Specialised Medicines Service (SMS) Guideline ~ Guanfacine for attention deficit hyperactivity disorder (ADHD) in children and adolescents aged 6 – 17 years

This guideline has been reviewed by relevant stakeholders across Devon and is intended for use in accordance with locally commissioned services.

Specialist: Please complete 'Specialist Request to GP Letter' and send together with a copy of this guideline to the GP.

GP: GPs are invited to participate. Please indicate whether you wish to share patient's care by completing the appropriate 'GP Acceptance/Refusal Letter' and return to specialist.

Responsibilities remain with the specialist service until formally accepted by the GP. If a GP is not confident to undertake these roles, then they are under no obligation to do so. In such an event, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist. Training and education may be available from the specialist team to support GPs where required.

If the GP agrees to share the care of the patient, the patient should not be discharged from the care of their specialist, but rather the care of the patient is shared between the patient, GP and specialist in accordance with the responsibilities outlined in this guideline.

The prescriber has the clinical and legal responsibility for the drug and the consequences of its use. Responsibility for drug monitoring and acting on results remains with the prescriber.

Introduction and aims of treatment

This Devon wide Specialised Medicines Service (SMS) guideline covers the use of guanfacine for the treatment of ADHD in children and adolescents aged 6 years to 17 years where previous treatment with stimulants AND previous treatment with atomoxetine, is ineffective OR not tolerated OR these treatments are not suitable (see Commissioning Policy for more details).

Patients must be under the care of paediatric services or Child and Adolescent Mental Health Service (CAMHS) providers.

Guanfacine is a non-stimulant treatment, a selective alpha$_{2A}$-adrenergic receptor agonist and known antihypertensive agent used in the management of ADHD. Guanfacine should only be initiated by a healthcare professional with training and expertise in diagnosing and managing ADHD. Treatment should be tailored effectively to the individual needs of the child or young person and used as part of a comprehensive ADHD treatment programme, typically including psychological, educational and social measures.

The guideline details the responsibilities for the ongoing prescribing and monitoring required to enable a shared care agreement to be arranged between the primary and secondary care interface. Refer to the online British National Formulary for children (BNFC), individual summaries of product characteristics (SmPCs), or the Medicines and Healthcare products Regulatory Agency (MHRA) for up-to-date prescribing data.

Management of children under 6 years of age falls outside the scope of this guideline. Guanfacine is sometimes used off-label for other disorders however these indications fall outside the scope of this guideline.

Service transition for young people with existing ADHD diagnosis

Refer also to: NICE Guideline NG43 Transition from children's to adults' services for young people using health or social care services (2016).

Young people transferring from child/adolescent services to adult services should be offered a transition appointment ideally jointly with the child/adolescent and adult specialist providers (contact details are provided later in the guideline).

The routine commissioning of guanfacine for the management of attention deficit hyperactivity (ADHD) in adults is not accepted in Devon (see Commissioning Policy for more information). Guanfacine is not licensed for the treatment of patients aged 18 years and above. The manufacturer's SmPC states that the safety and efficacy of guanfacine in adults and the elderly with ADHD has not been established, therefore, guanfacine should not be used in this group. Children being treated with guanfacine should have this drug withdrawn prior to transition to adult services.

The ongoing treatment plan should be formulated collaboratively with the young person as part of the service transition to adult services.

Precise timing of transition arrangements may vary according to the needs and preferences of the individual patient but should usually be completed by the time the young person is 18 years old. If there are delays to treatment reviews for patients transitioning to adult services (or pending consideration of an individual funding request), GPs may agree on an individual patient basis to continue (*off-label*) prescribing for adults for a limited period that is appropriate to the circumstances. If this is the case, monitoring should continue in line with this shared care guideline.

During the service transition process there may be circumstances where adult services provide care for an individual below the age of 18 years. In these situations the specialist should provide the GP with age specific prescribing guidance (including dose) and monitoring requirements.

Where patient care is transferred from one specialist service to another, and/or the patient is initiated on a different ADHD treatment (excluding brand / formulation / dose changes) with associated SMS guidelines, a new shared care agreement must be completed between the specialist, the GP and the patient.

Specialist responsibilities

Specialists may decide to delegate some of these tasks to members of their team, however the responsibility for ensuring the following are undertaken remains with the named specialist overseeing the care of the individual patient:

- Assess the patient, establish diagnosis of ADHD, agree a management plan and the need for treatment with guanfacine. Ensure the patient and/ or the patient's parent/guardian/carer is involved in making an informed choice about their treatment.
- Update records with list of existing drugs from available resources and ensure there are no drug interactions of clinical significance with current medication, recreational drugs, or over the counter (OTC) medicines or supplements. Recommend the patient and/ or the patient's parent/guardian/carer consults a pharmacist before using OTC treatments.
- Provide the patient and/ or the patient's parent/guardian/carer with suitable written and verbal information about the medication prior to starting treatment, including benefits, side effects, cautions, frequency of dosing, monitoring requirements and treatment reviews (timing and by whom).
- Provide advice on the need for effective contraception, and the risks of pregnancy to individuals on initiation and at each review; the ongoing responsibility for providing this advice rests with both the specialist and the GP.
- Ensure the patient and/ or the patient's parent/guardian/carer understands that treatment may be stopped if they do not attend for monitoring & treatment review.
- Highlight the importance of safe and secure storage of medication at all times to the patient and/ or the patient's parent/guardian/carer.

