓ levels significantly • Grapefruit juice: ↑ levels	• Minimal effect on other drugs • No significant enzyme induction • No significant enzyme inhibition • No sedative potentiation	• With SSRIs/SNRIs: effective combination, monitor for serotonin syndrome • With antipsychotics: generally safe combination • With BZDs: can be used during BZD taper • With anticonvulsants: monitor for efficacy if enzyme inducers	• Elderly: standard dosing • Hepatic impairment: ↓ dose • Renal impairment: ↓ dose • Pregnancy: limited data, risk/ benefit assessment • Children: limited data on efficacy
☐ Hydroxyzine (Entringer, 2022)	• CNS depressants: additive effects • QT-prolonging drugs: additive QT prolongation • Anticholinergics: additive anticholinergic effects • Alcohol: enhanced sedation • Minimal effect on other drugs • No significant enzyme inhibition • Additive anticholinergic effects	• With antidepressants: monitor for anticholinergic effects • With antipsychotics: monitor QT, anticholinergic effects • With BZDs: generally avoid due to additive sedation • Elderly: avoid or ↓ dose, anticholinergic risk • Hepatic impairment: ↓ dose • Cardiac disorders: monitor QT interval • Pregnancy: limited data, generally considered safe		

MEDICATION	SIGNIFICANT INTERACTIONS	EFFECT ON OTHER DRUGS	COMBINATION STRATEGIES	SPECIAL POPULATIONS
			• With antihistamines: avoid combination (additive effects)	• Children: established pediatric dosing

Pregabalin (Pope, 2023)	• CNS depressants: additive effects • Thiazolidinediones: additive edema risk • Alcohol: enhanced sedation • Opioids: respiratory depression risk • ACEIs: increased angioedema risk	• No significant CYP interactions • No enzyme induction • No enzyme inhibition • No protein binding issues	• With antidepressants: generally safe combination • With antipsychotics: monitor for sedation • With BZDs: monitor for excessive sedation • With opioids: monitor respiratory status • With anticonvulsants: often beneficial combinations	• Elderly: standard dosing, monitor for sedation • Renal impairment: dose adjustment required • Cardiac disorders: monitor for edema • Pregnancy: limited data, animal studies show toxicity • History of substance abuse: monitor closely
Gabapentin (Yasaei et al., 2024)	• CNS depressants: additive effects • Antacids: ↓ absorption (space by 2h) • Opioids: respiratory depression risk • Alcohol: enhanced sedation	• No significant CYP interactions • No enzyme induction • No enzyme inhibition • No protein binding issues	• With antidepressants: generally safe combination • With antipsychotics: monitor for sedation • With BZDs: monitor for excessive sedation • With opioids: monitor respiratory status • With anticonvulsants: often beneficial combinations	• Elderly: start low, titrate slowly • Renal impairment: dose adjustment required • Dialysis patients: supplemental dose after dialysis • Pregnancy: registry data relatively reassuring • Children: established pediatric dosing for epilepsy
Ramelteon	• CYP1A2 inhibitors: ↑ levels significantly • Fluvoxamine: contraindicated • CYP2C9 inhibitors: moderate effect • CYP3A4 inhibitors: moderate effect • Alcohol: additive effects • No significant effect on other drugs • No enzyme	induction • No enzyme inhibition • No hormonal contraceptive interactions	• With antidepressants: generally safe except fluvoxamine • With antipsychotics: generally safe combination	• With BZDs: can be used during BZD taper • Elderly: no dose adjustment needed • Hepatic impairment: avoid in

