## Guanfacine for patients within children and adult services

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| Version: | RDTC v1.0 | Replaces version: | NHSE v1.0 |
| Clinical content last reviewed: | April 2024 | Next review date: | April 2026 |

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| **Version** | **Date published** | **Changes since previous version** |
| RDTC v1.0 | 15/05/2024 | Clarified information regarding dose adjustments required with enzyme inducers/inhibitors. Included interaction with metformin. Added information about avoiding abrupt withdrawal to cautions and adverse effects sections. Added clarity to some information regarding management of adverse effects. Updated breastfeeding section to reflect information currently available. Hyperlinks and references updated to current versions. |
| HNY v1.1 | 28/04/2025 | The RDTC version has been adjusted to include children as well as clarified that it is only for adults for patients who have been started on the drug in childhood and then transferred to adults services.  Section3  For the treatment of ADHD in children and adolescents 6-17yrs for whom stimulants are not suitable, not tolerated or have been shown to be ineffective. For adults aged 18 years **who have previously responded to Guanfacine in childhood and transitioned into adult’s services.**  **Guanfacine remains Red for use adults when it is been considered for initiation in adults.**  Section 4: State that prescribing and monitoring should be transferred after at least 12 weeks.  Maximum dose:  Child 6–12 years (body-weight 25 kg and above): 4mg daily  Child 13–17 years (body-weight 34–41.4 kg): 4mg daily  Child 13–17 years (body-weight 49.5–58.4 kg): 6mg daily  Child 13–17 years (body-weight 58.5 kg and above): 7mg daily  Section 5: Baseline investigations   * Height, weight, and body mass index (BMI) - recorded on centile chart (not applicable in patients > 18 years) * Blood pressure (BP) and heart rate - recorded on centile chart (not applicable in patients > 18 years)   **Ongoing monitoring:**   * Before and after every change of dose: assess heart rate and blood pressure. For under 18s, record BP, height and weight on centile charts to detect clinically important changes.   Section 7  Administration details  Patients/ carers should be advised not to stop treatment abruptly. |

**Local review and adoption**

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| **Local approval** | **Date** |
| Local content added |  |
| Approved for use by HNY ICB |  |
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Clinical content has been reviewed and updated by the RDTC on the date indicated above. Every effort is made to keep the content up to date. These templates are provided to the North West and North East and Yorkshire ICBs for localisation and approval through standard ICB processes. The most recent version is available on the RDTC website at <https://rdtc.nhs.uk/prescribing-support-document/shared-care-protocol-guanfacine-in-adults/>.

Information requiring local completion is highlighted.

This document is intended for use by NHS healthcare professionals and cannot be used for commercial or marketing purposes.