- Inform the patient that guanfacine is not licensed for the treatment of patients aged 18 years and above.
- Oversee the transition process described above when the patient approaches adulthood.
- Confirm patient and/or the patient's parent/guardian/carer understands the treatment and record consent and acceptance of associated patient responsibilities in the patient's medical records.
- Undertake pre-treatment screening, including consideration to cautions and contraindications, and required baseline monitoring (see monitoring requirements below) before initiating guanfacine.
- **Prescribe guanfacine and continue to monitor the patient for the first 3 months of treatment or until the patient's condition/dose is stabilised whichever is longer.**
- Once treatment is optimised, ask the GP in writing whether they are willing to participate in shared care for a particular patient using the shared care agreement letter below. Include all relevant test results (GPs may not have access to these results in primary care).
- Prescribing and monitoring will remain in secondary care until the patient is stable and GP agrees to share care.
- Following the request to the patient's GP to participate in a shared care agreement, the specialist must ensure that the patient has an adequate supply of medication (usually 28 days) until shared care arrangements are in place. Further prescriptions will be issued by the specialist if, for unforeseen reasons, arrangements for shared care are not in place at the end of this period.
- If guanfacine is to be used for extended periods (over 12 months) the manufacturer recommends that **the specialist should re-evaluate the usefulness of guanfacine every 3 months for the first year and then at least yearly based on clinical judgement.**
- **The specialist will advise frequency of reviews on an individual patient basis.** During the review consider and discuss patient preferences, clinical effectiveness, and adverse effects with the patient and/ or the patient's parent/guardian/carer and liaise with school as required. Evaluate the long-term benefit and continuation of treatment; discuss trial periods off medication where indicated (preferably during times of school holidays). Treatment discontinuation is specialist-led unless stated otherwise. If continuing medication, document the reasons why.
- Support patient-held records for physical health monitoring where possible. This may be through provision of electronic document (e.g. App for use on phone) or paper document to best suit individual patient
- Ensure prompt written summary is sent to the GP whenever the patient is reviewed including any changes in treatment or monitoring requirements, results of monitoring undertaken, and assessment of adverse events.
- Urgent changes to treatment should be communicated electronically and directly to the GP surgery (and followed up by telephone as required) to ensure prompt and immediate update.
- Provide the GP with relevant contact information and clear arrangements for back-up advice and support.
- Ensure that the GP is informed in writing of any changes to the patient's specialist or their contact details.
- Where patient care is transferred from one specialist service to another, and/or the patient is initiated on a different ADHD treatment (excluding brand / formulation / dose changes) with associated SMS guidelines, a new shared care agreement must be completed between the specialist, the GP and the patient.
- Ensure formal communication is sent to the child/ young person's school regarding the use of guanfacine where indicated.
- Respond promptly to the GP and advise on action required when abnormal monitoring results are identified or adverse effects signs or symptoms are detected.
- Any individual who becomes pregnant or wishes to become pregnant will be referred back to the specialist for an individualised review.
- Report suspected side effects to the MHRA via yellow card scheme.

General practitioner responsibilities

GPs may decide to delegate some of these tasks to members of their team; however, the responsibility for ensuring the following are undertaken remains with the GP overseeing the care of the individual patient:

- Ensure a timely reply is sent to specialist in response to request for shared care agreement. Where possible this should be undertaken within 14 days of the request being made.

If GP has agreed to share care:

- Continue to prescribe and monitor guanfacine in accordance with these guidelines.
- If home monitoring is considered appropriate on an individual patient basis the requirements and expectations should be discussed and responsibilities agreed with the patient and / or patient's parent/guardian/carer. Advise the patient on suitable equipment to facilitate home monitoring.
- Review monitoring results including those reported by the patient and take any necessary action (see monitoring requirements below).
- Be alert to the possibility of interactions when initiating new medicines or recommending over the counter (OTC) medicines or supplements, or interactions with recreational drugs. See supporting information below for further information.
- It is the responsibility of the specialist to provide advice on the need for effective contraception to individuals on initiation and at each review however the ongoing responsibility for providing this advice rests with both the specialist and the GP.
- Support patient-held records for physical health monitoring where possible. This may be through provision of electronic document (e.g. App for use on phone) or paper document to best suit individual patient. Alternatively, a copy of measurements and growth charts should be provided to the patient on request prior to any upcoming specialist review to enable a continuous assessment of developing height and weight.
- Be alert to the possibility of adverse effects at every contact. Ensure prompt action in the case of a severe adverse effect or signs or symptoms (see monitoring requirements below).
- Ensure advice sought promptly from the specialist if there is a change in the patient's physical or mental health status which is of concern to the GP and may affect treatment.
- **Any individual who becomes pregnant or wishes to become pregnant should be referred back to the specialist for an individualised review. Guanfacine is not recommended during pregnancy and in individuals of childbearing potential not using contraception.**
- Respond promptly to advice from specialist regarding any changes in treatment or monitoring requirements.
- Ensure that the specialist is informed in writing of any changes to the patient's GP or their contact details.
- Where patient care is transferred from one GP practice to another a new shared care agreement must be completed.
- Report suspected side effects to specialist and the MHRA via yellow card scheme.

