Intuniv

(guanfacine ER)

Intuniv (guanfacine); not controlled

Full Prescribing Information	DailyMed Drug Information

Summary

Intuniv is extended-release guanfacine, a central alpha-2A adrenergic agonist approved for ADHD in patients 6 to 17 years, as monotherapy or added to a stimulant. It is a once-daily tablet dosed by body weight rather than by age, and its selectivity for the alpha-2A subtype makes it less sedating than clonidine. It is the alpha-2 agonist to reach for when a stimulant is insufficient or poorly tolerated and daytime sedation is the limiting concern. Not controlled; brand and generic.

Forms & Strengths

- **Tablets, extended release:** 1 mg, 2 mg, 3 mg, 4 mg; unscored
- **These are tablets, not capsules.** No guanfacine capsule exists in any form
- **Separate label:** immediate-release guanfacine tablets 1 mg and 2 mg (formerly Tenex), not interchangeable mg-for-mg

Dosing

- **Age:** 6-17 y/o; not established below 6 years
- **Onset:** sedation same day; ADHD benefit over weeks, trial endpoints at 5 to 8 weeks
- **Duration:** once daily, morning or evening, same time each day; half-life about 18 hours
- **Release Profile:** extended release from a matrix tablet; Cmax about 60% lower and AUC about 43% lower than immediate-release guanfacine, Tmax about 3 hours later, relative bioavailability 58%
- **Initial Dose:** 1 mg once daily
- **Titration:** no more than 1 mg every 7 days

- **Max Dose:** target 0.05 to 0.12 mg/kg/day, total 1 mg to 7 mg/day. Two age ceilings sit above the weight bands and both apply:
  - **6-12 y/o: do not exceed 4 mg/day**
  - **13-17 y/o: do not exceed 7 mg/day**
  - **As adjunct to a stimulant: do not exceed 4 mg/day** at any age
  - Under 25 kg: no weight band; dose from 0.05 to 0.12 mg/kg/day, starting at 1 mg
  - 25 to 33.9 kg: 2 to 3 mg/day
  - 34 to 41.4 kg: 2 to 4 mg/day
  - 41.5 to 49.4 kg: 3 to 5 mg/day
  - 49.5 to 58.4 kg: 3 to 6 mg/day
  - 58.5 to 91 kg: 4 to 7 mg/day
  - Over 91 kg: 5 to 7 mg/day
- **Considerations:** Swallow whole and do not give with a high-fat meal, which raises Cmax about 75%. Halve the dose with strong or moderate CYP3A4 inhibitors, and re-check the weight band as the child grows.

Pharmacology

- **Mechanism:** Central alpha-2 adrenergic agonist; reduces sympathetic outflow from the locus coeruleus and enhances prefrontal noradrenergic signalling. Alpha-2A selective, 15 to 20 fold. Mechanism in ADHD unknown.
- **Delivery / Release:** Matrix tablet; a high-fat breakfast raises Cmax about 75% and AUC about 40%.
- **Metabolism:** Primarily CYP3A4; neither inhibits nor induces major P450s. About 70% protein bound. Inhibits MATE1 and OCT1, which may raise OCT1 substrate exposure.
- **Pediatric exposure:** higher in 6-12 year olds than in adolescents at the same dose (4 mg: Cmax 10 vs 7 ng/mL, AUC 162 vs 116 ng.h/mL). Plasma level falls as weight rises, hence weight banding.
- **Cardiac:** a thorough QT study at 2 to 4 times maximum Intuniv concentrations showed no clinical QTc prolongation.
- **Class Positioning:** Less sedating than non-selective clonidine; once daily against twice-daily Kapvay, weight-banded, with a CYP3A4 profile clonidine lacks. Alpha-2 effect size about 0.7 against 1.0 for stimulants. (AAP 2019)

Indications

- **ADHD, as monotherapy** (ICD-10: F90.0, F90.1, F90.2, F90.8, F90.9): patients 6-17 y/o
- **ADHD, as adjunctive therapy to stimulants** (ICD-10: F90.0, F90.1, F90.2, F90.8, F90.9): patients 6-17 y/o

