Intuniv▼ (guanfacine hydrochloride) prolonged-release tablets Guide

Important Risk Minimisation Information for Healthcare Professionals

ADHD

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This website was developed by Takeda as part of a commitment made in the Risk Management Plan for Intuniv®

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Introduction

This information pack is to help you in the appropriate selection of patients and the prescribing of Intuniv® (guanfacine hydrochloride) prolonged-release tablets 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.

Intuniv® must be used as a part of a comprehensive ADHD treatment programme, typically including psychological, educational and social measures.

Treatment must be initiated under the supervision of an appropriate specialist in childhood and/or adolescent behavioural disorders.

The information pack provides information on risks associated with guanfacine treatment and resources to use prior to initiating treatment and for ongoing monitoring of patients while on treatment with guanfacine.

This information is also available for download from the website at www.intunivguide.com.

How to use these resources

As detailed in the summary of product characteristics (SmPC), specific concurrent conditions may exclude the use of Intuniv® (guanfacine hydrochloride) prolonged-release tablets or may warrant particular attention. Therefore, it is necessary to conduct a baseline evaluation to identify patients at increased risk of:

- Somnolence and sedation
- Hypotension and bradycardia
- QT-prolongation arrhythmia
- Weight increase/risk of obesity

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Careful dose titration and monitoring is necessary at the start of treatment with guanfacine since clinical improvement and risks for clinically significant adverse reactions (syncope, hypotension, bradycardia, somnolence and sedation) are dose- and exposure-related. Once guanfacine treatment is initiated, it is also necessary to regularly monitor the patient's safety.

Resources

Checklist for use prior to initiating treatment with guanfacine: A patient management resource to support you in the appropriate selection of patients for guanfacine treatment

Checklist for the ongoing monitoring and management of patients during guanfacine treatment: A patient management resource to support you in the ongoing monitoring during treatment with guanfacine

Checklist for discontinuation of guanfacine including monitoring blood pressure and pulse of patients during downward titration: A patient management resource to support you in the monitoring of patients during the discontinuation and downward titration of guanfacine. It is recommended that this checklist be used in conjunction with the Intuniv® SmPC

Chart for ongoing monitoring (vital signs, height, weight) of patients during guanfacine treatment: A patient management resource to support you in the initiation and ongoing monitoring of patients during treatment with guanfacine. This chart should be used in conjunction with the checklists provided

Intuniv® resources

Summary of Product Characteristics (SmPC)

Patient Information Leaflet

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About ADHD

- Attention-deficit/hyperactivity disorder (ADHD) is a neurocognitive, developmental, behavioural disorder whose core features are inattention, hyperactivity and impulsivity, in addition to impairments in executive functions[1,2]
- The mean worldwide ADHD prevalence was estimated to be between 5.29% and 7.1%[3,4] with a prevalence of just under 5% in Europe in children and adolescents (<18 years)[3]
- Diagnosis is normally made in children and adolescents, owing to problems in learning, school performance or social behaviour.[2] However, recent evidence suggests that symptoms and functional impairment may change or diminish with age.[5] ADHD is generally found to be more prevalent in males[4]
- ADHD can impair a patient's academic, social and interpersonal functioning[6,7]
- Patients with ADHD require a comprehensive, individualised, multimodal treatment strategy.[8,9] Treatment includes psychological, educational and social interventions, as well as pharmacotherapy[2,8,9]
- Pharmacotherapy should be used as part of a comprehensive, multimodal treatment programme.[8,9] When considering pharmacotherapy for the treatment of ADHD it is important to consider potential comorbid conditions, the adverse effect profile and abuse potential of the medication[9]

References

1. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. Fifth edition. Arlington, Virginia, USA: American Psychiatric Association; 2013, p59–66

2. European Medicines Agency (EMA). Guideline on the clinical investigation of medicinal products for the treatment of attention deficit hyperactivity disorder (ADHD) available at: http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2010/08/WC500095686.pdf, accessed March 2018

3. Polanczyk et al. *Am J Psychiatry* 2007;164:942–948

4. Willcutt. *Neurother* 2012;9:490–499

5. Lara et al. *Biol Psychiatry* 2009;65:46–54

6. Coghill et al. *Child Adolesc Psychiatry Ment Health* 2008; 2: 31

7. Holmberg et al. *J Atten Disord* 2014; 18: 635-645

8. Taylor et al. *Eur Child Adolesc Psychiatry* 2004;13 Suppl 1:I7–30.

9. National Institute for Health and Care Excellence (NICE). CG72 Attention deficit hyperactivity disorder (ADHD): full guideline available at: guidance.nice.org.uk/CG72/Guidance, accessed March 2018