Patient and/ or patient's parent/guardian/carer responsibilities

- Understand the importance of monitoring treatment and attend specialist appointments and GP appointments to ensure timely monitoring can be completed in accordance with the guideline.
- If home monitoring has been agreed, ensure recommended equipment is used. Report results to the GP in a timely manner.
- Understand that treatment will be stopped if they do not attend for monitoring and treatment review. Ensure contact details are kept up to date with both the GP and the Specialist.
- Ensure handheld growth charts, where provided, are taken to all GP and specialist appointments. If handheld records are not available a copy of recent measurements and growth charts recorded by the GP should be requested and obtained prior to attending specialist reviews; providing this information to the specialist will facilitate a continuous assessment of developing height and weight.
- Read the guanfacine patient information leaflet. Request information in different format(s) if required to aid understanding. Understand treatment, expected benefits and potential side effects.

- Take (or support administration of) medication as directed by the prescriber. Patients wishing to reduce their dose or stop guanfacine treatment should discuss with their specialist before doing so. **Avoid abrupt withdrawal unless advised by the prescriber.**
- If one dose is missed, the prescribed dose can resume the next day. If two or more consecutive doses are missed, re-titration may be required – seek advice from initiating specialist
- Seek guidance from a pharmacist, GP or specialist on medication safety and potential interaction with guanfacine if engaging in recreational drug use, or using over the counter (OTC) medicines or supplements.
- Report any adverse effects or newly presenting signs or symptoms to the GP and/or specialist.
- **Report the following signs and symptoms without delay:**
  - Fatigue, dizziness, palpitations, feeling faint or fainting (potential bradycardia or hypotension)
  - Distressing thoughts or feelings including suicidal ideation or behaviour
- Use appropriate contraception while taking guanfacine. Individuals should avoid pregnancy and should take a pregnancy test if they think there is a possibility they could be pregnant, and inform the GP or specialist immediately if they become pregnant or wish to become pregnant.
- Avoid recreational drugs. Abstain from alcohol during treatment, as it may make some side effects worse.
- Avoid grapefruit juice whilst taking guanfacine. Drink plenty of other fluids alongside treatment.
- Store medicines safely and securely at all times; it must not be shared with anyone else. Dispose of any unused medication appropriately.
- Do not operate heavy equipment, drive or cycle until response to treatment with guanfacine is known due to potential side effects such as sedation, somnolence, dizziness and syncope. It is illegal to drive with prescription medicines in your body if it impairs your driving, see Drugs and driving: the law. Patients must inform the DVLA if their ADHD or ADHD medication affects their ability to drive safely.
- Report suspected side effects to the GP or specialist and the MHRA via yellow card scheme.

Monitoring requirements

Baseline assessment to be completed by the specialist before initiating treatment in children and young people:

Full history and physical examination to include:

- Medical history including past and present co-morbid medical and psychiatric disorders or symptoms
- Concomitant medication
- Consideration of cautions and contraindications associated with guanfacine
- Social circumstances including a risk assessment for substance misuse and drug diversion
- Identification of patients at increased risk of somnolence and sedation, hypotension and bradycardia, QT-prolongation arrhythmia and weight increase/risk of obesity.
- Pulse and blood pressure measured with an appropriately sized cuff and compared with the normal range for age
- Height, weight and body mass index (BMI) measured and recorded against the normal range for age and gender on a growth chart.
- Cardiovascular assessment to include (but not limited to) the following considerations:
  - Presence of cardiac disease, history of exercise syncope, undue breathlessness, signs of heart failure, chest pain suggesting cardiac origin, palpitations and heart murmur
  - Family history of cardiovascular disease and sudden cardiac/unexplained death; consideration of major lifestyle risk factors such as smoking and obesity
  - Electrocardiogram (ECG) to be carried out if clinically indicated based on patient medical history, cardiovascular assessment or if the patient is being treated with a medicine that may pose an increased cardiac risk.
  - Specialist cardiac evaluation to be requested if the ECG shows abnormalities or if the cardiovascular assessment raises concerns.
- Before initiating treatment it is essential to consider and discuss effective contraception and/ or, where appropriate, the risks of pregnancy (including risk to the foetus and risks associated with stopping or changing

medication). If there is any possibility that the individual may be pregnant, it is important to exclude this prior to starting treatment. Refer also to supporting information below.

Monitoring to be completed by the specialist service provider before initiation of shared care agreement:

- Monitoring at baseline and during initiation is the responsibility of the specialist. Clinical improvement and risks for several clinically significant adverse reactions (syncope, hypotension, bradycardia, somnolence and sedation) are dose- and exposure-related. Weekly monitoring should be performed during titration. Specialist will discontinue if no symptom improvement is observed after one month.
- **Only once the patient is optimised on guanfacine with no anticipated further changes expected in immediate future will prescribing and monitoring be transferred to primary care.**
- Continue to monitor the patient until shared care agreement is accepted, and ongoing prescribing and monitoring responsibilities are transferred to the GP.
- Respond promptly with advice on action required if adverse effects signs or symptoms are reported by the patient, either directly or through their GP.

Monitoring to be completed by the GP once shared care agreement in place:

The specialist should provide the GP with age specific prescribing guidance (including dose) and monitoring requirements.

