Pan Mersey
Area Prescribing Committee

SHARED CARE FRAMEWORK

The Pan Mersey Area Prescribing Committee recommends the prescribing of GUANFACINE (Intuniv®▼) for ADHD in accordance with NICE NG87.

SHARED CARE

NHS Halton CCG for the treatment of adults only
NHS Knowsley CCG for the treatment of adults only
NHS St Helens CCG for the treatment of adults only
NHS Warrington CCG for the treatment of adults only

Background

Attention deficit hyperactivity disorder (ADHD) is a chronic, neurodevelopmental disorder associated with inattention, hyperactivity and impulsiveness.

The National Institute for Health and Clinical Excellence (NICE) issued a clinical guideline, Attention Deficit Hyperactivity Disorder: diagnosis and management (NG87) in 2018. This document advises that treatment for ADHD should only be initiated by a healthcare professional with expertise in ADHD and should be based on a comprehensive assessment and diagnosis. Continued prescribing and monitoring of drug therapy may be performed by the primary care clinicians, under shared care arrangements.

NICE states: Offer guanfacine to children aged 5 years and over and young people if they cannot tolerate methylphenidate or lisdexamfetamine or their symptoms have not responded to separate 6-week trials of lisdexamfetamine and methylphenidate, having considered alternative preparations and adequate doses.

Symptoms of ADHD can persist into adulthood in about two thirds of all patients. For patients transitioning into adulthood, specialists should ensure appropriate arrangements are made for referral into adult services. In such circumstances a new shared care agreement will need to be made between the primary care clinician and the new specialist provider.

Treatment must be initiated by a specialist in the treatment of ADHD, such as a paediatrician, child/adolescent psychiatrist, or psychiatrist.

Mode of action

Guanfacine is a selective central alpha 2A-adrenergic receptor agonist and it is a non-stimulant. Preclinical research suggests guanfacine modulates signalling in the prefrontal cortex and basal ganglia through direct modification of synaptic noradrenalin transmission at the alpha 2- adrenergic receptors.

Licensed Indications

Guanfacine is indicated for the treatment of ADHD in children and adolescents 6 – 17 years old for whom stimulants are not suitable, not tolerated or have been shown to be ineffective. It must be used as a part of a comprehensive ADHD treatment programme, typically including psychological, educational and social measures.

Locally agreed off-label use

This document supports the following off label uses:

- Continuing treatment in adults from 18 years old and above whose symptoms persist into adulthood and who have shown clear benefit from treatment
- Children aged 6 years old and above weighing less than 25kg
- Children aged 5-6 years

Initiation and ongoing dose regime

Transfer of monitoring and prescribing to primary care is after the dose has been stabilised and the patient has been reviewed by the specialist. The duration of treatment will be determined by the specialist based on clinical response and tolerability.

Dosing information

All dose adjustments will be the responsibility of the initiating specialist unless directions have been discussed and agreed with the primary care clinician.

For all patients, the recommended starting dose is 1 mg of guanfacine, taken orally once a day.

The dose may be adjusted in increments of not more than 1 mg per week. The initial dose should be titrated against symptoms and adverse effects in line with the BNF or BNF for Children until dose optimisation is achieved, that is, reduced symptoms, positive behaviour change, improvements in education, employment and relationships, with tolerable adverse effects[2].

The recommended maintenance dose range is 0.05 - 0.12 mg/kg/day.

The recommended **dose titration** for children and adolescents is provided below (see under specialist initiation and titration). Dose adjustments (increase or decrease) to a maximum tolerated dose within the recommended optimal weight-adjusted dose range based upon clinical judgement of response and tolerability may occur at any weekly interval after the initial dose.