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Off-Label Uses

- **Tic disorders and Tourette syndrome** (ICD-10: F95.1, F95.2): a positive double-blind trial for tic severity, the better tic evidence of the two alpha-2 agonists. (AACAP 2013)
- **Oppositional defiant disorder, irritability and aggression** (ICD-10: F91.3): no eligible controlled pediatric evidence identified; insufficient
- **Irritability in autism spectrum disorder** (ICD-10: F84.0): limited data
- **Where the evidence does not support use:**
  - **Anxiety disorders** (ICD-10: F41.x): insufficient; no graded pediatric evidence identified
  - **Children under 6** (ICD-10: F90.x): insufficient (AHRQ 2018), and exposure rises as weight falls

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Contraindications & Warnings

- **Warning, rebound hypertension:** abrupt discontinuation has caused **persistent** rebound hypertension above baseline, with **hypertensive encephalopathy reported**
- **Contraindicated:** hypersensitivity to Intuniv, its excipients, or other guanfacine products; rash and pruritus reported
- **Use with caution:**
  - Hypotension, heart block, bradycardia, cardiovascular or cerebrovascular disease; titrate slowly
  - Syncope, orthostatic hypotension, or a tendency to dehydration; avoid overheating
  - Conduction abnormality, concurrent sympatholytics or CNS depressants; risk of AV block and additive sedation
  - Significant renal or hepatic impairment; reduce the dose
  - Any child prone to vomiting illness; missed doses are a labeled rebound risk
- **Screen before starting:**
  - Heart rate and blood pressure, supine and standing; the label makes this mandatory
  - Accurate weight, since the dose ladder is banded by it; renal and hepatic function
  - Medication list, screened for CYP3A4 inhibitors and inducers, sedating and sympatholytic agents, and any syncope or conduction history

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Drug Interactions

- **Strong and moderate CYP3A4 inhibitors** (ketoconazole, fluconazole, itraconazole, clarithromycin, erythromycin, grapefruit juice): exposure rises. **Halve the dose;** restore it when the inhibitor stops
- **Strong and moderate CYP3A4 inducers** (rifampin, efavirenz, carbamazepine): exposure falls. **Consider up to double the dose** over 1 to 2 weeks, and reverse when

the inducer stops
- **CNS depressants and alcohol** (benzodiazepines, antihistamines, opioids): additive sedation; advise avoiding alcohol
- **Antihypertensives and rate-lowering drugs:** additive hypotension and syncope; check orthostatic vitals after any dose change
- **Sympatholytics** (beta-blockers, calcium channel blockers, digitalis): may worsen sinus node dysfunction and AV block; titrate slowly
- **Stimulants:** the labeled combination, but featured in the rebound hypertension cases; taper the guanfacine even when the stimulant continues

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Administration

- Once daily, morning or evening, at about the same time each day
- **Swallow whole.** Do not crush, chew or break; the tablet is unscored, so 1 mg is the smallest deliverable dose
- **Do not give with a high-fat meal.** A prohibition, not a consistency instruction
- **Missed doses:** after two or more in a row, consider re-titrating rather than resuming maintenance
- **Switching from immediate-release guanfacine:** stop it and titrate from 1 mg; relative bioavailability is 58%, so never convert mg-for-mg
- Re-check the weight band at every visit in a growing child
- No liquid guanfacine exists; Onyda XR is the only liquid alpha-2 agonist, and it is clonidine
- Do not stop abruptly; see Discontinuation & Taper

Side Effects

- **Common** (fixed-dose monotherapy trials, all doses and the 4 mg column against placebo):
  - Somnolence 38%, **51% at 4 mg,** vs 11% placebo; fatigue 14 / 15 vs 3%
  - Hypotension 7 / 8 vs 3%; dizziness 6 / 10 vs 4%; dry mouth 4 / 7 vs 1%; lethargy 6 vs 3%; nausea 6 vs 2%
  - Stopped for adverse effects: 3% at 1 mg, 7% at 2 mg, 10% at 3 mg, **18% at 4 mg,** vs 3% placebo
- **Serious:**
  - Persistent rebound hypertension on abrupt discontinuation, with hypertensive encephalopathy reported; taper
  - Dose-dependent hypotension, bradycardia and syncope; hold or reduce, and any syncope stops titration
  - Conduction abnormality including first-degree AV block; obtain an ECG and stop
  - Convulsion; discontinue and evaluate
  - Rash, pruritus, dermatitis and exfoliative dermatitis; discontinue

    - Hallucinations and confusion; discontinue and reassess
    - Raised ALT; check liver enzymes if hepatic injury is suspected