**Shared Care Protocol**

## Guanfacine for patients within children and adult services

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| Background | Guanfacine is a centrally acting alpha2-adrenergic agonist indicated for the treatment of attention deficit hyperactivity disorder (ADHD) in children and adolescents. Use in adults is off-label and should only be considered on the advice of a tertiary ADHD service. It may be recommended for people who have not responded to one or more stimulants, and one non-stimulant (see [NG87](https://www.nice.org.uk/guidance/ng87) ADHD: diagnosis and management). NICE recommends that people with ADHD have a comprehensive, holistic shared treatment plan that addresses psychological, behavioural, and occupational or educational needs.  Guanfacine should be used as part of a comprehensive treatment programme, typically including psychological, educational, and social measures.  Where a person with ADHD is treated by a Child and Adolescent Mental Health Service (CAMHS) but is approaching their 18th birthday, it is expected that CAMHS will refer to the appropriate adult service if need for ongoing treatment is anticipated. NICE Guidance [NG43](https://www.nice.org.uk/guidance/ng43) Transition from children’s to adults’ services for young people using health or social care services should be followed.  Long-term usefulness of guanfacine for extended periods (over 12 months) should be periodically re-evaluated for the individual patient. Consider trial periods of stopping medication or reducing the dose when assessment of the overall balance of benefits and harms suggests this may be appropriate. |
| Licensed and agreed off-label indications | * Attention deficit hyperactivity disorder in children and adults ǂ   ǂ Off-label indication – not licensed in adults. See [section 1](#_Background) for circumstances where NICE recommends use in adults.  This shared care protocol applies to adults and children aged 6 years and over. |
| Locally agreed indications | For the treatment of ADHD in children and adolescents 6-17yrs for whom stimulants are not suitable, not tolerated or have been shown to be ineffective. For adults aged 18 years **who have previously responded to Guanfacine in childhood and transitioned into adult’s services.**  **Guanfacine remains Red for use adults when it is been considered for initiation in adults.** |
| Initiation and ongoing dose regime | Transfer of monitoring and prescribing to primary care is normally after at least 12 weeks, and when the patient’s dose has been optimised and with satisfactory investigation results.  The duration of treatment and frequency of review will be determined by the specialist, based on clinical response and tolerability.  All dose or formulation adjustments will be the responsibility of the specialist unless directions have been discussed and agreed with the primary care clinician.  Termination of treatment will be the responsibility of the specialist.  **Initial stabilisation:**  1mg once daily, adjusted in increments of not more than 1mg every week, if necessary and tolerated.  **The loading period must be prescribed by the initiating specialist.**  **Maintenance dose (following initial stabilisation):**  0.05-0.12 mg/kg/day. Maximum daily dose up to 7mg daily.  Maximum dose:  Child 6–12 years (body-weight 25 kg and above): 4mg daily  Child 13–17 years (body-weight 34–41.4 kg): 4mg daily  Child 13–17 years (body-weight 49.5–58.4 kg): 6mg daily  Child 13–17 years (body-weight 58.5 kg and above): 7mg daily    **The initial maintenance dose must be prescribed by the initiating specialist.**  Adults who have shown clear benefit from guanfacine in childhood or adolescence may continue treatment into adulthood at the same daily dose.  **Conditions requiring dose adjustment:**  Hepatic or renal insufficiency:  Dose reduction may be required in patients with hepatic impairment, severe renal impairment (GFR 29-15 mL/min), end stage renal disease (GFR <15 mL/min) or in patients requiring dialysis.  Patients taking moderate or strong CYP3A4 and CYP3A5 inhibitors:  A 50% reduction in guanfacine dose is recommended, and further dose titration may be required (see [section 9](#_Significant_drug_interactions)).  Patients taking strong CYP3A4 inducers:  An increase in guanfacine dose may be required (see [section 9](#_Significant_drug_interactions)). |
| Baseline investigations, initial monitoring, and ongoing monitoring to be undertaken by specialist | Monitoring at baseline and during initiation is the responsibility of the specialist; only once the patient is optimised on the chosen medication with no anticipated further changes expected in the immediate future will prescribing and monitoring be transferred to primary care.  **Baseline investigations:**   * A full assessment, as recommended by [NICE guidance for ADHD](https://www.nice.org.uk/guidance/ng87/chapter/Recommendations" \l "medication). This should ensure that the patient meets the criteria for ADHD and that pharmacological treatment is required. The assessment should also include a medical history and cardiovascular assessment, considering conditions that may be contraindications for guanfacine. * Height, weight, and body mass index (BMI) - recorded on centile chart (not applicable in patients > 18 years) * Blood pressure (BP) and heart rate - recorded on centile chart (not applicable in patients > 18 years) * Electrocardiogram (ECG) and cardiology opinion are recommended if the patient has any of the following:   + history of congenital heart disease or previous cardiac surgery   + sudden death in a first-degree relative under 40 years suggesting a cardiac disease   + shortness of breath on exertion compared with peers   + fainting on exertion or in response to fright or noise   + palpitations that are rapid, regular, and start and stop suddenly   + chest pain suggestive of cardiac origin   + signs of heart failure, heart murmur or hypertension * ECG is recommended if the patient has a co-existing condition treated with a medicine that may increase cardiac risk.   **Initial monitoring:**   * Weekly monitoring for signs and symptoms of somnolence, sedation, hypotension and bradycardia during dose titration and stabilisation. * Assessment of symptom improvement. Discontinue if no improvement is observed after one month.   **Ongoing monitoring:**   * Before and after every change of dose: assess heart rate and blood pressure. For under 18s, record BP, height and weight on centile charts to detect clinically important changes. * Monitoring for signs and symptoms of somnolence or sedation during any dose adjustments or discontinuation.   Ensure the patient receives a review at least annually with a healthcare professional with training and expertise in managing ADHD. This may be in primary or secondary care, depending on local arrangements, and should include a review of ADHD medication, including patient preferences, benefits, adverse effects, and ongoing clinical need. Consider trial periods of stopping medication or reducing the dose when assessment of the overall balance of benefits and harms suggests this may be appropriate. If continuing medication, document the reasons why.  Review outcomes should be communicated to the primary care prescriber in writing, with any urgent changes also communicated by telephone. After each review, advise primary care whether treatment should be continued, confirm the ongoing dose, and whether the ongoing monitoring outlined in [section 6](#_Ongoing_monitoring_requirements) remains appropriate. |

