
ANTI-HISTAMINES (Diphenhydramine, others) Fact Sheet [G]

Bottom Line:

Antihistamines can be very effective sleep aids for many patients, although some patients may experience too much grogginess (“hangover”) in the morning. They are good first-line agents due to a low risk of drug tolerance, dependence, or abuse, but exercise caution in the elderly, who are more sensitive to cognitive and peripheral effects.

FDA Indications:

Insomnia (adults, children 12–17 years); allergies; motion sickness; **antiparkinsonism**.

Off-Label Uses:

Extrapyramidal symptoms (EPS); nausea and vomiting (morning sickness).

Dosage Forms:

- **Tablets, chewable tablets, caplets, capsules, and oral solutions, varies by brand:** 25 mg, 50 mg.
- **Common brand names:**
 - **Diphenhydramine:** Benadryl, Compoz, Nytol, Simply Sleep, Sleep-Eze, Sominex, Unisom SleepGels, Unisom SleepMelts, and generic.
 - **Doxylamine:** NyQuil, Unisom SleepTabs, and generic.
 - **Hydroxyzine:** Atarax, Vistaril, and generic (see hydroxyzine fact sheet in this chapter).

Dosage Guidance:

Insomnia: Start 25 mg, 30 minutes before bedtime. The dose required to induce sleep can be as low as 6.25 mg, but usual dose is 25 mg. Some patients may require 50 mg at bedtime.

Monitoring: No routine monitoring recommended unless clinical picture warrants.

Cost: \$

Side Effects:

- Most common: Dry mouth, ataxia, urinary retention, constipation, drowsiness, memory problems.
- Serious but rare: Blurred vision, tachycardia.
- Pregnancy/breastfeeding: Considered safe.

Mechanism, Pharmacokinetics, and Drug Interactions:

- Histamine H1 antagonist.
- Metabolized by liver, primarily CYP2D6; $t_{1/2}$: for diphenhydramine, 3.5–9 hours; for doxylamine, 10 hours (12–15 in elderly).
- Avoid use with other antihistamines or anticholinergics (additive effects).

Clinical Pearls:

- These antihistamines non-selectively antagonize central and peripheral histamine H1 receptors. They also have secondary anticholinergic effects, which can cause side effects including dry mouth, constipation, and urinary retention, as well as cognitive impairment in susceptible populations.
- Be aware that anticholinergic drugs are often used to treat or prevent EPS in patients taking antipsychotics; diphenhydramine is often chosen and dosed at night to take advantage of its sedative effect.
- Antihistamines can be helpful for some patients with anxiety. See hydroxyzine fact sheet.

Fun Fact:

The name NyQuil is a portmanteau of “night” and “tranquil.”