Monitoring results should be compared against the normal range for age, height and gender. The patient's height and weight should be plotted on growth charts to enable a visual representation of continuous individualised growth over time. A continuous record enables any deviation from the patients expected growth pattern and centile to be detected. The Royal College of Paediatrics and Child Health (RCPCH) website provides UK-WHO growth charts which are accessible here. Apps may be available to download from online stores for use on electronic devices to aid calculation of growth centiles. Consideration should be given as to whether the App is endorsed by recognised professional bodies such as the RCPCH.

Nationally agreed normal range values for children's heart rate (based on age) can be viewed in the table below replicated from the following resource: Advanced Paediatric Life Support: A Practical Approach to Emergencies, Sixth Edition. Edited by Martin Samuels and Susan Wieteska, 2016.

Age	**Pulse** (5^{th}-95^{th} centile)
6-7 years	80-130 bpm
8-11 years	70-120 bpm
12 years	65-115 bpm
14 years	60-110 bpm
Adult	60-100 bpm.

Monitoring parameters to be measured by the GP and recommended frequencies:

Monitoring Parameter	**Children and adolescents aged 6 – 17 years**
Height, weight and BMI	Every three months for the first 12 months. Usually six monthly thereafter. *Additional monitoring may be temporarily required following any dose adjustments due to change in clinical circumstances, age progression, or concomitant CYP3A4/5 inhibitors or inducers etc. The initiating specialist will advise.*
Pulse and blood pressure *(use appropriately sized cuff for the size of the child's upper arm and repeat blood pressure manually as required)*	Every three months for the first 12 months. Usually six monthly thereafter. *Measure one week after any dose adjustment advised by the specialist due to change in clinical circumstances, age progression, or concomitant CYP3A4/5 inhibitors or inducers etc.*
Adverse events	Be alert to the possibility of adverse effects at every contact including (but not limited to): • Cardiovascular effects such as syncope • Psychological changes including suicidal ideation or behaviour • Somnolence and sedation
Assessment of adherence	As required, based on the patient's needs and individual circumstances

Compare results to baseline and/or previous measurements. As well as responding to absolute values, a rapid change or a consistent trend in any value should prompt caution and extra vigilance.

Where abnormal results are identified during routine monitoring consider the actions below, consider treatment adherence, concordance and potential for any other contributing factors such as interacting medication.

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. Include a copy of measurements recorded by the GP since the previous specialist review and where possible include a copy of the growth chart to enable a continuous assessment of results.

Monitoring Parameter	Result prompting further action	Action to be taken by GP
Weight and BMI	Weight or BMI outside healthy range	Continue treatment and contact initiating specialist for advice
Pulse and blood pressure	Marked decrease from baseline, previous result, or deviation from the trend for an individual child or adolescent *OR* The individual is symptomatic *OR* Orthostatic hypotension *See table below for patient reported cardiovascular signs and symptoms.*	Consider the normal range for age which changes with increasing age. Use clinical judgement when assessing results and determining need for specialist input. Exclude other potential causes for unexpected results. If appropriate, repeat measurement within 1-2 weeks e.g. uncertainty surrounding result accuracy or if result is within normal range for age, unless there is a deterioration or increased severity in associated symptoms before this. Contact initiating specialist for advice and review of treatment. Refer for prompt cardiology review if indicated. Give lifestyle advice where appropriate e.g. drinking plenty of fluids, getting up slowly from standing or sitting. Manage ongoing symptoms in accordance with local guidelines and specialist advice.

Important: When stopping treatment, the dose must be tapered – see discontinuation guidance below

Presentation of the following adverse effects, signs or symptoms and associated actions should be noted. Any serious adverse reactions should be reported to the MHRA via the Yellow Card scheme. See also adverse effects in supporting information below.

Adverse effects, signs and symptoms	Action to be taken by GP
Worsening behaviour	Continue treatment and contact initiating specialist for review
Somnolence and sedation *Symptoms typically occur during the start of treatment and with dose increases.*	If symptoms are judged to be clinically concerning or persistent, a dose decrease or treatment discontinuation should be considered; seek specialist advice.
Dizziness and drowsiness	Patients should be advised that if affected, they should avoid potentially hazardous activities such as driving or operating machinery. Seek advice from initiating specialist as required.
Development of symptoms such as palpitations, exertional chest pain, unexplained syncope, dyspnoea or other symptoms suggestive of cardiac disease or arrythmia. *See table above for bradycardia detected during routine monitoring*	Exclude other potential causes. Contact initiating specialist for urgent advice and review of treatment. Refer for prompt cardiology review if indicated. Manage ongoing symptoms in accordance with local guidelines and specialist advice.
Development or worsening of psychiatric disorders e.g. suicidal tendency and/or ideation, aggression, hostility	Contact initiating specialist for advice and review of treatment. Follow local guidelines for referral to mental health services depending on clinical findings.

Supporting Information

This section provides additional information regarding guanfacine. Refer to the online BNFC, SmPCs, the MHRA or NICE websites for up-to-date information on any medicine.

The specialist should provide the GP with age specific prescribing guidance (including dose) and monitoring requirements.

Refer to NICE Guideline NG87: ADHD: diagnosis and management (2018) for guidance on the management of ADHD.