## Ongoing monitoring requirements to be undertaken by primary care

If monitoring results are forwarded to the specialist team, please include clear clinical information on the reason for sending, to inform action to be taken by secondary care.

| **Monitoring** | **Frequency** |
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| * Blood pressure and heart rate * Somnolence and sedation * Weight and appetite * Signs or symptoms of cardiovascular adverse effects, e.g. syncope, bradycardia * Suicidal ideation or behaviour, aggressive behaviour, or hostility | Every 3 months for the first year, and every 6 months thereafter.  More frequent monitoring is recommended following dose adjustment, which may be done in primary care if directions have been discussed and agreed with the specialist service. |
| Assessment of adherence | As required, based on the patient’s needs and individual circumstances. |
| Review to ensure patient has been offered and attended an annual review with a healthcare professional with expertise in ADHD. | Annually |

## Pharmaceutical aspects

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| Route of administration: | Oral |
| Formulation: | Guanfacine hydrochloride (Intuniv®▼)  Prolonged-release tablets: 1mg, 2mg, 3mg, 4mg |
| Administration details: | Guanfacine can be taken with or without food but should not be given with high fat meals due to increased exposure.  Tablets should be swallowed whole and not split, crushed or chewed.  Guanfacine should be taken once daily in the morning or evening.  If a dose is missed, then the next scheduled dose should be taken as usual; a double dose should not be taken to make up for a missed dose. If two or more consecutive doses are missed, re-titration is recommended. A lower starting dose may be required based on the patient’s tolerance to guanfacine. Discuss with the specialist team or HCP with expertise in ADHD who conducts the annual review for advice on re-titrating guanfacine. Patients/ carers should be advised not to stop treatment abruptly. |
| Other important information: | Grapefruit juice should be avoided during treatment with guanfacine (see [section 9](#_Significant_drug_interactions)).  Due to risk of blood pressure increase upon discontinuation, guanfacine should be gradually tapered at a rate of no more than 1mg every 3 to 7 days. Blood pressure and pulse should be monitored when discontinuing treatment. Discontinuation should be managed by the specialist team or HCP with expertise in ADHD who conducts the annual review. |

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| Cautions and contraindications | This information does not replace the Summary of Product Characteristics (SPC) and should be read in conjunction with it. Please see [BNF](https://bnf.nice.org.uk/) & [SPC](https://www.medicines.org.uk/emc/search?q=guanfacine) for comprehensive information.  **Contraindications:**   * Hypersensitivity to guanfacine or to any of the excipients * Hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption.   **Cautions:**   * Risk factors for torsades de pointes: bradycardia, heart block, hypokalaemia, history of QT interval prolongation, concomitant use of other medicines which may prolong the QT interval. * History of cardiovascular disease, hypotension, orthostatic hypotension, or syncope. * Family history of cardiac or unexplained death. * Dehydration (may increase risk of syncope). * Alcohol consumption (not recommended during treatment). * Concomitant treatment with centrally acting depressants or antihypertensives (see [section 9](#_Significant_drug_interactions)). * Avoid abrupt discontinuation: increased risk of withdrawal effects (see [section 7](#_Pharmaceutical_aspects)). * Suicidal ideation or behaviour. * Prescribing in the elderly is potentially inappropriate. See [BNF information on prescribing in the elderly.](https://bnf.nice.org.uk/guidance/prescribing-in-the-elderly.html) |
| Significant drug interactions | The following list is not exhaustive. Please see [BNF](https://bnf.nice.org.uk/) & [SPC](https://www.medicines.org.uk/emc/search?q=guanfacine) for comprehensive information and recommended management.   * **Drugs which prolong the QT interval**: concomitant use with guanfacine is not recommended. * **Moderate or strong CYP3A4 and CYP3A5 inhibitors**, e.g. ketoconazole, clarithromycin, erythromycin, ciprofloxacin, diltiazem, fluconazole, verapamil, grapefruit juice, ritonavir: increased exposure to guanfacine. A 50% reduction in guanfacine dose is recommended, and further dose titration may be required (see [section 4](#_Initiation_and_ongoing)). * **CYP3A4 inducers**, e.g. carbamazepine, modafinil, phenytoin, rifampicin, St John’s wort: reduced exposure to guanfacine. Dose increase may be required. * **Valproic acid**: concomitant use may increase concentrations of valproic acid. Dose adjustments for guanfacine and/or valproic acid may be required. * **Antihypertensive medicines**: risk of additive effects, e.g. hypotension, syncope. * **CNS depressants**, e.g. alcohol, sedatives, hypnotics, benzodiazepines, barbiturates, antipsychotics: risk of additive effects, e.g. sedation, somnolence. * **Metformin:** concomitant use may increase concentration of metformin. * Administration with high fat meals: increased exposure to guanfacine. |