Age	**Weight Group**	**Recommended max dosage frequency**
6 – 12 years	<34kg	4mg once daily
13 – 17 years	34 – 41.4kg	4mg once daily
	41.5 – 49.4kg	5mg once daily
	49.5 – 58.4kg	6mg once daily
	58.5kg and above	7mg once daily
Adult aged 18 years and over		Continue treatment at the stabilised dose

Specialist Initiation and Titration

Dose Titration Schedule for Children Aged 6-12 years				
For children aged 6 and above weighing < 25kg, initiate starting dose of 0.05 – 0.12mg/kg/day; adjust dose in increments of not more than 1mg per week according to the patient's response and tolerability. Max 4mg once a day.				
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

Dose Titration Schedule for Adolescents (Aged 13-17 Years)/ Adolescent patients must weigh at least 34 kg.							
Weight Group	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

Adolescents weighing 58.5 kg and above may be titrated to a 7 mg/day dose after the patient 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.

Dose reduction may be required in patients with different degrees of hepatic or renal impairment – please refer to current SPC for further information.

Ongoing prescribing

Shared Care may only be commenced following initiation, stabilisation and review of treatment. In addition, formal agreement must have been received from the primary care prescriber. Termination will be the responsibility of the specialist.

Review the use of guanfacine at least once a year and discuss with the patient (and their families and carers as appropriate) whether the medication should be continued (NICE NG87).

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. This will be undertaken and supervised by the specialist who will advise the patient and GP of the outcome.

For extended periods of treatment (over 12 months) 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.

Baseline investigations and initial monitoring to be undertaken by the specialist

Baseline: Pre-Treatment Screening

Before starting medication for ADHD, a full assessment should be completed which should include:

- a review to confirm they continue to meet the criteria for ADHD and need treatment
- a review of mental health and social circumstances, including:
    - presence of coexisting mental health and neurodevelopmental conditions
    - current educational or employment circumstances
    - risk assessment for substance misuse and drug diversion
    - care needs
- a review of physical health, including:
    - a medical history, taking into account conditions that may be contraindications for specific medicines
    - current medication
    - height and weight (measured and recorded against the normal range for age, height and sex)
    - baseline pulse and blood pressure
    - A cardiovascular assessment.

An electrocardiogram (ECG) is not needed before starting guanfacine, unless the person has any of the features mentioned in recommendation 1.7.5 of the NICE 2018 Attention deficit hyperactivity disorder diagnosis and management guidelines or a co-existing condition that is being treated with a medicine that may pose an increased cardiac risk.

During dose titration, weekly monitoring for signs and symptoms of somnolence and sedation, blood pressure for hypotension and pulse for bradycardia, clinical response is required.

Ongoing monitoring requirements to be undertaken by primary care

Monitoring	Frequency
Blood pressure and pulse (appropriate for age, using information supplied in attached request letter – children & adolescents only)	At every adjustment of dose or visit to the specialist service and then every 6 months. Primary care – every 6 months.
Weight (in adults); Height and weight (in children and adolescents	At every adjustment of dose or specialist visit or at least every 6 months. Primary care – every 6 months. Weight every 3 months in children 10 years and under.
Signs and symptoms of somnolence/sedation	Every 6 months. Also, at every adjustment of dose or visit to the specialist service.
Side effects and compliance	Every 6 months.
Clinical need, benefits, side effects	Annual review by Specialist.

Cardiovascular monitoring (blood pressure and heartrate) should be undertaken before and after each dose adjustment.

Refer to '*Adverse Drug Reactions*' section for advice and actions to be taken.

Pharmaceutical aspects

Route of administration

Oral

Formulation

Prolonged release tablets in 1mg, 2mg, 3mg and 4mg

Administration details

Tablets should be swallowed whole, and should not be administered with high fat meals, to avoid increased guanfacine exposure. The prolonged release properties will be lost by crushing, chewing or breaking tablets before swallowing. Guanfacine should not be administered together with grapefruit juice.

Other Important Information

- Patients/carers are advised not to discontinue guanfacine without consulting their specialist.
- Blood pressure and pulse may increase following discontinuation of guanfacine.
- Tapering guanfacine dosing during withdrawal is recommended to minimise these potential withdrawal effects.
- Monitoring of blood pressure and pulse is recommended during dose downward titration.

