BNSSG Shared Care Guidance
Please complete all sections

Section 1: Heading

Drug	**Guanfacine (Intuniv®)**
Amber ***three months***	

Indication	As part of a comprehensive treatment programme for attention deficit hyperactivity disorder (ADHD) in children and adolescents of 5* years of age and over, where:
	• Treatment with methylphenidate or lisdexamfetamine has been considered to be:
	  ○ Inadequate (Their symptoms have not responded to separate 6-week trials of each medicine.)
	  ○ Not tolerated
	  ○ Contraindicated
	  ○ Inappropriate (e.g. concerns about misappropriation of stimulants).
	
	*Guanfacine is licensed from 6 years, 'off-label' use for 5 year old patients, but supported by NICE Guideline (NG87; 1.5.13)

Section 2: Treatment Schedule

Usual dose and frequency of administration *(Please indicate if this is licensed or unlicensed and any relevant dosing information)*	Guanfacine is a non-stimulant selective alpha2A-adrenergic receptor agonist. Treatment must be initiated by a specialist in the treatment of ADHD, such as a paediatrician, child/adolescent psychiatrist, or ADHD specialist non-medial prescriber. **Dose in children 5-12 years** Body-weight 25kg and above: Initially 1mg once daily, adjusted in steps of 1mg every week if needed and if tolerated. Maintenance: 0.05-0.12mg/kg (max 4mg/dose). **Dose in young people 13-17 years** Body-weight 34-41.4kg: Initially 1mg once daily; adjusted in steps of 1 mg every week if necessary and if tolerated; maintenance 0.05–0.12 mg/kg once daily (max. per dose 4 mg). Body-weight 41.5–49.4 kg Initially 1mg once daily; adjusted in steps of 1 mg every week if necessary and if tolerated; maintenance 0.05–0.12 mg/kg once daily (max. per dose 5 mg).

	<u>Body-weight 49.5–58.4 kg:</u> Initially 1mg once daily; adjusted in steps of 1 mg every week if necessary and if tolerated; maintenance 0.05–0.12 mg/kg once daily (max. per dose 6 mg). <u>Body-weight 58.5 kg and above:</u> Initially 1mg once daily; adjusted in steps of 1 mg every week if necessary and if tolerated; maintenance 0.05–0.12 mg/kg once daily (max. per dose 7 mg). *For optimal weight-adjusted dose titrations, consult product literature.* Patients who have shown clear benefit from guanfacine in childhood or adolescence may continue treatment into adulthood at the same daily dose.
Route and formulation	Oral. Guanfacine hydrochloride (Intuniv®▼) 1 mg, 2 mg, 3 mg and 4 mg modified-release tablets. Guanfacine can be taken with or without food, but should not be given with high fat meals due to increased exposure.
Duration of treatment	Long term Efficacy should be seen within four – eight weeks of therapeutic dose being reached. If no clinical benefit seen during the titration period, treatment should be stopped – this is the responsibility of secondary care. Long-term usefulness of guanfacine for extended periods (over 12 months) should be periodically re-evaluated. 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.

Section 3: Monitoring

Please give details of any tests that are required before or during treatment, including frequency, responsibilities (please state whether they will be undertaken in primary or secondary care), cause for adjustment and when it is required to refer back to the specialist.

Baseline tests - where appropriate
Monitoring at baseline and during initiation is the responsibility of the specialist; once the patient is optimised on the chosen medicine, with no anticipated changes expected in the immediate future, prescribing will be transferred to the GP. Monitoring will remain the with the specialist clinician in secondary care unless specific arrangements are made with GP. **Baseline investigations:** • A medical and medication history and full cardiovascular assessment (this should include consideration of any family history of sudden cardiac/unexplained death), taking into account conditions which may be contraindicated, risk of pregnancy (where applicable).

- Height, weight, and body mass index (BMI) on growth chart and risk of obesity
- Blood pressure (BP) and heart rate (including risk of hypotension, bradycardia and QT prolongation
- Risk of somnolence and sedation
- Suicidal ideation or behaviour

Blood tests, ECG and other parameters are not required unless specifically indicated for individual patients. N.B. Electrocardiogram (ECG) is recommended only 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, chest pain suggestive of cardiac origin, signs of heart failure, heart murmur or hypertension, or a co-existing condition that is being treated with a medicine that may pose an increased cardiac risk

Initial monitoring during dose titration:

- Weekly monitoring for signs and symptoms of somnolence, sedation, suicidal ideation or behaviour, hypotension and bradycardia during dose titration and stabilisation
- Assessment of symptom improvement. Discontinue if no improvement is observed after one month.