MEDICATION	SIGNIFICANT INTERACTIONS	EFFECT ON OTHER DRUGS	COMBINATION STRATEGIES	SPECIAL POPULATIONS
			• With melatonin: avoid combination (similar mechanism)	animal studies show no harm • Sleep apnea: generally safe
☐ Suvorexant (Cecilio Álamo et al., 2024)	• CYP3A4 inhibitors: ↑ levels significantly • CYP3A4 inducers: ↓ levels significantly • CNS depressants: additive effects • Alcohol: enhanced sedation	• No significant effect on other drugs • No enzyme induction • No enzyme inhibition • No hormonal contraceptive interactions	• With antidepressants: generally safe combination • With antipsychotics: monitor for excessive sedation • With BZDs: avoid combination • With alcohol: avoid combination	• Elderly: lower starting dose (5mg) • Hepatic impairment: avoid in severe impairment • Women: higher blood levels than men • Obesity: higher blood levels • Narcolepsy: contraindicated

☐ Neuropsychiatric Effects and Cognitive Impact

MEDICATION	COGNITIVE EFFECTS	NEUROPSYCHIATRIC EFFECTS	LONG-TERM CONSIDERATIONS	PATIENT SELECTION FACTORS
☐ Benzodiazepines	• Anterograde amnesia • Psychomotor slowing • Attention/ concentration deficits • Word-finding difficulties • Impaired learning	• Paradoxical reactions (elderly, children) • Depression (long term use) • Disinhibition • Emotional blunting • Increased suicide risk in some studies	• Cognitive effects may persist after discontinuation • Tolerance to anxiolytic effects develops • Dependence risk increases with duration • Withdrawal can be protracted • Possible link to dementia (controversial)	• Better for acute, short-term anxiety • Avoid in cognitive impairment • Avoid in substance use disorders • Avoid in elderly when possible • Caution in depression
☐ Z-drugs • Less anterograde amnesia than BZDs • Less next-day cognitive effects • Complex sleep behaviors • Hallucinations (rare) • Parasomnia behaviors • Depression (less than BZDs) • Suicidal ideation (rare)				

	• Cognitive effects generally resolve with discontinuation • Tolerance develops but possibly less than BZDs • Dependence risk increases with • Better for sleep	onset insomnia • Avoid in substance use disorders • Caution in elderly (falls risk) • Avoid with		

MEDICATION	COGNITIVE EFFECTS	NEUROPSYCHIATRIC EFFECTS	LONG-TERM CONSIDERATIONS	PATIENT SELECTION FACTORS
	possible • Driving impairment next day • Memory consolidation effects	• Aggression/agitation (rare)	duration • Withdrawal similar to BZDs but possibly milder • Less evidence for dementia link	alcohol • Caution with respiratory disorders
☐ Buspirone (Wilson & Tripp, 2023)	• Minimal cognitive effects • No significant memory impairment • No psychomotor impairment • No attention deficits • No anterograde amnesia	• Dizziness • Headache • Nervousness/ activation • No depression risk • No disinhibition	• No cognitive decline with long-term use • No tolerance to anxiolytic effects • No dependence potential • No withdrawal syndrome • No rebound anxiety	• Better for generalized anxiety • Good for elderly patients • Good with cognitive concerns • Good for substance use disorders • Not effective for panic attacks
☐ Hydroxyzine	• Sedation/ drowsiness • Mild anticholinergic effects • Attention/ concentration effects • Less amnesia than BZDs • Tolerance to cognitive effects develops	• Confusion (elderly) • Delirium risk (anticholinergic) • No depression risk • No disinhibition • No paradoxical reactions	• Tolerance to sedative effects develops • No dependence potential • No withdrawal syndrome • No rebound anxiety • Anticholinergic burden in elderly	• Better for anxiety with insomnia • Good for situational/acute anxiety • Good for substance use disorders • Avoid in elderly (anticholinergic) • Avoid in dementia

☐ Pregabalin • Somnolence/ sedation • Attention/ concentration effects • Dizziness • Word-finding difficulties • Less amnesia than BZDs • Euphoria (abuse potential) • Mild mood elevation • Visual disturbances • Rare psychosis • Weight gain	• Cognitive effects generally resolve with discontinuation • Minimal tolerance to anxiolytic effects • Physical dependence possible • Withdrawal syndrome with abrupt discontinuation • Weight gain may continue • Better for anxiety with neuropathic pain •	Good for somatic anxiety symptoms • Caution in substance use disorders • Caution in suicidal ideation • Avoid in