About Intuniv® (guanfacine hydrochloride) prolonged-release tablets[1]

- Guanfacine prolonged-release 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 prolonged-release must be used as a part of a comprehensive ADHD treatment programme, typically including psychological, educational and social measures.
- Treatment must be initiated under the supervision of an appropriate specialist in childhood and/or adolescent behavioural disorders.
- Prior to prescribing, it is necessary for you to conduct a baseline evaluation to identify patients at increased risk of somnolence and sedation, hypotension and bradycardia, QT-prolongation, arrhythmia and weight increase /risk of obesity.
- In addition, monitoring of your patients should occur during dose titration (weekly) and during ongoing therapy (at least every 3 months in the first year) for signs and symptoms of some of the risks associated with guanfacine (i.e. somnolence and sedation, hypotension, bradycardia and weight increase/risk of obesity).

Risks associated with guanfacine prolonged-release

- Guanfacine prolonged-release can cause **syncope (uncommon), hypotension (or decreased blood pressure) and bradycardia (both common).** Syncope may involve risks of falls or accidents, which could result in serious harm.

Prior to the initiation of treatment:

- Patient's cardiovascular status including heart rate and blood pressure parameters, family history of sudden cardiac death/ unexplained death, should be assessed to identify patients at increased risk of hypotension, bradycardia and QT-prolongation/risk of arrhythmia.
- Caution is advised when treating patients with guanfacine prolonged-release who have a history of hypotension, heart block, bradycardia, or cardiovascular disease, or who have a history of syncope or a condition that may predispose them to syncope, such as hypotension, orthostatic hypotension, bradycardia or dehydration.
- Caution is also advised when treating patients with guanfacine prolonged-release who are being treated concomitantly with antihypertensives or other medicinal products that can reduce blood pressure or heart rate or increase the risk of syncope.

Monitoring during treatment:

- Monitoring of heart rate and blood pressure parameters should continue on a weekly basis during dose titration and stabilisation and at least every 3 months for the first year, taking into consideration clinical judgement.
- Six monthly monitoring should follow thereafter with more frequent monitoring following any dose adjustment.

- Guanfacine prolonged-release may cause **somnolence (very common)** and **sedation** (common) predominantly at the start of treatment and typically lasts for 2–3 weeks, in some cases longer

  - It is recommended that patients should be closely monitored weekly during dose titration and stabilisation and every 3 months during the first year, taking into consideration, clinical judgement.
  - Before guanfacine prolonged-release is used with other centrally active depressants (such as alcohol, sedatives, phenothiazines, barbiturates or benzodiazepines) the potential for additive sedative effects should be considered.
  - Patients are advised against operating heavy equipment, driving or cycling until they know how they respond to treatment with guanfacine prolonged-release.

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- **Patients/caregivers should be instructed not to discontinue guanfacine prolonged-release without consulting their physician.**
    - In post marketing experience, hypertensive encephalopathy has been very rarely reported following abrupt discontinuation.
    - Tapering guanfacine prolonged-release dosing during withdrawal is recommended to minimise these potential withdrawal effects.
    - It is also recommended that blood pressure and pulse should be monitored in all patients during downward dose titration (decrements of no more than 1mg every 3¬7 days) and following discontinuation of guanfacine prolonged-release.
    - In the event of patient abruptly discontinuing guanfacine prolonged-release treatment, monitor blood pressure regularly and assess for possible risks of hypertensive emergencies.

- Patients treated with guanfacine prolonged release may show an increase in their body mass index (BMI) (possibly due to **weight increase**)
    - Monitoring of height, weight and BMI should be done prior to initiation of therapy and then every 3 months for the first year, taking into consideration clinical judgement.
    - Six monthly monitoring should follow thereafter, with more frequent monitoring following any dose adjustment.

- **For further information, please see the Intuniv® SmPC**
- **Before prescribing guanfacine prolonged-release, prescribers should consider the full product profile; including contraindications, special warnings and precautions for use, and adverse reactions**

Reference

1. Intuniv summary of product characteristics (SmPC)

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