Dosage and administration in children and adolescents aged 6 – 17 years (to be determined by specialist)

Guanfacine is available as a prolonged-release tablet. Refer to Devon formulary for list of preparations approved for use locally.

Guanfacine tablets should be swallowed whole once daily either morning or evening. Administration in the evening may be preferred due to potential for drowsiness. Guanfacine can be administered with or without food but should not be administered with high fat meals or grapefruit juice.

The SmPCs recommend a starting dose of 1 mg taken orally once a day. The dose may be adjusted in increments of not more than 1 mg per week. Dose should be individualised; depending on the patient's response and tolerability the recommended maintenance dose range is 0.05-0.12 mg/kg/day. Dose adjustments (increase or decrease) to a maximum tolerated dose within the recommended optimal weight-adjusted dose range based upon clinical judgement may occur at any weekly interval after the initial dose.

Manufacturer's recommended dose titrations for children and adolescents shown in tables 1 and 2 below.

Table 1: Dose titration schedule for children aged 6-12 years

Weight Group	Week 1	Week 2	Week 3	Week 4
25 kg and up Max Dose= 4 mg	1 mg	2 mg	3 mg	4 mg

Table 2: Dose titration schedule for adolescents (aged 13-17 Years)

Weight Group[a]	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 7
34-41.4 kg Max Dose= 4 mg	1 mg	2 mg	3 mg	4 mg			
41.5-49.4 kg Max Dose= 5 mg	1 mg	2 mg	3 mg	4 mg	5 mg		
49.5-58.4 kg Max Dose= 6 mg	1 mg	2 mg	3 mg	4 mg	5 mg	6 mg	
58.5 kg and above Max Dose= 7 mg	1 mg	2 mg	3 mg	4 mg	5 mg	6 mg	7 mg[b]

[a] Adolescent subjects must weigh at least 34 kg.
[b] Adolescents weighing 58.5 kg and above may be titrated to a 7 mg/day dose after the subject has completed a minimum of 1 week of therapy on a 6 mg/day dose and the physician has performed a thorough review of the subject's tolerability and efficacy.

If one dose is missed, the prescribed dose can resume the next day. If two or more consecutive doses are missed, re-titration may be required – specialist will advise.

Renal and liver impairment

Dose reduction may be required in patients with hepatic impairment or renal impairment however the impact of hepatic or renal impairment on the pharmacokinetics of guanfacine in paediatric patients has not been assessed. Seek advice from initiating specialist who will advise on any necessary dose adjustments.

Patients treated with CYP3A inhibitors or inducers

CYP3A4/5 inhibitors have been shown to have a significant effect on the pharmacokinetics of guanfacine when co-administered. Dose adjustment is recommended with concomitant use of moderate/strong CYP3A4/5 inhibitors (e.g. ketoconazole, grapefruit juice), or strong CYP3A4 inducers (e.g. carbamazepine). See interactions section below for further examples.

Seek advice from initiating specialist on any necessary dose adjustments and any additional monitoring required following a dose change.

In case of concomitant use of strong and moderate CYP3A inhibitors, a 50% reduction of the guanfacine dose is recommended. Due to variability in interaction effect, further dose titration may be needed.

If guanfacine is combined with strong enzyme inducers, a re-titration to increase the dose up to a maximum daily dose of 7 mg may be considered if needed. If the inducing treatment is ended, re-titration to reduce the guanfacine dose is recommended during the following weeks.

Treatment discontinuation

Treatment discontinuation is specialist-led unless stated otherwise. The duration of treatment will be determined by the specialist, based on clinical response and tolerability.

Other circumstances surrounding treatment, such as adherence to medication schedule, side effects and motivation should be considered when evaluating treatment effectiveness.

When stopping treatment, the dose must be tapered with decrements of no more than 1 mg every 3 to 7 days, and blood pressure and pulse should be monitored in order to minimise potential withdrawal effects, in particular increases in blood pressure and heart rate. In post-marketing experience, hypertensive encephalopathy has been very rarely reported upon abrupt discontinuation of guanfacine. Monitor patients for signs of suicide-related events, somnolence and sedation during drug discontinuation.

Contraindications

- Hypersensitivity to guanfacine or any of the excipients (refer to SmPC)
- Current Devon Formulary listed brand contains lactose – do not use in hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption.

Precautions

In addition to the points listed below, refer to the monitoring section above for further cautions to be noted during treatment depending on patient medical history and actions to take in the case of a severe adverse effect or patient reported signs or symptoms. Precautions for use include:

- 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.
- Family history of cardiac or unexplained death.
- Concomitant treatment with antihypertensives or other medicinal products that can reduce blood pressure or heart rate or increase the risk of syncope
- History of QT prolongation, risk factors for torsade de pointes (e.g. heart block, bradycardia, hypokalaemia) or patients who are taking medicinal products known to prolong the QT interval
- Concomitant use of any other centrally active depressants (such as alcohol, sedatives, phenothiazines, barbiturates, or benzodiazepines) the potential for additive sedative effects should be considered
- Underlying psychiatric disorders, suicidal ideation or behaviour
- Dehydration, alcohol consumption

Adverse effects

This list is not exhaustive. Refer to the online BNFC and SmPCs for full prescribing data. Seek specialist advice where necessary. See also adverse effects, signs and symptoms in monitoring requirements section above.