Legal category

Guanfacine is a prescription only medicine (POM). It is not a controlled drug.

Contraindications

For a comprehensive list consult the BNF or Summary of Product Characteristics.

Significant drug interactions

For a comprehensive list consult the BNF or Summary of Product Characteristics.

Adverse effects and management

For a comprehensive list consult the BNF or Summary of Product Characteristics.

The occurrence of somnolence/sedation and hypotension is most prominent in the first few weeks of treatment and diminishes gradually thereafter.

In children, parents/patients will have been advised by the ADHD specialist to report any suspected side effects directly to them. GPs should refer any patients with suspected side effects to the ADHD specialist irrespective of the advice in the following table.

Adverse effect	Management
Clinically concerning or persistent somnolence / sedation Severe and persistent headache Syncope	Exclude other causes and seek ADHD specialist advice if appropriate.
Depression	Exclude other causes and seek immediate ADHD specialist advice if suicidal ideation becomes apparent.
Bradycardia Significant changes in blood pressure (hypotension)	Exclude other causes. Repeat monitoring (blood pressure and pulse) on another occasion by GP. If symptoms thought secondary to the drug, seek ADHD specialist advice if appropriate.
Weight gain or increased body mass index (BMI)	Exclude other causes and seek ADHD specialist advice if appropriate.

Guanfacine is a black triangle drug. Any suspected adverse reaction should be reported to the MHRA via the "Yellow Card" scheme on http://yellowcard.mhra.gov.uk/

Advice to patients and carers

The specialist will counsel the patient regarding 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 GP without delay:

- Patient with emergent suicidal ideation or behaviour

In children, parents/patients will have been advised by the ADHD specialist to report the above signs or symptoms directly to them.

WARNING: Guanfacine may have a moderate to severe effect on the ability to drive, use machines or cycling. Patients will be warned of these possible effects during treatment initiation and be advised that if affected, they should avoid these activities.

Pregnancy and breast feeding

Seek advice from initiating specialist service for prescribing decision.

Specialist contact information

If stopping medication or needing advice
Please refer to the shared care agreement (Appendix 2)

Additional information

Where patient care is transferred from one specialist service or GP practice to another, a new shared care agreement must be completed.

References

1. Bolea-Alamanac et al. Evidence-based guidelines for the pharmacological management of attention deficit hyperactivity disorder: Update on recommendations from the British Association for Psychopharmacology Journal of Psychopharmacology 2014; 28(3): 179-203
2. NICE guidelines NG87 March 2018: Attention deficit hyperactivity disorder: diagnosis and management; https://www.nice.org.uk/guidance/ng87
3. NICE quality standard (QS39) 2013 (updated March 2018): Attention deficit hyperactivity disorder; https://www.nice.org.uk/guidance/qs39

4. Summary of Product Characteristics (Intuniv ®), updated 02/07/19, accessed 12/08/19; https://www.medicines.org.uk/emc/product/5099/smpc
5. BNF for Children BNF British National Formulary - NICE
6. NICE ESNM70: ADHD in children and young people: guanfacine prolonged- release (Mar 2016); https://www.nice.org.uk/advice/esnm70/resources/attention-deficit-hyperactivity-disorder-in-children-and-young-people-guanfacine-prolongedrelease-pdf-1502681158970053

To be read in conjunction with the following documents.

1. Policy for Shared Care
2. Shared care agreement.

Appendix 1

Policy for Shared Care

Shared care is only appropriate if it provides an optimum solution for the patient and it meets the criteria outlined in the Shared Care section of the Pan Mersey Definitions and Criteria for Categorisation of Medicines in the Pan Mersey Formulary document.

Before prescribing responsibilities are transferred to primary care:

- Prescribing responsibility will only be transferred when the consultant and the patient's GP agree that the patient's condition is stable.
- All information required by the shared care framework for the individual medicine has been provided to the patient's GP.
- Patients will only be referred to the GP once the GP has agreed to the Shared Care Agreement and returned signed copies.

Inherent in any shared care agreement is the understanding that participation is at the discretion of the GP, subject to the availability of sufficient information to support clinical confidence.

Specialist Responsibilities in Shared Care

- To initiate the medicine, prescribe, monitor for toxicity and efficacy as described by the shared care framework until the patient is stabilised.
- To ensure the patient or their carer:
    - Is counselled with regard to the risks and benefits of the medicine.
    - Provide any necessary written information to the patient with regard to the individual medicine including patient information leaflets on individual drugs.
    - Obtain and document informed consent from the patient when any medicines is prescribed for an off-label indication for any condition
- To be familiar with the shared care framework.
- To provide all information to the patient's GP as required by the shared care framework when prescribing responsibility is initially transferred and at any subsequent times as necessary for safe and effective treatment of the patient.
- To assess the patient regularly as necessary for the duration of therapy.
- To review the patient promptly if required by the GP concerned.
- To meet any additional requirements as required by the individual medicine shared care framework.
- To communicate failure of a patient to attend a routine hospital review and advise the GP of appropriate action to be taken.

Primary Care Responsibilities in Shared Care

- To reply to a written request for Shared Care within 21 days ensuring both copies of the Shared Care Agreement are signed if appropriate.

If agreeing to shared care, the GP is asked to:

- To provide prescribe or manage and monitor the medicine as advised by the Specialist and in line with the individual Shared Care Framework.
- To review the patient as required by the Shared Care Framework
- To make appropriate and contemporaneous records of prescribing and/or monitoring and to note the existence of the Shared Care Agreement on the patient`s clinical record. A READ code of "6652 Shared Care-Specialist/GP" can be used.
- To be familiar with the individual Shared Care Framework.
- To report any adverse effects of treatment to the specialist team.
- To inform the Specialist of any relevant change in the patient's circumstances.
- To seek Specialist advice as appropriate.
- To meet any additional requirements as required by the individual Shared Care Framework.
- To respond to Specialist communication relating to any change or addition to the patient's treatment covered by the Shared Care Agreement.

Where the GP wishes to withdraw prescribing, for example when the patient fails to attend for monitoring, they need to give the specialist team a minimum of 14 days' notice of their need to resume responsibility for prescribing. The specialist is required to acknowledge this request within the 14-day time period.

Appendix 2

Shared Care Agreement

Guanfacine

Request by Specialist Clinician for the patient's GP to enter into a shared care agreement

Part 1

To be signed by Consultant / Associate Specialist / Specialist registrar or Specialist Nurse (who must be a prescriber)

Date _____

Name of patient_____

Address _____

_____

Patient NHS No _____

Patient hospital unit No _____

Diagnosed condition _____

Dear Dr_____

I request that you prescribe

GUANFACINE

for the above patient in accordance with the enclosed shared care framework.

Last Prescription Issued: ..... / ..... / ..... Next Supply Due: ..... / ..... / .....

I confirm that the patient has been stabilised and reviewed on the above regime in accordance with the Shared Care Framework and Policy.

I confirm that if this is a Shared Care Agreement for a drug indication which is unlicensed or off label, informed consent has been received.

Details of Specialist Clinicians

Name _____Date_____

Consultant / Prescribing member of the Specialist Team *circle or underline as appropriate

Signature _____

In all cases, please also provide the name and contact details of the Consultant.

When the request for shared care is made by a prescriber who is not the consultant, it is the supervising consultant who takes medico-legal responsibility for the agreement.

Consultant: _____

Contact details:

Shared Care Framework

Telephone number: _____Ext:_____

Address for return _____

of documentation

_____

_____

Please add patient addressograph here

Part 2

To be completed by Primary Care Clinician

I agree to prescribe _____for the above patient in accordance with the enclosed shared care framework.

GP signature _____Date _____

GP name _____Please print

GP: Please sign and return a copy within 21 calendar days to the address above

OR

GP- If you do not agree to prescribe, please delete the section above and provide any supporting information as appropriate below: