BETA-ADRENERGIC ANTAGONIST

Propranolol

Inderal LA, InnoPran XL, Hemangeol

Nonselective, CNS-penetrant beta-blocker used off-label for performance anxiety, akathisia, and lithium tremor.

ANXIETY DOSE	HALF-LIFE	METABOLISM	ONSET
10-40 mg PO 30-60 min prior	3-6 h IR; 8-11 h LA	CYP2D6, 1A2, 2C19; 1st-pass	1-2 h; peak effect 1-1.5 h

No FDA boxed warning on the current US label.

INDICATIONS

- FDA-approved for hypertension, angina, atrial fibrillation, post-myocardial infarction protection, essential tremor, and migraine prophylaxis.
- FDA-approved for pheochromocytoma as an adjunct to alpha blockade and for hypertrophic subaortic stenosis; Hemangeol treats infantile hemangioma.
- Used off-label for performance or situational anxiety, where a single dose before a speech, audition, or examination blunts tremor and palpitations.
- Used off-label for antipsychotic-induced akathisia, where a Cochrane review supports central beta-blockers despite small and older trials.
- Used off-label for lithium-induced postural tremor, typically at low divided doses that do not compromise blood pressure.
- Used off-label for aggression and agitation after traumatic brain injury, where higher divided doses have modest supportive evidence.

DOSING & TITRATION

- Performance anxiety off-label: **10-40 mg** PO taken 30 to 60 minutes before the event, with a test dose at home before first real use.
- Akathisia off-label: **10-20 mg** PO two to four times daily, usually **30-80 mg/day**, titrated against pulse and blood pressure.
- Lithium-induced tremor off-label: **10-40 mg/day** PO in divided doses, or as needed before situations where tremor matters most.
- Essential tremor on label: start **40 mg** PO twice daily and titrate to 120-320 mg/day divided, using the long-acting form for adherence.
- Reduce the dose in hepatic impairment and in known CYP2D6 poor metabolizers, who show substantially higher plasma concentrations.
- Taper over 1 to 2 weeks when stopping chronic therapy, since abrupt withdrawal can precipitate angina, arrhythmia, or myocardial infarction.

MECHANISM OF ACTION

- Nonselective competitive antagonist at beta-1 and beta-2 adrenergic receptors, reducing heart rate, contractility, and peripheral tremor.
- Blocking peripheral beta receptors removes the somatic feedback of anxiety, including tachycardia, tremor, and voice quivering.
- High lipophilicity gives good central nervous system penetration, which is thought to underlie its benefit in akathisia and aggression.
- It does not treat the cognitive or worry component of anxiety, so it complements rather than replaces psychotherapy or serotonergic agents.
- Beta-2 blockade in bronchial smooth muscle causes the bronchoconstriction that makes it dangerous in asthma.

PHARMACOKINETICS

- Almost completely absorbed but heavily first-pass metabolized, so oral bioavailability is only about 25 percent and varies widely.
- Immediate-release half-life is 3-6 hours, while long-acting capsules provide 8-11 hours of exposure and once-daily dosing.
- Metabolized by CYP2D6, CYP1A2, and CYP2C19, so both CYP2D6 poor metabolizer status and enzyme inhibitors raise concentrations.
- Highly protein bound at about 90 percent and highly lipophilic, giving rapid brain penetration and central effects.
- Hepatic impairment markedly increases exposure and requires lower doses, while renal impairment has little effect on clearance.

ADVERSE EFFECTS

- Fatigue, bradycardia, hypotension, dizziness, and cold extremities are the common dose-related effects across all indications.
- Bronchospasm can be severe or fatal in asthma and in significant chronic obstructive pulmonary disease, which are effective contraindications.
- It masks the adrenergic warning signs of hypoglycemia except sweating and can delay glucose recovery in insulin-treated diabetes.
- Sleep disturbance, vivid dreams, and fatigue are reported, while the historical association with depression is weak and inconsistent.
- Abrupt discontinuation after chronic use can cause rebound tachycardia, hypertension, angina, and myocardial infarction.
- Sexual dysfunction, exercise intolerance, and worsening peripheral vascular symptoms are common reasons patients stop the drug.

MONITORING

- Check heart rate and blood pressure before starting and after each dose increase; hold or reduce the dose for pulse below 55 beats per minute.
- Screen specifically for asthma, chronic obstructive pulmonary disease, decompensated heart failure, and high-degree atrioventricular block.
- In diabetes, review glucose monitoring practice, since the usual adrenergic hypoglycemia warning signs will be blunted.
- For akathisia, measure response with the Barnes Akathisia Rating Scale and reassess the offending antipsychotic dose at the same time.
- Confirm that as-needed users know a single dose is for a discrete event and that daily escalation is not the intended pattern.

INTERACTIONS & CAUTIONS

- CYP2D6 inhibitors such as fluoxetine, paroxetine, bupropion, and quinidine substantially raise propranolol levels and adverse effects.
- CYP1A2 inhibitors including fluvoxamine, ciprofloxacin, and viloxazine also increase exposure, while smoking cessation raises levels further.
- Additive bradycardia and atrioventricular block with verapamil, diltiazem, digoxin, amiodarone, and cholinesterase inhibitors.
- Propranolol raises thioridazine and chlorpromazine concentrations and can potentiate hypotension with antipsychotics.
- Blunts the effect of beta-agonist rescue inhalers and can antagonize epinephrine used for anaphylaxis, complicating emergency treatment.

SPECIAL POPULATIONS

- Pregnancy: crosses the placenta and may cause fetal growth restriction, bradycardia, and neonatal hypoglycemia; use when clearly indicated.
- Lactation: relative infant dose is low and propranolol is generally considered compatible with breastfeeding with routine infant monitoring.
- Pediatric: Hemangeol is labeled for infantile hemangioma, and off-label psychiatric use in children requires cardiac screening first.
- Geriatric: start low because of bradycardia, orthostatic hypotension, fall risk, and reduced hepatic clearance with age.
- Hepatic impairment requires dose reduction, while renal impairment generally does not because metabolism is hepatic.

PRESCRIBING PEARLS

- It treats the body of anxiety, not the worry; pair it with therapy rather than using it daily.
- Asthma is a hard stop, and in diabetes it hides every hypoglycemia cue except sweating.
- Never stop chronic beta-blockade abruptly; taper over 1 to 2 weeks to avoid rebound ischemia.

References

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NOTE

References follow APA 7th edition style. Dosing, boxed warnings, and interaction data change; confirm every clinical decision against the current FDA prescribing information (DailyMed) and your institution's formulary. This sheet is an educational quick reference and does not replace the full label or clinical judgment.