The most frequently reported adverse reactions include somnolence, headache, fatigue, abdominal pain upper, and sedation. Somnolence and sedation occurred predominantly at the start of treatment and may typically last for 2-3 weeks and longer in some cases. The most serious adverse reactions commonly reported include hypotension, weight increase, bradycardia and syncope.

The BNFC reports the following adverse effects:

Very common (≥1/10) or common (**≥1/100 to <1/10):** Anxiety; appetite decreased; arrhythmias; asthenia; constipation; depression; diarrhoea; dizziness; drowsiness; dry mouth; gastrointestinal discomfort; headache; hypotension; mood altered; nausea; skin reactions; sleep disorders; urinary disorders; vomiting; weight increased

Uncommon (**≥1/1000 to <1/100)**: Asthma; atrioventricular block; chest pain; hallucination; loss of consciousness; pallor; seizure; syncope

Rare (≥1/10,000 to <1/1,000) or very rare (<1/10,000): Hypertension; hypertensive encephalopathy; malaise

Frequency not known: Erectile dysfunction

Interactions

The following interaction list is not exhaustive. Consider interaction with prescription and recreational drugs. Refer to the online BNFC and SmPCs for full prescribing data. Seek specialist advice where necessary and / or refer to specialist Medicines Information services for additional support (and reference to Stockley's Drug Interactions where paid subscription available) if concomitant administration of interacting medicines is clinically indicated.

Seek advice from initiating specialist on any necessary dose adjustments and any additional monitoring required following a dose change.

- **Concomitant CYP3A4/5 inhibitors or inducers** (see Table 3):
  - Moderate and strong CYP3A4/5 inhibitors - a decrease in the dose of guanfacine may be recommended
  - CYP3A4 inducers - an increase in the dose of guanfacine may be recommended.
  - See dosage guidance above for further details
- **Products that are metabolised via CYP3A4/5:** guanfacine can increase plasma concentrations
- **Products known to cause sedation, somnolence, hypotension, syncope or QT prolongation,** guanfacine can have an additive effect:
  - **Drugs that prolong the QT interval** (refer to the BNFC and Devon Formulary)
  - **Antihypertensives**
  - **Central nervous system (CNS) depressants e.g. alcohol, sedatives, hypnotics, benzodiazepines, barbiturates, and antipsychotics**
- **Metformin**: guanfacine is predicted to increase the concentration
- **Valproic acid** and co-administration of guanfacine can result in increased concentrations of valproic acid. When unavoidable monitor for potential additive CNS effects; consider monitoring serum valproic acid concentrations. Adjustments in the dose of valproic acid and guanfacine may be indicated.
- **High fat meals or grapefruit juice**: guanfacine should not be administered with these foods due to increased exposure to guanfacine

Table 3: Example CYP3A4/5 inhibitors and CYP3A4 inducers (this list is not definitive)

Moderate CYP3A4/5 inhibitors	Strong CYP3A4/5 inhibitors	CYP3A4 inducers
Aprepitant	Boceprevir	Bosentan
Atazanavir	Chloramphenicol	Carbamazepine
Ciprofloxacin	Clarithromycin	Efavirenz
Crizotinib	Indinavir	Etravirine
Diltiazem	Itraconazole	Modafinil
Erythromycin	Ketoconazole	Nevirapine
Fluconazole	Posaconazole	Oxcarbazepine
Fosamprenavir	Ritonavir	Phenobarbital
Imatinib	Saquinavir	Phenytoin
Verapamil	Suboxone	Primidone
Grapefruit juice	Telaprevir	Rifabutin
	Telithromycin	Rifampicin
		St. John's wort

Pregnancy, lactation and fertility

Before prescribing in this area seek specialist advice and check up-to-date sources of information.

Devon Partnership NHS Trust have produced a Prescribing Guideline for the Pharmacological Management of Perinatal Mental Health Conditions which can be accessed here. Contact details for perinatal mental health services can be found below.

Pregnancy

The SmPC reports that there are no or limited amount of data from the use of guanfacine in pregnant women. Studies in animals have shown reproductive toxicity. The SmPC states that **guanfacine is not recommended during pregnancy and in women of childbearing potential not using effective contraception.**

Any individual who becomes pregnant or wishes to become pregnant will be referred back to the specialist for an individualised review.

The UK Teratology Information Service (UKTIS) provides a national service on all aspects of the toxicity of drugs and chemicals in pregnancy (Tel: 0344 892 0909), and provides the 'best use of medicines in pregnancy' (bumps) website for supportive patient information relating to individual treatments.

Lactation

It is unknown whether guanfacine and its metabolites are excreted in human milk. Available pharmacodynamic and toxicological data in animals have shown excretion of guanfacine and its metabolites in milk. Therefore, a risk on the breast-fed infant cannot be excluded.

A case-by-case specialist led decision must be made whether to discontinue breast-feeding or to discontinue and/or abstain from guanfacine therapy taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman.

The long half-life increases the risk of accumulation in breastfed infants. It may interfere with lactation, as guanfacine decreases prolactin levels in the mother. Infants should be monitored for decreased appetite/weight gain, sleep disturbances, gastrointestinal symptoms (e.g. pain, vomiting, constipation), although some of these may be difficult to detect.