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Monitoring & Labs

- **Heart rate and blood pressure,** supine and standing: baseline, 1 to 2 weeks after each 1 mg increment, then every 3 months; hold titration for bradycardia by age or any syncope
- **Blood pressure and pulse during any dose reduction:** at each step down and after the last dose
- **Sedation:** ask about school-day sleepiness at each titration visit and every visit for 3 months
- **Weight:** at every visit, to keep the dose in the right band
- **ADHD response:** rated scale at 5 to 8 weeks, matching the trial endpoints
- **CYP3A4 co-medication:** review at every visit and refill; starting or stopping one requires a dose change
- **ECG:** not routine; baseline if conduction disease, syncope history or sympatholytics, and promptly for new syncope
- **Renal and hepatic function:** baseline and annually
- **Laboratory:** none routine; check ALT if hepatic injury is suspected

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Discontinuation & Taper

- **Never stop abruptly.** Reduce by no more than 1 mg every 3 to 7 days; from 7 mg/day that is 3 to 6 weeks
- Abrupt cessation has caused **persistent** rebound hypertension with raised heart rate, and **hypertensive encephalopathy has been reported**
- Cases involved higher doses and concomitant stimulants; taper even when the stimulant continues
- **Monitor blood pressure and pulse at every taper step and after the final dose**
- A vomiting illness is de facto abrupt discontinuation; families should call, not let doses lapse
- After two or more consecutive missed doses, consider re-titrating
- **Drug holidays are not appropriate for this class;** weekend and summer breaks are a rebound hypertension risk here

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Pregnancy & Lactation

- **Pregnancy:** no drug-associated risk identified, but pregnancy use has been **infrequent.** No fetal harm in rabbits and rats at 3 to 4 times the maximum human dose; reduced fetal survival at 13.5 times.
- **Lactation: no human data;** guanfacine has not been measured in human milk. Present in rat milk at blood-comparable levels. Monitor an exposed infant for sedation, lethargy and poor feeding. (LactMed 2024)
- **Lactation, milk supply:** no published information; guanfacine lowers basal prolactin in men and non-nursing women. Other agents may be preferred while nursing a newborn. (LactMed 2024)
- **Exposure Registry:** National Pregnancy Registry for ADHD Medications, 1-866-961-2388

Counseling Points

- **Counsel the family on:**
  - Sleepiness early and dose related, half the children on 4 mg, while the ADHD benefit takes 5 to 8 weeks
  - Not taking it with a high-fat breakfast, and swallowing the unscored tablet whole
  - The dose being set by weight, so it is revisited as the child grows
  - Never stopping on their own: stopping suddenly can push blood pressure above where it started
  - Telling other prescribers before an antifungal, clarithromycin, or a seizure medicine
  - Calling if a stomach bug stops the medicine going down, or after two days of missed doses
- **Advise them to call for:**
  - Fainting, dizziness on standing that does not settle, or any seizure
  - A pulse that feels very slow or irregular, or heavy daytime sleepiness
  - Severe headache with blurred vision, especially after missed doses
  - A widespread rash, peeling skin, facial swelling, or new confusion or hallucinations
  - Any vomiting illness that stops the medicine going down

References

1. DailyMed. Intuniv (guanfacine) extended-release tablets prescribing information. Takeda Pharmaceuticals America, Inc. 2025. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=b972af81-3a37-40be-9fe1-3ddf59852528
2. LactMed. Guanfacine. Drugs and Lactation Database, National Institute of Child Health and Human Development. 2024. https://www.ncbi.nlm.nih.gov/books/NBK501522/
3. American Academy of Pediatrics. Clinical practice guideline for the diagnosis, evaluation, and treatment of attention-deficit/hyperactivity disorder in children and adolescents. Pediatrics. 2019. https://publications.aap.org/pediatrics/article/144/4/e20192528/81590/

4. AACAP. Practice parameter for the assessment and treatment of children and adolescents with tic disorders. Journal of the American Academy of Child and Adolescent Psychiatry. 2013. https://www.jaacap.org/article/S0890-8567(13)00695-3/fulltext
5. AHRQ. Attention deficit hyperactivity disorder: diagnosis and treatment in children and adolescents. Comparative Effectiveness Review No. 203. 2018. https://www.ncbi.nlm.nih.gov/books/NBK487764/
6. FDA. openFDA National Drug Code Directory, guanfacine, queried by generic name across all labelers. 2026. https://api.fda.gov/drug/ndc.json?search=generic_name:%22guanfacine%22&limit=1000

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