## Adverse effects and management

As well as responding to absolute values in laboratory tests, a rapid change or a consistent trend in any value should prompt caution and extra vigilance**.** For information on incidence of ADRs see relevant SPCs.

**Any serious adverse reactions should be reported to the MHRA via the Yellow Card scheme. Visit** <https://yellowcard.mhra.gov.uk>.

Advice based on shared care guidelines published by NHS England, and checked against current guidance.

| **Adverse effect** | **Management** |
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| **Cardiovascular**  Symptoms such as palpitations, exertional chest pain, unexplained syncope, dyspnoea or other signs or symptoms suggestive of cardiac disease. | Refer for urgent specialist cardiac evaluation. |
| Bradycardia | Discuss with specialist team; dose reduction or cardiac evaluation may be required. |
| Hypotension (BP less than 90/60 mmHg) or orthostatic hypotension | Give lifestyle advice (e.g. drinking plenty of fluids, getting up slowly from standing or sitting) and repeat monitoring.  Hypotension is most prominent in the first few weeks of treatment and diminishes gradually thereafter. If hypotension persists, reduce dose by 1mg and discuss with specialist team. |
| **Sedation and somnolence** | Sedation and somnolence typically occur during the start of treatment and with dose increases.  Review timing of dose; guanfacine may be taken in the morning or evening. Review lifestyle factors and reinforce that alcohol should be avoided. Seek specialist advice if sedation persists. Dose reduction or discontinuation may be indicated. |
| **Weight or BMI outside healthy range** | Provide appropriate support on multicomponent interventions to increase physical activity levels, improve eating behaviour and quality of diet.  Discuss with specialist if difficulty persists; dose reduction, or treatment break, or change of medicine may be required. |
| **Psychiatric disorders**  Suicidal ideation or behaviour, aggressive behaviour or hostility | Review patient and exclude other causes. Refer urgently for psychiatric assessment if suicidal ideation or behaviour is present.  Contact specialist team and discuss ongoing benefit of treatment. |
| **Withdrawal effects due to abrupt discontinuation**  Increased blood pressure, increased heat rate, and very rarely hypertensive encephalopathy. | When stopping treatment, the dose should be gradually reduced by no more than 1mg every 3 to 7 days. Blood pressure and pulse should be monitored. Discontinuation should be managed by the specialist team or HCP with expertise in ADHD who conducts the annual review. |

