PAN MERSEY APC

PAN MERSEY AREA PRESCRIBING COMMITTEE
SHARED CARE FRAMEWORK
REF: SC13 FINAL
APC BOARD DATE: 30 NOV 2016

NHS
Pan Mersey
Area Prescribing Committee

GUANFACINE

1. 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. Methylphenidate, atomoxetine, dexamfetamine, lisdexamfetamine and guanfacine are recommended within their licensed indications, as options for the management of ADHD. Some prescribing of ADHD medication is 'off-label' but clearly supported by the NICE guideline, British National Formulary (BNF) and BNF for Children. 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 secondary care provider.
2. Mode of Action	Guanfacine is a selective central alpha $_{2A}$-adrenergic receptor agonist and it is a non-stimulant. The mode of action of guanfacine in ADHD is not fully established. 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.
3. 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.
4. Locally agreed off -label indications	This document supports the following off label uses (denoted by *): • 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

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(or earlier if there is significant new evidence relating to this recommendation)

5. Contraindications

(Please note this does not replace the Summary of Product Characteristics (SPC) and should be read in conjunction with it. Refer to the manufacturers SPC for complete up-to-date list.)

Hypersensitivity to guanfacine or to any of the excipients listed in the SPC

6. Pharmaceutical aspects

(including route of administration, formulation, method of administration, legal category)

Route of Administration	Oral
Formulation	Prolonged release tablets in 1mg, 2mg, 3mg and 4mg
Method of administration	**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.
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.

7. 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 **0.05-0.12 mg/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
25kg and up	1mg	2mg	3mg	4mg (max dose)

Dose Titration Schedule for Adolescents (Aged 13 – 17 years)							
Weight Group	Week1	Week2	Week3	Week4	Week5	Week6	Week7
34 – 41.4kg	1mg	2mg	3mg	4mg (max dose)			
41.5 – 49.4kg	1mg	2mg	3mg	4mg	5mg (max dose)		
49.5 – 58.4kg	1mg	2mg	3mg	4mg	5mg	6mg (max dose)	
58.5kg and above	1mg	2mg	3mg	4mg	5mg	6mg	7mg (max dose)

Dose reduction may be required in patients with different degrees of hepatic impairment – refer to SPC

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.

8. Dosage regimen for continued prescribing in Primary Care

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

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

Duration of treatment *To be determined by the specialist based on clinical response and tolerability.*	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. Trial periods off medication (drug holiday) to assess the patient's condition without treatment may be deemed appropriate by the ADHD specialist, this will be undertaken and supervised by the specialist who will advise the patient and GP of the outcome
Termination of treatment	This will be carried out by the specialist

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

9. Significant Drug Interactions

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

Seek advice from the initiating Specialist if any of the following drugs are co-prescribed.

Drugs that prolong QT interval *(e.g. neuroleptics, class 1A and III anti-arrhythmias, moxifloxacin, erythromycin, methadone, mefloquine, tricyclic antidepressants, lithium or cisapride) – Guanfacine causes a decrease in heart rate.*

CYP3A4 and CYP3A5 inhibitors - elevates plasma guanfacine levels and increases risk of adverse reactions e.g. hypotension, bradycardia and sedation. *50% dose reduction is recommended; further dose titration may be needed due to variability in interaction effect.*

CYP3A4 inducers – reduces plasma guanfacine levels and exposure *Re-titration to increase the dose may be considered if needed. If the inducing treatment is ended, retitration to reduce guanfacine dose is recommended during the following weeks.*

Valproic acid – Increased plasma valproic acid levels and potential additive central nervous system effects.

Antihypertensives – additive pharmacodynamics effects e.g. hypotension, syncope

CNS depressants (e.g. alcohol, sedatives, hypnotics, benzodiazepines, barbiturate and antipsychotics) – additive CNS effects e.g. sedation and somnolence.

