Mechanism of action

intuniv®
(guanfacine hydrochloride)
Modified Release Tablets 1•2•3•4 mg

The only approved selective α2A-adrenergic receptor agonist for ADHD treatment[1,2]

3 weeks

Significant improvement in ADHD core symptoms within 3 weeks vs placebo[3,4*]

*Statistically significant effect was reached in all dose groups at 3 weeks ($p<0.05$).[4] ADHD-RS-IV score per study week showed significant improvement in ADHD core symptoms vs placebo by week 2 for INTUNIV 2mg.[4]

24 hours

ADHD core symptom control for up to 24 hours[4†]

†Primary outcome: Significant improvement in ADHD core symptoms vs placebo ($p<0.0001$)[4]. Secondary outcome: Significant improvement from baseline on CPRS-R ($p<0.05$) and CTRS-R ($p<0.0001$) mean total scores vs placebo.[4] For the 3mg and 4mg groups, significant improvements were observed at 12 ($p<0.0030$ and $p<0.0001$, respectively) and 24 ($p<0.0398$ and $p<0.005$, respectively) hours as measured by CPRS-R.[4]

1 daily

Once daily flexible dosing: morning or evening[1,5]

ADHD, attention deficit hyperactivity disorder; **ADHD-RS-IV**, attention deficit hyperactivity disorder rating scale; **CPRS-R**, Conners' Parent Rating Scale-Revised: Short Form; **CTRS-R**, Conners' Teacher Rating Scale-Revised: Short Form.

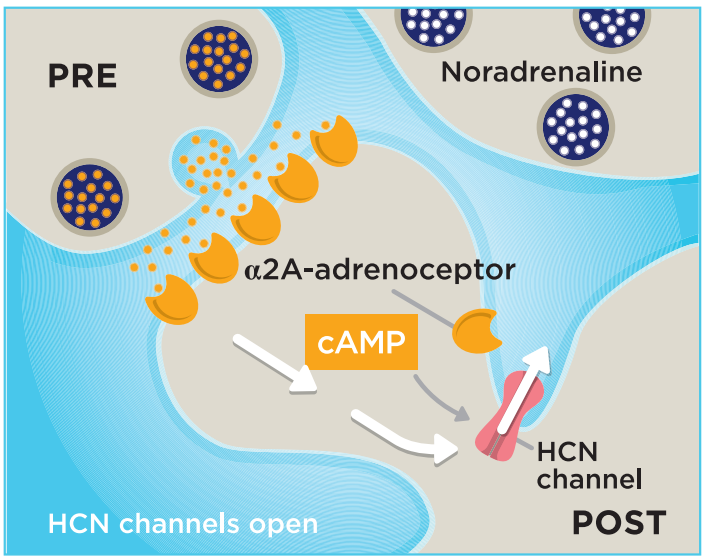
Mechanism of action[6]

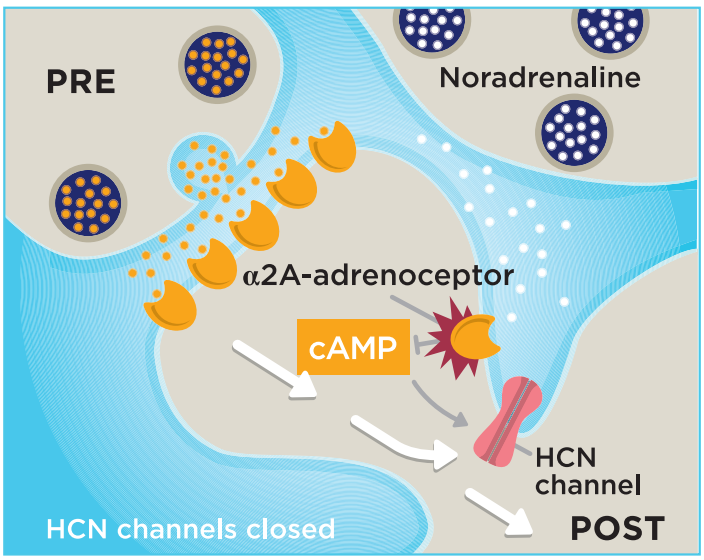
Guanfacine targets post-synaptic α2A-adrenergic receptors, mimicking noradrenaline.[6]

Preclinical evidence suggests guanfacine can modulate synaptic transmission in the PFC according to the following post-synaptic effect:

Effect on HCN channels[6]

- HCN channels are opened in the presence of cAMP, and the resulting current 'shunts' synaptic input. Stimulation of α2A-adrenergic receptors by guanfacine reduces cAMP production, closing HCN channels and **improving the efficiency of synaptic transmission**[6]





Adapted from Wang et al. 2007[6]

Mechanism of action of guanfacine in ADHD is not fully established.[1]
In vitro and animal data do not necessarily predict clinical effects in ADHD patients.

cAMP, cyclic adenosine monophosphate; **HCN**, hyperpolarisation-activated cyclic nucleotide; **PFC**, pre-frontal cortex.

Please review Product Information before prescribing. Product Information is available from Takeda Pharmaceuticals Australia Pty Ltd. Phone: 1800 012 612. Email: medinfoAPAC@takeda.com

For further information about the appropriate selection of patients and prescribing of INTUNIV, please visit http://www.intunivguide.com/au (password: onetakeda)

PBS Information: Authority required (Streamlined). Attention deficit hyperactivity disorder (ADHD); patient must be or have been diagnosed between the ages of 6 and 17 years inclusive. EITHER as monotherapy in patients who are contraindicated or intolerant to stimulants; OR as adjunctive therapy with a maximum tolerated dose of stimulant, in patients experiencing residual moderate to severe ADHD symptoms.

Minimum Product Information. INTUNIV® (guanfacine hydrochloride) 1mg, 2mg, 3mg and 4mg modified release tablets. **Indication:** INTUNIV is indicated for the treatment of attention deficit hyperactivity disorder (ADHD) in children and adolescents 6-17 years old, as monotherapy (when stimulants or atomoxetine are not suitable, not tolerated or have been shown to be ineffective) or as adjunctive therapy to psychostimulants (where there has been a sub-optimal response to psychostimulants). INTUNIV must be used as part of a comprehensive ADHD management programme, typically including psychological, educational and social measures. **Dosage and Administration:** Once daily either morning or evening. The modified-release tablet should not be crushed, chewed, or broken before swallowing. Recommended starting dose is 1mg for both monotherapy and when co-administered with psychostimulants. Dose adjustments in increments of no more than 1 mg/week. **Contraindications:** History of hypersensitivity to INTUNIV, its excipients, or other products containing guanfacine. **Precautions:** Syncope, hypotension, bradycardia; dizziness, aggression, sedation, fatigue and somnolence; suicidal ideation; effects on height, weight and body mass index; Rebound effects (Blood pressure and heart rate increase) upon discontinuation or treatment interruption (in postmarketing experience, hypertensive encephalopathy has been very rarely reported upon abrupt discontinuation). Caution in pregnancy (B3), breastfeeding and while driving or using machines. Safety and efficacy not studied in patients under 6 years of age, adults and elderly. No data in paediatric patients 6 – 17 years old with hepatic impairment. Dose reduction in patients with severe renal impairment and end stage renal disease or requiring dialysis. **Interactions:** CYP3A4/5 inhibitors, CYP3A4 inducers, transporters, valproic acid, antihypertensive drugs. **Adverse Effects:** Very Common reactions: Somnolence, headache, abdominal pain, fatigue. Common reactions: decreased appetite, insomnia, anxiety, affect lability, middle insomnia, nightmare, depression, sedation, dizziness, lethargy, bradycardia, hypotension, orthostatic hypotension, asthma, nausea, vomiting, diarrhoea, dry mouth, constipation, abdominal/stomach discomfort, rash, enuresis, irritability, blood pressure decreased, weight increased. (pi-00686. V5.0)

References: 1. INTUNIV® (guanfacine hydrochloride) Approved Product Information. **2.** Australian Register of Therapeutic Goods. Available at: https://www.tga.gov.au/australian-register-therapeutic-goods **3.** Hervas A et al. Eur Neuropsychopharmacol 2014;24:1861-1872. **4.** Biederman J et al Pediatrics 2008;121:e73-e84. **5.** Newcorn JH et al. J Am Acad Child Adolesc Psychiatry 2013:52:921-930. **6.** Wang M et al. Cell 2007;129:397-410.

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