Subsequent tests - where appropriate *(Please indicate who takes responsibility for taking bloods and interpreting results)*

Ongoing monitoring:

- Before and after every change of dose: assess heart rate and blood pressure.
- Ensure the patient receives a review at least annually with a healthcare professional with training and expertise in managing ADHD. This remains the responsibility of the specialist.
- 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 below remains appropriate.

Test	Frequency	Who by	Action/management For paediatric patients the use of a centile chart is recommended
Blood pressure and heart rate. **Signs or symptoms of cardiovascular adverse effects, e.g. bradycardia and hypotension**	Every 3 months for the first year of treatment, and every 6 months thereafter. N.B. More frequent monitoring is recommended following dose adjustment or discontinuation. Additional monitoring to be carried out by team initiating the dose change (usually	CAMHS or Community Paediatrics department unless local arrangements have been made for individual patients (can also be managed by primary care under advice from secondary care)	Compare with normal range for age. **Hypotension** Give lifestyle advice (e.g. drinking plenty of fluids, getting up slowly from standing or sitting) and repeat monitoring. If BP decreases markedly from baseline, reduce dose by 1mg and discuss with specialist team. **Hypertension** If there is a clinically significant increase in blood pressure or systolic blood pressure is greater than 95th percentile (measured on 2 occasions), refer to paediatric hypertension specialist; consider dose adjustment or alternative ADHD treatment. **Low heart rate:** Discuss with specialist team; dose reduction or cardiac evaluation may be required.

	secondary care).		**Raised heart rate:** NICE guidance suggest to investigate a resting tachycardia of > 120pbm; we suggest to monitor and possibly investigate a sustained resting tachycardia >100bpm; consider ECG; discuss with paediatric physical health colleagues as needed.
Height, weight and BMI (on growth chart)			If there is evidence of significant weight gain, loss or nil weight gain where expected, measure BMI and discuss with patient and family/ carer as appropriate. Plot height and weight of children and young people on a growth chart and ensure review by clinician responsible for treatment.
Somnolence and sedation			Sedation and somnolence typically occur during the start of treatment and with dose increases. Seek specialist advice if sedation persists. Dose reduction or discontinuation may be indicated.
Assessment of adherence	As required based on the patient's needs and individual circumstances	CAMHS or Community Paediatrics department and primary care	Primary care to seek advice from secondary care
Suicidal ideation or behaviour	Annually or if dose is adjusted / titrated or discontinued.	CAMHS or Community Paediatrics department unless arrangements have been made for individual patients.	Primary care to seek advice from secondary care
Monitoring for effectiveness and adverse effects.	During any dose adjustments or discontinuation and every 3 months for the first year and then at least annually.		This should include a review of ADHD medication, including patient preferences, benefits, adverse effects, and ongoing clinical need. Consider trial periods off medication to assess the patient's functioning without pharmacotherapy, preferably during times of school holidays, when assessment of the overall balance of benefits and harms suggests this may be appropriate. If continuing medication, document rationale.
Review to ensure patient has been offered and attended an annual review with a healthcare professional with expertise in ADHD	Annually	Primary care to confirm that review by CAMHS or Community Paediatrics has occurred.	Primary care to seek advice from secondary care

*Children and Adolescent Mental Health Service

Section 4: Side Effects

Please list only the most pertinent side effects and management. Please provide guidance on when the GP should refer back to the specialist. For everything else, please see BNF or SPC.