MEDICATION	COGNITIVE EFFECTS	NEUROPSYCHIATRIC EFFECTS	LONG-TERM CONSIDERATIONS	PATIENT SELECTION FACTORS
				significant weight concerns
☐ Gabapentin	• Somnolence/ sedation • Attention/ concentration effects • Dizziness • Word-finding difficulties • Less amnesia than BZDs	• Mood changes • Irritability • Visual disturbances • Rare psychosis • Weight gain	• Cognitive effects generally resolve with discontinuation • Minimal tolerance to anxiolytic effects • Physical dependence possible • Withdrawal syndrome with abrupt discontinuation • Weight gain may continue	• Better for anxiety with neuropathic pain • Good for somatic anxiety symptoms • Variable absorption limits reliability • Caution in substance use disorders • Avoid in significant weight concerns

Ramelteon	• Minimal cognitive effects • No significant memory impairment • No psychomotor impairment • No attention deficits • No anterograde amnesia	• Headache • Dizziness • Somnolence • Worsening insomnia (rare) • Abnormal dreams	• No cognitive decline with long-term use • No tolerance to hypnotic effects • No dependence potential • No withdrawal syndrome • No rebound insomnia	• Better for circadian rhythm disorders • Good for elderly patients • Good with cognitive concerns • Good for substance use disorders • Limited overall efficacy
Suvorexant	• Minimal next day cognitive effects • Somnolence • Less amnesia than BZDs • Minimal psychomotor effects • Abnormal dreams	• Sleep paralysis • Hypnagogic hallucinations • Complex sleep behaviors (rare) • Worsening depression (monitor) • Suicidal ideation (rare)	• Minimal cognitive effects with long-term use • Minimal tolerance to hypnotic effects • Low dependence potential • Mild withdrawal possible • Minimal rebound insomnia	• Better for sleep maintenance insomnia • Good for elderly patients • Good with cognitive concerns • Caution in depression • Contraindicated in narcolepsy

Clinical Pearls and Practical Considerations

MEDICATION CLASS	UNIQUE ADVANTAGES	CLINICAL PEARLS	COMMON PITFALLS	PATIENT EDUCATION POINTS

Benzodiazepines (Bounds & Nelson, 2024)	• Rapid onset of action • High efficacy for acute anxiety • Multiple formulations available • Established safety profile • Flexible dosing	• Clonazepam has less abuse potential than alprazolam • Lorazepam/ oxazepam safer in hepatic impairment • Diazepam has smoother offset due to metabolites • Taper by 10-25% every 1-2 weeks • Consider adjunctive CBT during taper	• Prescribing for longer than intended • Inadequate monitoring for misuse • Failure to address underlying disorders • Overlooking fall risk in elderly • Overlooking drug interactions	• Take exactly as prescribed • Do not stop abruptly • Avoid alcohol completely • Do not drive if sedated • Report any unusual mood changes
Z-drugs (Gunja, 2013)	• Less muscle relaxation than BZDs • Potentially less cognitive impact • Shorter half-life options available • Less respiratory depression • Extended-release formulations available	• Zolpidem affects women more than men • Eszopiclone has longer duration of action • Zaleplon useful for middle-of-night awakening • Take on empty stomach for faster onset • Sublingual formulations for faster onset	• Prescribing higher than recommended doses • Overlooking complex sleep behaviors • Failure to ensure adequate sleep opportunity • Overlooking fall risk in elderly • Prescribing for longer than FDA approved duration	• Take immediately before bedtime • Ensure 7-8 hours available for sleep • Do not take with or after a meal • Report any sleep behaviors (eating, driving) • Avoid alcohol completely
Buspirone (Wilson & Tripp, 2023)	• No dependence potential • No withdrawal syndrome • No cognitive impairment • No sedation • Safe in elderly	• Requires 2-4 weeks for full effect • Often underdosed (target: 15-30mg daily) • TID dosing more effective than BID • Food increases absorption by 50% • Can be safely combined with SSRIs	• Inadequate dosing • Discontinuing too early (before effect) • Expecting immediate relief • Missing significant drug interactions • Using for panic disorder (ineffective)	• May take 2-4 weeks for full effect • Continue even if initially ineffective • Take consistently with/ without food • Not addictive or sedating • Report dizziness or nausea

