AWTTC
All Wales Therapeutics & Toxicology Centre
Canolfan Therapiwteg a Thocsicoleg Cymru Gyfan

Evidence status report for a limited assessment

Guanfacine (Intuniv®) prolonged release (PR) tablet

Indication

Treatment of attention deficit hyperactivity disorder (ADHD) in children and adolescents 6 to 17 years old for whom stimulants are not suitable, not tolerated or have been shown to be ineffective. Intuniv® must be used as a part of a comprehensive ADHD treatment programme, typically including psychological, educational and social measures.

Company

Takeda

Background

The management of ADHD in children and young people consists of a multi-faceted approach combining behavioural therapy and where appropriate pharmacotherapy that addresses the individual needs of a patient. Treatment guidelines published by the National Institute of Health and Care Excellence (NICE) recommend psychostimulant medicines as first-line treatment, which must be part of a comprehensive treatment programme. The use of non-stimulant medicines is recommended in children and adolescents who cannot tolerate or do not respond to stimulants.

Guanfacine is a non-stimulant medicine, with a different mechanism of action to the existing licensed treatments and is positioned joint third-line in treatment pathway guidelines with atomoxetine, the only other licensed non-stimulant treatment for ADHD.

AWMSG appraised guanfacine following a full submission by the company and issued a negative recommendation in May 2016. Therefore, guanfacine is not recommended for use in NHS Wales for the treatment of ADHD in children 6 years and older. AWMSG determined that the case for cost-effectiveness had not been proven and the key factors for influencing this recommendation were the considerable uncertainties and limitations in the economic model provided in the company's submission and that the applicant company did not present sufficiently robust economic analyses to gain approval by AWMSG. The company was encouraged to re-submit for reassessment by AWMSG and made a new submission in 2020. However, after review, it was determined that the new evidence submitted was not substantially different to that presented in the original appraisal and so revaluation of the AWMSG recommendation issued in 2016 was not warranted.

Guanfacine is routinely available for patients in Scotland following health technology assessment by the Scottish Medicines Consortium who issued a positive recommendation for the full indication in 2016. Guanfacine has not been assessed by NICE HTA and NICE have no plans for doing so; however, it is included in the NICE

guideline NG87: Attention deficit hyperactivity disorder: diagnosis and management published in 2018. This recommends the use of atomoxetine or guanfacine in children and young people aged 5 years and older 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; in England, patients can access guanfacine through local trust protocols (for example Tees, Esk and Wear Valleys NHS Foundations Trust, East London NHS Foundation Trust and Oxford Health/Buckinghamshire Healthcare NHS Trusts; list not exhaustive).

In their original assessment AWMSG was satisfied that the case for clinical effectiveness was established. The AWMSG Scrutiny Panel was also satisfied that, as use of guanfacine is included in national guidelines, is nationally commissioned elsewhere and considered standard of care, the case for clinical effectiveness is established and does not warrant further review. No new safety concerns have been reported since the original submission in 2016.

Despite the AWMSG negative recommendation, between 2018 and 2024 three health boards in Wales have made the decision to routinely fund guanfacine as a joint third-line non-stimulant treatment option in-line with the NICE NG87 guideline. In response to stock shortages of atomoxetine, one additional health board has made guanfacine available (as a non-formulary request) for suitable patients who cannot obtain their usual atomoxetine; if a good response is achieved, the patient is able to remain on guanfacine even if atomoxetine subsequently becomes available.

The differences in availability of guanfacine within NHS Wales has created an inequity of access. Clinicians from health boards where this treatment is not routinely available have raised lack of access as an issue with AWTTC. They consider that guanfacine provides a useful option in the treatment pathway fulfilling an unmet clinical need for a small sub-group of patients. The 2025 change to the AWMSG assessment process has allowed AWMSG to proceed with a re-assessment of guanfacine for the indication under consideration without the need for an updated submission from the company.

Marketing authorisation date: 17 September 2015

Criteria for limited assessment

The Scrutiny panel reviewed the clinical request for re-assessment of guanfacine and considered that guanfacine was suitable for a limited assessment via the Licensed One Wales Medicines Assessment Group (LOWMAG). They cited the following reasons for this decision:

- Guanfacine is included in the NICE clinical guideline NG87; clinicians state this guideline is followed in NHS Wales for the diagnosis and management of ADHD. It has been made routinely available in some Welsh health boards thus creating an inequity of access to guanfacine resulting in an unmet clinical need in some areas of Wales

- It is available to patients in both England and Scotland
- It is considered that making guanfacine routinely available throughout NHS Wales will have a low budget impact and service impact.
- The clinical effectiveness of guanfacine is established.

The AWMSG Scrutiny Panel agreed that as the case for clinical effectiveness is established it does not warrant further review. Therefore, the limited assessment should give an overview of current use, equity of access and budget impact only.

Comparator(s) and place in pathway

Guanfacine is positioned in the NICE NG87 guideline at the same point in the clinical pathway as atomoxetine. Atomoxetine was the comparator in the 2016 AWMSG appraisal.

In clinical practice, Welsh clinicians indicate that guanfacine is mainly given after atomoxetine has proved ineffective or led to worsening of symptoms. However, clinicians also highlight that guanfacine may be used in preference to atomoxetine for a small sub-group of patients with ADHD and other co-morbidities.

Clinicians indicate that clonidine (which is not licensed for use in children) or best supportive care (which may include non-pharmacological options) would be next-line treatments after atomoxetine in the absence of guanfacine.

Budget impact

The recommended starting dose of guanfacine is 1 mg, taken orally once a day. The dose may be adjusted in increments of not more than 1 mg per week and should be individualised according to the patient's response and tolerability. The recommended maintenance dose range is 0.05–0.12 mg/kg/day. The maximum dose for children aged 6 to 12 years is 4 mg daily; for young people aged 13 to 17 years the maximum dose is dependent on weight, with a maximum dose of 7 mg daily for young people weighing 58.5 kg and above.

Guanfacine is costed at list price of £56 (28 x 1 mg), £58.52 (28 x 2 mg), £65.52 (28 x 3 mg) and £76.16 (28 x 4 mg).). The cost of guanfacine is unchanged from the original AWMSG assessment in 2016. Atomoxetine is usually initiated under specialist recommendation with a shared care agreement. NHS Wales prescribing data for 2024 shows that over 90% of atomoxetine is dispensed via primary care at list price which is between £50.55 (28 x 10 mg) to £53.67 (28 x 60 mg). It should be noted that a proprietary oral solution (4 mg/1 ml) of atomoxetine (Strattera) is available with a list price of £85 for 300 ml. This may be prescribed as an alternative formulation for younger children or for those with difficulties in swallowing capsules. The medicine acquisition costs and cost differences given in Tables 1 and 2 are calculated using atomoxetine capsules only. All calculations exclude VAT.

Table 1. Range of estimated medicine acquisition costs per patient per year

	Minimum daily dose (mg)	Maximum daily dose (mg)	Minimum medicine acquisition cost per annum	Maximum medicine acquisition cost per annum
Guanfacine	1	7	£728.00	£1,841.84
Atomoxetine *	25	100	£695.37	£1,385.67 (single daily dosing) £2,781.48 (twice daily dosing)
*The usual maintenance dose for children and adolescents aged 6–17 (body weight up to 70 kg) is 1.2 mg/kg of atomoxetine daily. The average weight of a six-year-old child is approximately 20 kg; this has been used to guide the lower estimate. The maximum maintenance dose for atomoxetine is 100 mg usually administered as a single daily dose (40 mg + 60 mg tablets daily). However, patients not achieving a satisfactory clinical response when taking atomoxetine as a single daily dose may benefit from taking it as twice daily evenly divided doses (4 x 25 mg tablets daily). Costs for both regimens have been provided. All prices exclude VAT.				

It is estimated that 3,678 children and adolescents aged between 6 and 17 years with ADHD would be pharmacologically treated. This has been calculated using Welsh mid-year 2023 population estimates and THIN data (2012) which gives the proportion of ADHD patients treated with medication in the UK. It is assumed that there are no changes over time in the total population size, and the predicted prevalence remains constant in the budget impact analyses calculations. This is comparable to the estimate of 3,511 provided by the company in their original submission with the slight increase due to population growth. More recent data on UK prevalence of pharmacologically treated ADHD has been published by Bachmann et al (2017) and Raman et al (2018); however, AWTTC consider these data less reflective of the target 6-17 years age group as prevalence was calculated for wider age ranges (from 0 to 19 years and 3 to 18 years respectively). The original company estimate of 10% for the market share for non-stimulants has been used; this agrees with clinicians in Wales who estimate that about 1 in 10 children/adolescents with ADHD requiring treatment with medication may benefit from guanfacine. The number of eligible patients is therefore assumed to be 368. The original company predictions for the percentage uptake of guanfacine over 5 years have also been used. These factor in new patients starting treatment, patients stopping treatment and existing patients continuing treatment.