Side effects and management

Side effect	Frequency/ severity	Action/management
Cardiac related	Uncommon - Severe	Refer for urgent specialist cardiac evaluation: Palpitations, exertional chest pain, syncope, dyspnoea or marked bradycardia (from baseline)
Marked decrease from baseline in heart rate	Common	Discuss with specialist team; dose reduction or cardiac evaluation may be required.
Hypotension or orthostatic hypotension	Common	Give lifestyle advice (e.g. drinking plenty of fluids, getting up slowly from standing or sitting) and repeat monitoring. If BP decreases markedly from baseline, reduce dose by 1mg and discuss with specialist team.
Sedation and somnolence	Very Common	Sedation and somnolence typically occur during the start of treatment and with dose increases. Closely monitor during initiation and stabilisation and every 3 months for first year. Seek specialist advice if sedation persists. Dose reduction or discontinuation may be indicated.
Weight increase	Common	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, treatment break or change of medicine may be required.
Psychiatric disorders Suicidal ideation or behaviour	Common Unknown	Review patient and exclude other causes. Refer urgently to ADHD specialist team. Consider discontinuing guanfacine
Dry mouth	Common	Supportive management. Discuss with specialist if symptoms persist.

Referral back to specialist

Refer back to specialist when:

- Patients become pregnant or starts breastfeeding while taking guanfacine.
- Suicidal behaviour or ideation, syncope, or other signs or symptoms of cardiovascular adverse effects occur (all urgent referral).
- Any loss of clinical efficacy is suspected (e.g. worsening of ADHD symptoms) or intolerance to therapy occurs.
- Any significant change in physical health and comorbidities for example hepatic or renal insufficiency

Section 5: Other Issues

(e.g. Drug Interactions, Contra-indications, Cautions, Special Recommendations)

Please list only the most pertinent action for GP to take (For full list please see BNF or SPC)

Issues

Significant drug interactions of guanfacine

CNS depressants and melatonin	Enhanced sedative effect
Antihypertensives and baclofen	Risk of hypotension
Some anticonvulsants	Greater exposure to either anticonvulsant or guanfacine side effects
CYP3A4 – moderate-potent inhibitors	Reduce dose by half (e.g. with ciprofloxacin, clarithromycin, erythromycin, fluconazole and itraconazole)
CYP3A4 – potent inducers	Increase dose up to max. 7 mg daily (e.g. with carbamazepine, phenobarbital, phenytoin, rifampicin, St. John's Wort and glucocorticoids).
QT prolonging medicines	Risk of additive effect of decreased heart rate

Contraindications

- Hypersensitivity to guanfacine or to any excipients of formulation.

Cautions

- Cardiac issues, e.g. risk of torsade de pointes with bradycardia, heart block and hypokalaemia; caution in patients with history of hypotension, cardiovascular disease or of QT-interval prolongation
- Sedation and somnolence – predominantly at the start of treatment and typically lasts for 2-3weeks, closely monitor during initiation and stabilisation and every 3 months for first year
- Suicidal ideation – post-marketing reports of suicide-related events, monitor closely especially during initiation, optimisation and discontinuation
- Aggression- Behavioural changes- Hostility (predominantly aggression, oppositional behaviour and anger) - patients should closely monitor for worsening of aggressive behaviour
- Pregnancy- avoid during pregnancy
- Refer back to specialist services for advice if patient breastfeeding

Other cautions:

Periods off medication (including poor compliance) for more than 48 hours require re-titration. Do not restart at the previous dose.

Treatment cessation

Avoid abrupt withdrawal. Due to risk of blood pressure increase upon discontinuation, guanfacine should be gradually tapered at a rate of no more than 1 mg every 3 to 7 days. Blood pressure and pulse should be monitored when discontinuing treatment. This is the responsibility of the CAMHS or Community Paediatrics department managing treatment cessation.

Reminder to ask patient about specific problems	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 • Signs and symptoms of bradycardia or hypotension, e.g. fatigue, dizziness, palpitations, feeling faint or fainting

Section 6: Advice to the patient

Advice for prescribing clinician to inform patient

The patient and/or family/carer should be advised:

1. To drink plenty of fluids; dehydration can increase the risk of fainting.
2. Not to drive, cycle, or operate machines if guanfacine affects their ability to do so safely, e.g. by causing dizziness or drowsiness - review timing of dose as guanfacine may be taken in the morning or evening.
3. Avoid alcohol while taking guanfacine, as it may make side effects worse.
4. Avoid grapefruit juice while taking guanfacine (theoretical increase in guanfacine blood levels).
5. Not to stop taking guanfacine without talking to their doctor. Due to risk of discontinuation effects, it is important to gradually reduce the dose of guanfacine under medical supervision. Let your specialist or GP know if you miss more than one dose.
6. To take a pregnancy test if they think there is a possibility they could be pregnant and inform the specialist or GP immediately if they become pregnant or wish to become pregnant (women of child-bearing potential).
7. Avoid taking with high fat meals as this may increase absorption.
8. Information on drug prescribed including a patient information leaflet (PIL). Information on mental health conditions, treatments and medication can be found at:

Choice and Medication
NHS – Attention Deficit Hyperactivity Disorder
Guanfacine Patient Information Leaflet

Section 7: Generic principles of shared care for SECONDARY CARE

Please do not amend.