☐ Hydroxyzine

MEDICATION CLASS	UNIQUE ADVANTAGES	CLINICAL PEARLS	COMMON PITFALLS	PATIENT EDUCATION POINTS
	• No dependence potential • Rapid onset of action • Multiple formulations available • Antihistamine properties beneficial for allergic symptoms • PRN or scheduled dosing options	• Higher doses for anxiety than for allergies • Tolerance to sedation develops • Anticholinergic burden in elderly • QT prolongation risk at high doses • Can be used for sleep or anxiety	• Overlooking anticholinergic effects in elderly • Missing QT prolongation risk • Inadequate dosing for anxiety • Overlooking drug interactions • Sedation limiting daytime use	• May cause drowsiness • Dry mouth common side effect • Avoid driving until effects known • Tolerance to sedation may develop • Not addictive
☐ Pregabalin	• Rapid onset compared to antidepressants • Effective for somatic anxiety • Beneficial for comorbid pain • Minimal drug interactions • Linear pharmacokinetics	• Schedule V controlled substance • Start low, titrate gradually • BID dosing sufficient due to high bioavailability • Dose adjustment needed in renal impairment • Weight gain monitoring important	• Overlooking abuse potential • Failure to adjust dose in renal impairment • Overlooking weight gain • Abrupt discontinuation • Underdosing for anxiety	• Take exactly as prescribed • Do not stop abruptly • Monitor for weight gain • May cause dizziness initially • Report any swelling or visual changes

☐ Gabapentin	• Minimal drug interactions • Beneficial for comorbid pain • No hepatic metabolism • Multiple formulations available • Off-label but widely used	• Absorption decreases with increasing doses • Take with food to increase absorption • TID dosing necessary due to short half-life • Higher doses needed for anxiety than epilepsy • Dose adjustment needed in renal impairment	• Overlooking saturable absorption • Inadequate dosing frequency • Failure to adjust dose in renal impairment • Overlooking abuse potential • Abrupt discontinuation	• Take with food to increase absorption • Do not stop abruptly • Monitor for weight gain • May cause dizziness initially • Report any swelling or visual changes

☐ Ramelteon • No dependence potential • No withdrawal syndrome • No cognitive • Take 30 minutes before bedtime • Avoid high-fat meals before dosing • Most effective for

• Using for sleep maintenance insomnia • Taking too close to bedtime • Take 30 minutes before bedtime • Avoid high-fat meals before dosing

MEDICATION CLASS	UNIQUE ADVANTAGES	CLINICAL PEARLS	COMMON PITFALLS	PATIENT EDUCATION POINTS
	impairment • No restrictions on duration of use • Minimal drug interactions	sleep onset • Not effective for sleep maintenance • No dose adjustment in elderly	• Taking with high fat meal • Overlooking CYP1A2 interactions • Expecting significant hypnotic effects	• Not addictive or sedating • May cause dizziness • Report abnormal dreams
☐ Suvorexant	• Novel mechanism of action • Effective for sleep maintenance • Minimal tolerance development • Less respiratory depression than BZDs/Z-drugs • Studied for longer term use	• Schedule IV controlled substance • Take 30 minutes before bedtime • Lower doses in women and elderly • Significant CYP3A4 interactions • Contraindicated in narcolepsy	• Overlooking drug interactions • Using in narcolepsy patients • Failure to ensure adequate sleep opportunity • Overlooking next day effects • Combining with other sedatives	• Take 30 minutes before bedtime • Ensure 7-8 hours available for sleep • May cause drowsiness the next day • Report sleep paralysis or hallucinations • Avoid alcohol completely