UK Drugs in Lactation Advisory Service (UKDILAS) provides evidence-based information on the use of drugs during the breastfeeding period to all UK healthcare professionals. Information relating to guanfacine can be

accessed here. Information relating to safety in lactation, specifically for drugs used to treat ADHD is also available.

Fertility

There are no or limited amount of data regarding effect on fertility from the use of guanfacine in humans. Animal studies indicate an effect on male fertility

Paternal exposure

No evidence regarding adverse outcomes following paternal exposure was identified.

Support

Local child and adolescent ADHD service providers	
Children and Family Health Devon https://childrenandfamilyhealthdevon.nhs.uk Email: CFHD.DevonSPA@nhs.net Telephone: 0330 0245 321	**University Hospitals Plymouth NHS Trust** Email: plh-tr.cdcplymouth@nhs.net Telephone 01752 439400
Royal Devon and Exeter NHS Foundation Trust Email: rde-tr.exeterchildhealth@nhs.net	**Livewell Southwest** https://www.livewellsouthwest.co.uk/childrens-services/camhs Telephone: 01752 434476
Torbay and South Devon NHS Foundation Trust www.torbayandsouthdevon.nhs.uk/services/camhs/ Telephone: 01803 655692	

Local adult ADHD service providers	
Devon Adult Autism & ADHD Service (DAANA); Devon Partnership NHS Trust Email: dpt.adhd@nhs.net Telephone: 01392 674250	**Livewell Southwest** Email: livewell.adultadhdassessment@nhs.net Telephone: 01752 434034

Additional ADHD service providers with an NHS Devon ICB Contract
Refer to the DRSS ADHD and Autism FAQ for a list of additional providers with an NHS Devon contract (and Devon shared care agreements): North & East Devon | South & West Devon

Perinatal mental health teams	
Exeter Email: dpn-tr.PerinatalTeamExeter@nhs.net Telephone: 01392 674964	**North Devon** Email: dpn-tr.perinatalNorth@nhs.net Telephone: 01271 322772
Plymouth Email: livewell.perinatalmht@nhs.net Telephone: 01752 431607	**South Hams and West Devon** Email: dpt.perinatalteamwestdevon@nhs.net Telephone: 01822 813 070
Torbay Email: dpn-tr.PerinatalTeamTorbay@nhs.net Telephone: 01803 396590	

For further support and information in relation to individual shared care agreements please contact your practice pharmacist or alternatively please contact the Medicines Optimisation Team.

Email: D-ICB.medicinesoptimisation@nhs.net

Date ratified: September 2023

Amended to reflect NHS Devon commissioning policy in respect of guanfacine for adults (November 2025)

Link to DRSS ADHD and Autism FAQ added (December 25)

Shared Care Agreement Letter - Specialist Request to GP

To	**GP name**	
	Practice address	
Patient name		
Hospital number		
NHS number		
Date of birth		
Address		

GPs are invited to participate in shared care agreements, but if the GP is not confident to undertake these roles then they are under no obligation to do so. If so, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist. If asked to prescribe this drug the GP should reply to this request as soon as practical. Continuing the care assumes communication between the specialist, GP and patient; the intention should be explained to the patient and accepted by them.

The prescriber has the clinical and legal responsibility for the drug and the consequences of its use. Responsibility for drug monitoring and acting on results remains with the prescriber.

NHS England 'Responsibility for prescribing between Primary & Secondary/Tertiary care' guidance (2018) states that "when decisions are made to transfer clinical and prescribing responsibility for a patient between care settings, it is of the utmost importance that the GP feels clinically competent to prescribe the necessary medicines. It is therefore essential that a transfer involving medicines with which GPs would not normally be familiar should not take place without full local agreement, and the dissemination of sufficient, up-to-date information to individual GPs."

I have discussed and agreed the following treatment with the patient:

Guanfacine prolonged-release tablets (state dose and frequency)

……

For the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in a child or young person aged ……

Treatment was started on ……

The patient has been on the optimised dose stated for ……..

This patient is now suitable for prescribing to move to primary care. The patient fulfils criteria for shared care therefore I am writing to request your agreement to continue the care of this patient according to the Specialised Medicines Service (SMS) Guideline for guanfacine.

In accordance with the SMS Guideline the transfer of monitoring and prescribing to the GP is after at least 3 months, or once the patient's condition/dose is stabilised whichever is longer.

I have provided the patient with sufficient medication to last until ……

Please undertake prescribing and monitoring from …… in line with the SMS Guideline.

The next monitoring is due on …….

I have arranged a follow up with this patient in ……..

I can confirm that the following has happened with regard to this treatment:

	Specialist to complete (YES/NO)
Baseline investigation and monitoring as set out in the SMS Guideline have been completed and were satisfactory	
The condition being treated has a predictable course of progression and the patient can be suitably maintained by primary care	
The risks and benefits of treatment have been explained to the patient	
The roles of the Specialist / GP / Patient have been explained and agreed	
The patient has agreed to this shared care arrangement, understands the need for ongoing monitoring, and has agreed to attend all necessary appointments	
I have enclosed a copy of the SMS Guideline which covers this treatment. The guideline can also be found here	
I have included with this letter copies of the information the patient has received	

The results of baseline tests, early monitoring and any additional supportive information are included below and/or attached:

GP please sign response letter and return promptly (where possible this should be within 14 days of the request being made).