Core responsibilities

1. Initiating treatment and prescribing for the length of time specified in **section 1.**
2. Undertaking the clinical assessment and monitoring for the length of time specified in **section 1** and thereafter undertaking any ongoing monitoring as detailed in **section 3.**
3. Communicate details of the above in 1 and 2 to GP within the first month of treatment. This information should be transferred in a timely manner.
4. Communicate changes of medication form, strength or dose to the GP before the next repeat prescription is due (ie within 28 days). Note that a change of dose does not itself imply instability, and is usually done as a response to patient growth. If the secondary care clinician feels the medication is not at a stable dose, the GP will be informed that the secondary care provider will supply medication until this is again stable
5. Refer patients to GP and provide information of further action where appropriate e.g. if blood test is due.
6. To provide advice to primary care when appropriate, including queries about medication efficacy and side effects.
7. Review concurrent medications for potential interaction prior to initiation of drug specified in **section 1.**
8. Stopping treatment where appropriate or providing advice on when to stop.
9. Reporting adverse events to the MHRA.
10. Reminder to ask patients about particular problems see **section 5.**

Section 8: Generic principles of shared care for PRIMARY CARE

Please do not amend.

Core responsibilities

1. Responsible for taking over prescribing after the length of time specified in **section 1.**
2. Responsible for any clinical assessment and monitoring if detailed in **section 3** after the length of time specified in **section 1.**
3. Review of any new concurrent medications for potential interactions.
4. Reporting adverse events to the MHRA.
5. Refer for advice to specialist where appropriate.
6. Reminder to ask patients about particular problems see **section 5.**

Section 9: Contact Details

Name	Organisation	Telephone Number	E mail address
Initiating Clinician	AWP	As provided on correspondence	As provided on correspondence
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Section 10: Document Details

Date prepared	28th April 2023
Prepared by	Sarah Steel
Date approved by JFG	6th Feb 2024
Date of review	Feb 2027
Document Identification: Version	V1

Section 11: Collaboration

All shared care protocols should be BNSSG wide where possible. Specialists in any one discipline are encouraged to collaborate across the health community in preparing shared care guidance. Please give details

1. Sarah Steel - Highly Specialised Clinical Pharmacist, AWP
2. Samantha Hayer - CAMHS Consultant, AWP
3. Alfred Perrera - CAMHS Consultant, AWP
4. Richard Williams - Consultant Paediatrician, Sirona Care & Health
5. Richard Lee-Kelland - Consultant Community Paediatrician, Sirona Care & Health – from June 2023

Section 12: References

Please list references

1. Specialist Pharmacy Service. Guanfacine Lactation Safety Information. Last updated October 2022. Accessed on 15/12/2022.

2. Cortese S, Del Giovane C, Chamberlain S*, et al.* Pharmacological and non-pharmacological interventions for adults with ADHD: protocol for a systematic review and network meta-analysis *BMJ Open* 2022;**12:**e058102. Accessed May 2023.
3. eBNF. Guanfacine, last updated 14th December 2022. Accessed via on 15/12/2022.
4. SmPC: Guanfacine hydrochloride 1 mg prolonged-release tablets (Intuniv®). Date of revision of the text 2nd March 2022. Accessed on 15/12/2022.
5. NICE NG87: Attention deficit hyperactivity disorder: diagnosis and management. Last updated 13th September 2019. Accessed on 15/12/2022.
6. EMC: Guanfacine risk minimisation materials. Updated June 2022. Accessed via on 15/12/2022.
7. Specialist Pharmacy Service. Safety in Lactation: Drugs for ADHD. Last updated October 2020. Accessed on 15/12/2022