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| Advice to patients and carers The specialist will counsel the patient with regard to the benefits and risks of treatment and will provide the patient with any relevant information and advice, including patient information leaflets on individual drugs. | **The patient should be advised to report any of the following signs or symptoms to their primary care prescriber without delay:**   * New or worsening psychiatric symptoms, such as suicidal ideation or behaviour, aggressive behaviour, or hostility. * Signs and symptoms of bradycardia or hypotension, e.g. fatigue, dizziness, palpitations, feeling faint or fainting. * Pregnancy or planning to become pregnant or breastfeed.   **The patient should be advised:**   * To drink plenty of fluids; dehydration can increase the risk of falls or fainting. * Not to drive, cycle, or operate machines if guanfacine affects their ability to do so safely, e.g. by causing dizziness or drowsiness, and to inform the DVLA if their ability to drive safely is affected. See <https://www.gov.uk/adhd-and-driving>. * Avoid alcohol while taking guanfacine, as it may make side effects worse. * Avoid grapefruit juice while taking guanfacine. * Not to stop taking guanfacine without talking to their doctor. Due to risk of side effects, it is important to gradually reduce the dose of guanfacine under medical supervision.   Patient information:   * Royal College of Psychiatrists – ADHD in adults. <https://www.rcpsych.ac.uk/mental-health/problems-disorders/adhd-in-adults> * NHS – Attention Deficit Hyperactivity Disorder. <https://www.nhs.uk/conditions/attention-deficit-hyperactivity-disorder-adhd/>   Patient information leaflets are also available from <https://www.medicines.org.uk/emc/search?q=guanfacine> |
| Pregnancy, paternal exposure and breastfeeding | It is the responsibility of the specialist to provide advice on the need for contraception to male and female patients on initiation and at each review, but the ongoing responsibility for providing this advice rests with both the primary care prescriber and the specialist.  **Pregnancy**:  Guanfacine is not recommended for use during pregnancy. There are no or limited data from the use of guanfacine in pregnant women, and animal studies have shown reproductive toxicity.  Patients who become pregnant while taking guanfacine, or who are planning a pregnancy, should be referred to the specialist team for review.  **Breastfeeding**:  There is no published evidence on the safety of guanfacine in breastfeeding. Animal studies have shown excretion of guanfacine and its metabolites in milk. Therefore, a risk to the breastfed infant cannot be excluded. Decisions on whether to use guanfacine while breastfeeding should be made on a case-by-case basis with specialist input e.g. [UK Drugs in Lactation Advisory S](https://www.sps.nhs.uk/home/about-sps/get-in-touch/medicines-information-services-contact-details/breastfeeding-medicines-advice-service/)ervice, taking into account the risks to the infant and benefits of therapy.  **Paternal exposure**:  No evidence regarding paternal exposure was identified. |
| Specialist contact information and arrangements for referral | Details for contacting specialist must be included on clinic letter. |
| Additional information | Where patient care is transferred from one specialist service or GP practice to another, a new shared care agreement must be completed. Ensure that the specialist is informed in writing of any changes to the patient’s GP or their contact details.  Notify specialist immediately (within 2 weeks) if transfer of prescribing and monitoring responsibility is not accepted so that alternative arrangements can be put in place.  Contact specialist if communication of prescribing & monitoring requirements is unclear. |
| References | 1. eBNF. Guanfacine. Accessed via <https://bnf.nice.org.uk/drug/guanfacine.html> on 02/04/2024. 2. Guanfacine hydrochloride 1mg prolonged-release tablets (Intuniv®). Date of revision of the text 15/05/2023. Accessed via <https://www.medicines.org.uk/emc/product/5099> on 02/04/2024. 3. NICE NG87: Attention deficit hyperactivity disorder: diagnosis and management. Last updated September 2019. Accessed via <https://www.nice.org.uk/guidance/ng87/> on 02/04/2024. 4. NICE NG43: Transition from children’s to adults’ services for young people using health or social care services. Last updated February 2016. Accessed via <https://www.nice.org.uk/guidance/ng43/> on 02/04/2024. 5. Guanfacine risk minimisation materials. Updated June 2022. Accessed via <https://www.medicines.org.uk/emc/product/7507/rmms#about-medicine> on 02/04/2024. 6. Drugs and Lactation Database (LactMed®). Guanfacine. Last updated February 2023. Accessed via <https://www.ncbi.nlm.nih.gov/books/NBK501522/> on 23/04/2024. 7. Regional Medicines Optimisation Committee (RMOC). February 2021. Shared Care for Medicines Guidance – A Standard Approach. Available via [FutureNHS](https://future.nhs.uk/connect.ti/PrescribingMedicinesOptimisation/view?objectId=44553232) (log in required). |
| To be read in conjunction with the following documents | * NHSE guidance – Responsibility for prescribing between primary & secondary/tertiary care. Available from <https://www.england.nhs.uk/publication/responsibility-for-prescribing-between-primary-and-secondary-tertiary-care/>. * General Medical Council. Good practice in prescribing and managing medicines and devices. Shared care. Available from <https://www.gmc-uk.org/ethical-guidance/ethical-guidance-for-doctors/good-practice-in-prescribing-and-managing-medicines-and-devices/shared-care>. * NICE NG197: Shared decision making. Last updated June 2021. <https://www.nice.org.uk/guidance/ng197/>. |