Medicines Information Bulletin

Oxford Health NHS
NHS Foundation Trust

Vol. 14 No. 5 **Guanfacine (Intuniv) for ADHD** **June 2016**

DTG decision: Formulary

The Drugs and Therapeutics Group has included guanfacine on the Trust formulary to be used in accordance with its product licence: "*Guanfacine is indicated for the treatment of attention deficit hyperactivity disorder (ADHD) in children and adolescents 6-17 years old for whom stimulants are not suitable, not tolerated or have been shown to be ineffective. Guanfacine must be used as a part of a comprehensive ADHD treatment programme, typically including psychological, educational and social measures.*"[1]

Guanfacine is currently a secondary care only medicine.

What is it?

Guanfacine was launched in the UK on 29th January by Shire Pharmaceuticals. It is a non-stimulant, licensed for the treatment of attention deficit hyperactivity disorder (ADHD) in children and adolescents 6-17 years old for whom stimulants are not suitable, not tolerated or have been shown to be ineffective.[1] It is not licensed for use in combination with stimulants or for adults with ADHD.

Guanfacine is a selective alpha2A-adrenergic receptor agonist. It has 15‑20 times higher affinity for this receptor subtype than for the alpha2B or alpha2C subtypes, whereas clonidine binds equally to alpha2A, alpha2B, and alpha2c receptors. The mode of action of guanfacine in ADHD is not fully established. Preclinical research suggests guanfacine modulates signalling in the prefrontal cortex and basal ganglia through direct modification of synaptic noradrenaline transmission at the alpha 2- adrenergic receptors.[1] Guanfacine appears less sedating and hypotensive than clonidine.

Treatment cost ranges for comparison[2]

Daily dose	***per year £***
Concerta XL 18mg – 108mg	379.47 – 1471.68
Medikinet XL 5mg – 90mg	292.49 – 1228.59
Equasym XL 10mg – 90mg	304.16 – 1277.50
Atomoxetine 10mg – 100mg	814.21 – 1085.61
Lis-dexamfetamine 30mg – 70mg	759.20 – 1084.05
Guanfacine 1mg – 7mg	730.00 – 1842.98

What is the dose?

Guanfacine is a prolonged release preparation and the starting dose for *all* patients is 1mg daily.[1]

The dose is increased at weekly intervals according to response and tolerability and is also based on age and weight – see below or refer to SPC:

Schedule for children aged 6 – 12 years old

Weight	Week 1	Week 2	Week 3	Week 4
25kg upward	1mg	2mg	3mg	4mg (max)

Schedule for adolescents aged 13 – 17 years old

Weight	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 7
34-41.4 kg	1mg	2mg	3mg	4mg (max)			
41.5-49.4 kg	1mg	2mg	3mg	4mg	5mg (max)		
49.5-58.4 kg	1mg	2mg	3mg	4mg	5mg	6mg (max)	
58.5 kg	1mg	2mg	3mg	4mg	5mg	6mg	7mg (max)

What about missed doses?

If one dose is missed, the dose can resume the following day. If doses are missed on two days or more, then re-titration based on individual tolerability is recommended.

Are there any contraindications or precautions?

For information please refer to the manufacturer's literature (SPC).

How does guanfacine compare with other treatments for ADHD?

Guanfacine has not been directly compared with any other medicines for ADHD. Six short term studies have been conducted, one of which included an active reference arm (atomoxetine). Whilst not powered to specifically detect differences, guanfacine may have a faster onset of action than atomoxetine. Short term studies produced similar effect sizes as those seen in studies with methylphenidate. Long term studies are limited to two open label extensions studies with high attrition rates (~80%) and an as yet unpublished withdrawal study.

What tablet strengths are available?

1mg, 2mg, 3mg and 4mg

How is it taken?

- In the morning or evening
- Swallow whole (do not crush or chew)
- Take with or without food, but do not take with a high-fat meal as this increases the exposure

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What is the required monitoring? For recommended pre-treatment screening refer to the SPC.