Specialist signature		**Date**	
Specialist name, role, speciality			
Daytime telephone number			
Email address			
Alternative contact **e.g. clinic or specialist nurse**			
Out of hours contact details **e.g. duty doctor**			

Remember to keep a copy of this letter for the patient's records.

Shared Care Agreement Letter – GP Acceptance Letter to Specialist

To	Specialist name	

Patient name	
Hospital number	
NHS number	
Date of birth	
Address	

GPs are invited to participate in shared care agreements, but if the GP is not confident to undertake these roles then they are under no obligation to do so. If so, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist. If asked to prescribe this drug the GP should reply to this request as soon as practical. Continuing the care assumes communication between the specialist, GP and patient; the intention should be explained to the patient and accepted by them.

The prescriber has the clinical and legal responsibility for the drug and the consequences of its use. Responsibility for drug monitoring and acting on results remains with the prescriber.

NHS England 'Responsibility for prescribing between Primary & Secondary/Tertiary care' guidance (2018) states that "when decisions are made to transfer clinical and prescribing responsibility for a patient between care settings, it is of the utmost importance that the GP feels clinically competent to prescribe the necessary medicines. It is therefore essential that a transfer involving medicines with which GPs would not normally be familiar should not take place without full local agreement, and the dissemination of sufficient, up-to-date information to individual GPs."

Thank you for your request for me to accept prescribing responsibility for this patient under a shared care agreement and to provide the following treatment:

Medicine	Formulation	Route	Dose and frequency
Guanfacine	Prolonged-release tablets	Oral	

I can confirm that **I am willing to take on this responsibility** from …….. and will maintain the prescribing and monitoring responsibilities as set out in the Specialised Medicines Service (SMS) Guideline for guanfacine for attention deficit hyperactivity disorder (ADHD) in children and adolescents aged 6 – 17 years.

GP signature		**Date**	
GP name			
Practice address			
Telephone number			
Email address			

Remember to keep a copy of this letter for the patient's records. If this letter is not returned sharing of the care for this patient will not commence.

Shared Care Agreement Letter – GP Refusal Letter to Specialist

To	Specialist name	

Patient name	
Hospital number	
NHS number	
Date of birth	
Address	

GPs are invited to participate in shared care agreements, but if the GP is not confident to undertake these roles then they are under no obligation to do so. If so, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist. If asked to prescribe this drug the GP should reply to this request as soon as practical. Continuing the care assumes communication between the specialist, GP and patient; the intention should be explained to the patient and accepted by them.

The prescriber has the clinical and legal responsibility for the drug and the consequences of its use. Responsibility for drug monitoring and acting on results remains with the prescriber.

NHS England 'Responsibility for prescribing between Primary & Secondary/Tertiary care' guidance (2018) states that "when decisions are made to transfer clinical and prescribing responsibility for a patient between care settings, it is of the utmost importance that the GP feels clinically competent to prescribe the necessary medicines. It is therefore essential that a transfer involving medicines with which GPs would not normally be familiar should not take place without full local agreement, and the dissemination of sufficient, up-to-date information to individual GPs."

In the interest of patient safety NHS Devon, in conjunction with local acute trusts have classified guanfacine as a "shared care" drug which requires a number of conditions to be met before transfer can be made to primary care.

Thank you for your request for me to accept prescribing responsibility for this patient. I regret to inform you that in this instance **I am unable to take on responsibility** due to the following:	**Tick all applicable**
The prescriber does not feel clinically confident in managing this individual patient's condition, and there is a sound clinical basis for refusing to accept shared care. As the patients GP I do not feel clinically confident to manage this patient's condition. I have consulted with other GPs in my practice who support my decision. This is not an issue which would be resolved through adequate and appropriate training of prescribers within my practice. **I have discussed my decision with the patient and request that prescribing for this individual remain with you as the specialist, due to the sound clinical basis given below.**	

The condition does not fall within the criteria defining suitability for inclusion in a shared care arrangement. As the condition requested to be treated is not included on the locally recognised list of indications for shared care for guanfacine I am unable to accept clinical responsibility for prescribing this medication at this time. **Until this condition is identified locally as requiring shared care with guanfacine the responsibility for providing this patient with their medication remains with you.**	
A minimum duration of supply by the initiating specialist. As the patient has not had the minimum supply of medication to be provided by the initiating specialist I am unable to take clinical responsibility for prescribing this medication at this time. Therefore can you please contact the patient as soon as possible in order to provide them with the medication that you have recommended. **Until the patient has had the appropriate length of supply the responsibility for providing the patient with their medication remains with you.**	
Initiation and optimisation by the initiating specialist. As the patient has not been optimised on this medication I am unable to take clinical responsibility for prescribing this medication at this time. Therefore can you please contact the patient as soon as possible in order to provide them with the medication that you have recommended. **Until the patient is optimised on this medication the responsibility for providing the patient with their medication remains with you.**	
Other (GP to complete if there are other reasons why shared care cannot be accepted):	

I would be willing to consider prescribing for this patient once the above criteria have been met for this treatment.

Please do not hesitate to contact me if you wish to discuss any aspect of my letter in more detail and I hope to receive more information regarding this shared care agreement as soon as possible.

GP signature		**Date**	
GP name			
Practice address			
Telephone number			
Email address			

Remember to keep a copy of this letter for the patient's records.