Table 2. Costs associated with use of guanfacine for the treatment of ADHD in children and adolescents 6 to 17 years old for whom stimulants are not suitable, not tolerated or have been shown to be ineffective.

	Year 1	Year 2	Year 3	Year 4	Year 5
No. eligible patients	368	368	368	368	368
Uptake of medicine	11%	24%	39%	56%	61%
No. patients receiving guanfacine	40	88	144	206	225
Minimum guanfacine acquisition cost	£29,120	£64,064	£104,832	£149,968	£163,800
Maximum guanfacine acquisition cost	£73,674	£162,082	£265,225	£379,419	£414,414
Minimum atomoxetine acquisition cost	£27,815	£61,193	£100,133	£143,246	£156,458
Maximum atomoxetine acquisition cost (single daily dosing)	£55,427	£121,939	£199,536	£285,448	£311,776
Maximum atomoxetine acquisition cost (twice daily dosing)	£111,259	£244,770	£400,533	£572,985	£625,833
Minimum net acquisition cost of guanfacine in comparison to atomoxetine	**£1,305**	**£2,871**	**£4,699**	**£6,722**	**£7,342**
Maximum net acquisition cost of guanfacine compared to atomoxetine (single daily dosing)	**£18,247**	**£40,143**	**£65,688**	**£93,971**	**£102,638**
Maximum net acquisition cost of guanfacine compared to atomoxetine (twice daily dosing)	**-£37,586**	**-£82,688**	**-£135,308**	**-£193,566**	**-£211,419**

It is estimated that enabling access to guanfacine is associated with an increased spend ranging between £1,305 to £18,247 in Year 1, and between £7,342 to £102,638 in Year 5. These estimates incorporate cost differences resulting from the displacement of atomoxetine capsules with the maximum estimates based on displacement of the highest recommended dose of atomoxetine for this age group given as a single daily dose. If twice-daily dosing of atomoxetine at the highest

recommended dose is considered, guanfacine is predicted to be cost-saving in comparison.

The actual budget impact will be lower than that predicted above as there is already a significant NHS Wales spend on guanfacine. As previously stated, three health boards covering approximately 41% of the Welsh population have enabled routine access to guanfacine; prescribing data show that [confidential data removed] was spent on guanfacine in 2024.

The budget impact considerations are limited to acquisition costs only; other resource use is not included (e.g. monitoring costs and costs associated with adverse events). However, these are expected to be similar for both guanfacine and atomoxetine.

Impact on health and social care services

Additional monitoring of heart rate and blood pressure is required for guanfacine especially in the dose titration. According to the SmPC, monitoring of heart rate and blood pressure parameters should continue on a weekly basis during dose titration and stabilisation and at least every 3 months for the first year, taking into consideration clinical judgement. Six monthly monitoring should follow thereafter, with more frequent monitoring following any dose adjustment. Atomoxetine has similar monitoring requirements (SmPC) although some clinicians indicate that guanfacine may require more frequent blood pressure checks, especially in the initial phase of treatment. The use of guanfacine is not expected to cause additional impact on social care services.

Patient factors

Clinicians in Wales with experience of prescribing guanfacine highlight it can be more effective and better tolerated than atomoxetine in children with ADHD and certain co-morbidities including autistic spectrum complex (ASC), learning disabilities, disordered sleep and hyperkinesis. For some young people with ADHD, stimulant medications and atomoxetine are either not effective or can exacerbate symptoms of their co-morbidity which may include anxiety, obsessions, sensory needs, tics, emotional lability and behavioural disturbance. Guanfacine can be a better balance for supporting ADHD symptoms whilst also not increasing co-morbidity-associated symptoms. Guanfacine also has less effect on appetite than other medications for ADHD including atomoxetine, which clinicians consider to be a huge benefit for some children and may be the main driver for prescribing.

Clinicians report that guanfacine has significantly improved quality of life for some of their patients and their families, allowing return to full-time schooling, being able to access coping strategies and participate in family events.

Equality impact assessment

AWTTC have completed an Equality and Health Impact Assessment in parallel with each development stage of the project. This follows the five ways of working for public bodies, and work to achieving the wellbeing goals, outlined in the Well-Being of Future Generations (Wales) Act 2015.

It is not expected that guanfacine will have a potential negative impact on people based on the protected characteristics of the Equality Act 2010. However, it would be expected that a positive recommendation will remove any existing inequity in access to guanfacine because of where patients live in Wales.

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