Monitoring during titration[1]	Ongoing monitoring[1]		Monitoring during discontinuation[1]
Weekly	**Every 3 months for the first year**	**6 monthly thereafter** *(or more frequently following dose adjustment)*	
signs and symptoms of: • somnolence • sedation • hypotension • bradycardia	signs and symptoms of: • somnolence • sedation • hypotension • bradycardia • weight increase / risk of obesity	signs and symptoms of: • somnolence • sedation • hypotension • bradycardia • weight increase / risk of obesity	Blood pressure and pulse (due to rebound effects) – *monitor during downward titration and following discontinuation*

What adverse effects does it cause?
As with all new drugs, guanfacine is a black triangle ▼ drug and all suspected adverse reactions should be reported to the MHRA via the yellow card scheme (www.mhra.gov.uk/yellowcard). Refer to the SPC for a full list of adverse effects.

Very common (=/>10%)	Somnolence*, headache, abdominal pain, fatigue.
Common (>/=1/100 to <1/10)	Sedation*, dizziness, lethargy, hypotension, orthostatic hypotension, bradycardia, nausea, constipation, diarrhoea, dry mouth, weight increased, nightmare.
Uncommon (>/=1/1000 to <1/100)	Syncope, agitation, hallucination, convulsion, dizziness, pallor, dyspepsia, asthenia, chest pain, first degree AV block, tachycardia, sinus arrhythmia, pollakiuria, pruritus.
Rare (>/= 1/10,000 to <1/1000)	Hypertension, hypersomnia, malaise.

**The adverse reactions somnolence and sedation occurred predominantly at the start of treatment and may typically last for 2-3 weeks, but can last longer in some cases.*

Are there any drug interactions?
Guanfacine is a substrate of CYP3A4 and CYP3A5, and guanfacine concentrations can be affected by CYP3A4 and CYP3A5 inducers and inhibitors.[1]

Drug	Effect
Medicines with hypotensive effects *e.g. antihypertensives, some antipsychotics*	**Caution.** Potential additive effects.
Medicines with sedative effects *e.g. sedatives, hypnotics, benzodiazepines, antipsychotics*	**Caution.** Potential additive sedative effects.
Medicines that prolong the QT interval	**Caution.** Potential additive effects.
Moderate and strong inhibitors of CYP3A4/5 *e.g. ciprofloxacin, diltiazem, erythromycin, fluconazole, clarithromycin, ketoconazole, ritonavir, saquinavir*	**Caution.** Significantly elevated plasma guanfacine levels can occur and increase the risk of adverse reactions such as hypotension, bradycardia, and sedation. Dose reduction may be necessary.
CYP3A4 inducers *e.g. carbamazepine, efavarenz, nevirapine, phenytoin, rifampicin*	**Caution.** Significantly reduced levels of guanfacine can occur. A dose increase may be necessary to maintain efficacy.
Valproic acid	**Caution.** Co-administration can result in increased valproic acid concentrations.
Grapefruit juice	**Avoid.** Grapefruit juice can increase guanfacine levels and is best avoided.
Alcohol	**Caution**. Potential additive sedative effects.

How should patients be switched from their current ADHD medication to guanfacine?
No switch studies have been conducted and the manufacturer has no recommendations about how to switch from existing ADHD medication to guanfacine. Guanfacine has been used to augment methylphenidate in one study, so a cross-taper from methylphenidate to guanfacine
would be appropriate, depending on the individual situation. For more advice about switch strategies please contact the Medicines Information Service.

How should guanfacine be stopped?
Guanfacine should not be stopped suddenly (unless a serious adverse effect has occurred). A downward titration in steps of no more than 1mg every 3 to 7 days is recommended.[1]

Need more information?

For more detailed prescribing information please refer to the SPC.

OR contact the Medicines Information Service on 01865 904365 or email: med.info@oxfordhealth.nhs.uk
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For patient information leaflets, click here →


For parent/ carer/ adolescent


For children

References
1. Shire Pharmaceuticals. Intuniv Summary of Product Characteristics. Date of revision of the text: 9/2015
2. The May 2016 Drug Tariff, NHS Prescription Services
3. Personal communication with Shire Pharmaceuticals Medical Information Department, June 2016