10. Adverse drug reactions

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

Very common (>10%): Somnolence, fatigue, headache, abdominal pain

Common (>1% to <10%): reduced appetite, depression, anxiety, lethargy, sedation, dizziness, bradycardia, hypotension, vomiting, diarrhea, rash, weight gain, irritability, enuresis

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 event	**Action to be taken and by whom**
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.*

<table>
<tr><td></td><td>WARNING: It 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.</td></tr>
<tr><td></td><td>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/</td></tr>
<tr><td>11. Advice to patient/carers</td><td>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.</td></tr>
<tr><td>12. Pregnancy and breast feeding</td><td>Seek advice from initiating specialist service for prescribing decision.</td></tr>
<tr><td>13. Baseline investigations to be undertaken by the specialist centre</td><td><u>Pre-treatment screening</u>
• Baseline evaluation of cardiovascular status including blood pressure and heart rate
• Comprehensive drug history (i.e. concomitant medications)
• Past and present co-morbid medical and psychiatric disorders or symptoms
• Family history of sudden cardiac/unexplained death
• Weight (in adults); height and weight plotted on a growth chart (in children and adolescents)
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.</td></tr>
<tr><td>14. Ongoing monitoring requirements to be undertaken by the specialist team and Primary Care</td><td>
<table>
<tr><th>Monitoring</th><th>Frequency</th></tr>
<tr><td>Blood pressure and pulse
(appropriate for age, using information supplied in attached request letter – children & adolescents only)</td><td>Every 6 months for the first year of treatment and 6 monthly thereafter or at every adjustment of dose</td></tr>
<tr><td>Weight (in adults); Height and weight (in children and adolescents)</td><td>Primary care – every 6 months

Weight every 3 months in children 10 years and under</td></tr>
<tr><td>Signs and symptoms of somnolence/sedation</td><td>Every 6 months</td></tr>
<tr><td>Side effects</td><td>Every 6 months</td></tr>
<tr><td>Clinical need, benefits, side effects</td><td><u>Annual review by Specialist</u></td></tr>
<tr><td colspan="2">Refer to ‘Adverse Drug Reactions’ section for advice and actions to be taken.</td></tr>
</table>
</td></tr>
<tr><td>15. Specialist contact information</td><td>If stopping medication or needing advice
Please refer to the shared care agreement (Appendix 2)</td></tr>
<tr><td>16. Additional information</td><td>Where patient care is transferred from one specialist service or GP practice to another, a new shared care agreement must be completed.</td></tr>
</table>

17. 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 3. NICE quality standard (QS39) 2013: Attention deficit hyperactivity disorder 4. Summary of Product Characteristics (Intuniv ®) 5. BNF for Children (when published) 6. NICE ESNM70: ADHD in children and young people: guanfacine prolonged-release (Mar 2016)
18. To be read in conjunction with the following documents	Shared Care Policy (appendix 1) Shared Care Agreement (appendix 2)

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 patients 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, prescribing and monitoring toxicity and efficacy as required until the patient is stabilised and reviewed as described by the shared care framework.
- To ensure the patient or their carer is counselled with regard to the medicine.

- To provide any necessary written information to the patient with regard to the individual medicine.
- To be familiar with the shared care framework.
- To provide all information to the patients 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 as specified in the individual medicine shared care framework.
- 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.
- Following the addition of a new drug to an existing regime covered by a Shared Care Agreement, the Specialist must recall the patient for re-titration, stabilisation and subsequent review and inform the GP of this. A new Shared Care Agreement must then be initiated.

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 monitor patient’s general wellbeing.
- To report any adverse effects of treatment to the consultant
- 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.

Appendix 2: **Shared Care Agreement**

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

Part 1 - to be signed by Consultant / Prescribing Member of Specialist Team

Date _____

Name of patient_____

Address _____

_____

Patient NHS No _____

Patient hospital unit No _____

Diagnosed condition _____

If using addressograph label please attach one to each copy

Dear Dr_____

I request that you prescribe

(1) _____

(2) _____

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 Specialist Team ***circle or delete 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*:*

Telephone number: _____Ext:_____

Address for return of documentation _____

_____

_____

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: