Scottish Medicines Consortium
Providing advice about the status of all newly licensed medicines
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2nd Resubmission

botulinum toxin A, 50 Allergan units, 100 Allergan units, 200 Allergan units, powder for solution for injection (Botox®) SMC No. (692/11)

Allergan Limited

13 January 2017

The Scottish Medicines Consortium (SMC) has completed its assessment of the above product and advises NHS Boards and AREA Drug and Therapeutic Committees (ADTCs) on its use in Scotland. The advice is summarised as follows:

ADVICE: following a resubmission

botulinum toxin A (Botox®) is accepted for restricted use within NHS Scotland.

Indication under review: Prophylaxis of headaches in adults with chronic migraine (headaches on at least 15 days per month of which at least 8 days are with migraine).

SMC restriction: use in adults with chronic migraine whose condition has failed to respond to ≥3 prior oral prophylactic treatments, where medication overuse has been appropriately managed.

In pooled analysis of the two pivotal phase III studies, botulinum toxin type A (Botox®) significantly reduced the frequency of headache days compared with placebo.

Overleaf is the detailed advice on this product.

Chairman,
Scottish Medicines Consortium

Published 13 February 2017

Indication

Prophylaxis of headaches in adults with chronic migraine (headaches on at least 15 days per month of which at least 8 days are with migraine).[1]

Dosing Information

155 Units to 195 Units administered intramuscularly as 0.1mL (5 Units) injections to 31 and up to 39 sites.

Botulinum toxin units are not interchangeable from one product to another. Doses recommended in Allergan Units are different from other botulinum toxin preparations.

It should only be administered by physicians with appropriate qualifications and expertise in the treatment and the use of the required equipment.

Refer to the summary of product characteristics for detail on sites of injection.

The recommended re-treatment schedule is every 12 weeks.[1]

Product availability date

July 2010

Summary of evidence on comparative efficacy

Botulinum toxin type A, Botox®, a purified neurotoxin complex derived from the bacterium *Clostridium botulinum*, blocks the release of neuromuscular transmitters. The presumed mechanism for headache prophylaxis is by blockade of peripheral signals to the central nervous system, which inhibits central sensitisation, as suggested by pre-clinical and clinical pharmacodynamic studies.[1]

The submitting company has requested that SMC considers the use of Botox® in adults with chronic migraine whose condition has failed to respond to ≥3 prior oral prophylactic treatments, where medication overuse has been appropriately managed.

The key evidence comes from two similarly designed, multi-centre, double-blind, placebo-controlled studies (PREEMPT 1 and 2) in adults with a history of chronic migraine meeting International Classification of Headache Disorders (ICHD-II) (2004) criteria.[2,3] During a 28-day baseline screening period, patients were required to have ≥15 headache days with each day consisting of ≥4 hours of continuous headache and with ≥50% of days being migraine or probable migraine days, and ≥4 distinct headache episodes, each lasting ≥4 hours. The studies had two phases, a 24-week double-blind, placebo-controlled phase with two injection cycles, followed by a 32-week open-label phase with three injection cycles.

Eligible patients were randomised equally to Botox® or placebo (saline injections), stratified based on the frequency of acute headache pain medication intake during the 28-day baseline period (yes/no), overuse of acute headache pain medications (defined as intake during baseline of

simple analgesics on ≥15 days or other medication types or combination of types for ≥10 days, with intake ≥2 days/week from the category of overuse). Botox® 155 Allergan units or placebo was administered in 31 fixed-site, fixed-dose injections across seven specific head/neck muscle areas. At the investigator's discretion, an additional 40 units could be administered into the temporalis, occipitalis and/or trapezius muscles using a follow-the-pain strategy, resulting in a maximum total dose of 195 units at 39 sites.[2,3]

Efficacy analyses in each study used the intent-to-treat population, which included all randomised patients. Data from each study were also pooled in a pre-specified analysis. In PREEMPT 1, the primary endpoint was mean change from baseline in frequency of headache episodes (patient-reported headache with a start and stop time indicating that the pain lasted at least 4 continuous hours) for the 28-day period ending with week 24. There was no significant difference between Botox® and placebo for this outcome.[2]

For PREEMPT 2 and for the pooled analysis, the primary efficacy endpoint was mean change from baseline in frequency of headache days for the 28-day period ending with week 24. A headache day was defined as a calendar day when the patient reported four or more continuous hours of a headache in the patient diary.[3,4] Statistically significant differences were observed for this outcome; results are presented in Table 1 below.

Table 1: Change in frequency of monthly headache days[2-4]

		Baseline	**Mean change from baseline at week 24**	**Mean intergroup difference (95% CI)**
Pooled analysis	Botox® (n=688)	19.9	-8.4	-1.8 (-2.52 to -1.13), p<0.001
	Placebo (n=696)	19.8	-6.6	
PREEMPT 2	Botox® (n=347)	19.9	-9.0	-2.3 (-3.25 to -1.31), p<0.001
	Placebo (n=358)	19.7	-6.7	
PREEMPT 1 (secondary outcome)	Botox® (n=341)	20.0	-7.8	-1.4 (-2.40 to -0.40), p=0.006
	Placebo (n=338)	19.8	-6.4	

CI = confidence interval

Relevant secondary outcomes including the change in frequency of moderate to severe headache days and frequency of migraine/probable migraine days were reduced with Botox® when compared with placebo in analyses of the pooled patient population (see Table 2). There were also clinically meaningful improvements in health-related quality of life (HRQoL) when measured by the changes from baseline to week 24 in total Headache Impact Test (HIT-6) score, and by the three domains of the Migraine-Specific Quality of life Questionnaire (MSQ), role-function restrictive, role-function preventative, and emotional function.[4]

Table 2: Selected secondary outcomes for the pooled patient population (analysis at week 24).[4]

		Botox® (n=688)	Placebo (n=696)
Responder rate*		47%	35%
Frequency of moderate to severe headache days/month	Baseline mean	18.1	18.0
	Mean change from baseline	-7.7	-5.8
	Difference (95% CI)	-1.9 (-2.6 to -1.3)	
Frequency of migraine or probable migraine days/month	Baseline mean	19.1	18.9
	Mean change from baseline	-8.2	-6.2
	Difference (95% CI)	-2.0 (-2.7 to -1.3)	

CI = confidence interval. * responder rate defined as a decrease from baseline of at least 50% in frequency of headache days.

To support the economic analysis, the company presented the findings of post-hoc subgroup analyses of patients from the pooled population who had a prior history of at least three oral prophylactic agents (n=479). Botox® improved the frequency of headache days, moderate or severe headache days, and migraine/probable migraine days when compared with placebo (Table 3). Patients also used less acute headache pain medication when compared with placebo patients, with a least squares mean reduction of 3.6 intakes and 1.3 days. Botox® was associated with a statistically significant improvement in total Headache Impact Test (HIT-6) score; however, the treatment difference of -2.08 points was smaller than the minimum clinically important difference of 2.3. Improvements in the three domains of the Migraine-Specific Quality of life questionnaire (role-function restrictive, role-function preventative, and emotional function) with Botox® when compared with placebo were clinically meaningful.[5,6]

Table 3: Selected outcomes in the subgroup of patients who received at least 3 prior prophylactic medications (analysis at week 24).[5]

		Botox® (n=231)	Placebo (n=248)
Frequency of headache days/month	Baseline LSmean	20.1	20.3
	LSMean change from baseline	-7.4	-4.7
	Difference (95% CI)	-2.65 (-3.82 to -1.48), p<0.001	
	Responder rate*	40% (n=76/189)	25% (n=51/207)
Frequency of moderate to severe headache days/month	Baseline LSmean	18.1	18.4
	LSMean change from baseline	-6.7	-3.9
	Difference (95% CI)	-2.87 (-4.02 to -1.73), p<0.001	
Frequency of migraine or probable migraine days/month	Baseline LSmean	19.4	19.4
	LSMean change from baseline	-7.1	-4.3
	Difference (95% CI)	-2.75 (-3.92 to -1.57), p<0.001	

LSmean = least squares mean. CI = confidence interval. * responder rate defined as a decrease from baseline of at least 50% and is based on observed data without imputation (p=0.001 versus placebo).

During the open-label phase in which all patients received treatment with Botox® at weeks 24, 36 and 48, the mean change in number of headache days fell in both groups ie those who had previously received Botox® and those who had previously received placebo. However, those patients who had received Botox® from the start of the studies continued to improve more during the open-label phase, resulting in a significant difference between the two patient groups at one year of 0.9 headache days per 28 days. Discontinuation rates at the end of the double-blind phase were 12% versus 9.6% compared to 25% versus 29% at the end of the open-label phase in patients that were initially assigned to the Botox® and placebo groups respectively.[7]

The company presented the findings of several real-world studies of using Botox® in patients with chronic migraine which provided supporting data for use beyond one year.[8-14]

Summary of evidence on comparative safety

There are limited safety data versus active comparators. In the pooled analysis of the PREEMPT studies, the frequency of treatment-related adverse events was 29% in the Botox® group and 13% in the placebo group. There were 33 (4.8%) versus 16 (2.3%) serious adverse events and 26 (3.8%) versus 8 (1.2%) discontinuations related to adverse events, respectively. No deaths were reported. Adverse events with an incidence ≥5% were neck pain (6.7% versus 2.2%) and muscular weakness (5.5% versus 0.3%). No unexpected treatment related adverse events were observed.[4] The Medicine and Healthcare products Regulatory Agency (MHRA) noted that the safety profile of Botox® is well known and the incidence of adverse reactions of concern is low.[15]

Summary of clinical effectiveness issues

Migraine is the most common severe primary headache disorder, with lifetime prevalence of 10% and 22% in males and females respectively. Migraines are classified by the absence or presence of aura (typically reversible visual, sensory or dysphasic speech symptoms). Recurrent migraine attacks can last between 4 and 72 hours. Chronic migraine is classified as migraine occurring on at least 15 days per month for >3 months in the absence of medication overuse.[16,17] UK treatment guidelines recommend several pharmacological treatments for the prophylaxis of migraine attacks including propranolol or topiramate. Alternative off-label treatments include amitriptyline, venlafaxine, valproate and other beta-blockers.[17,18] Botox® is the first non-oral product and the first medicine to be licensed in the UK for chronic migraine. No other botulinum toxins are licensed for use in headache or chronic migraine. Botulinum toxin units are not interchangeable from one product to another. Doses recommended in Allergan units are different from other botulinum toxin preparations.[1]

Clinical experts consulted by SMC considered that there is unmet need in this area, namely the lack of effective medical treatments.

The submitting company has requested that SMC considers the use of Botox® in adults with chronic migraine whose condition has failed to respond to ≥3 prior oral prophylactic treatments, where medication overuse has been appropriately managed.

The PREEMPT studies provide placebo-controlled efficacy data for six months treatment with Botox®. When the data from these similarly-designed studies were pooled, Botox® was found to reduce the frequency of headache days, migraine or probable migraine days and frequency of moderate to severe headache days when compared with placebo (approximately two fewer days per month, Table 1 and 2). The magnitude of the treatment effect appears to be larger in the population of patients who received at least three prior prophylactic medications (approximately 2.6 to 2.9 fewer days per month, Table 3). Botox® also led to clinically meaningful improvements in health-related quality of life when measured with instruments validated for headache conditions.

The International Headache Society (IHS) recommends that appropriate primary outcomes to be used in clinical studies are: number of headache days with moderate or severe intensity; number of migraine days or number of migraine episodes. The IHS notes that using migraine episodes is not appropriate when patients with continuous headache are recruited. These primary outcomes recommended by the IHS were secondary outcomes in the PREEMPT studies.[19] European Medicines Agency guidance recommends that migraine prophylaxis studies should measure frequency of migraine attacks. This guidance is under review, the scope of which includes consideration of efficacy outcomes (days versus episodes and consideration of the severity of symptoms).[20,21]

Post-hoc subgroup analysis in patients who received at least 3 prior prophylactic medications was presented to support the company's proposed positioning. While reported baseline characteristics were similar between the groups, there may be an imbalance in unrecorded confounding factors since there was no stratification in the treatment allocation randomisation for this criterion.

There are no comparative data against other recommended prophylactic migraine treatments. The submitting company has proposed that best supportive care is the most relevant comparator when Botox® is positioned after the use of ≥3 prior oral prophylactic treatments. UK guidelines provide recommendations for first, second and third line treatments in migraine prophylaxis.[18,22] Comparing use of Botox®against best supportive care (BSC) after at least three other oral treatments seems reasonable.

A substantial proportion (68%) of the PREEMPT studies' patient population's acute headache medication usage was classified as overuse. The company's proposed positioning is for use of Botox® in those whose medication overuse has been appropriately managed; no comparative data were presented for these patients.

There was a high placebo response rate which may have confounded the results. The reason for this high placebo response rate is unexplained. It should be noted that in patients with medication overuse headache, discontinuation of treatment may lead to improvement of headache. The company noted that a high placebo response rate is common in chronic migraine studies and noted a similar response in a placebo-controlled study of topiramate.[23]

The company argued that the high placebo effect of the PREEMPT studies suggest that treatment allocation was not unblinded due to recognition of muscle relaxation effects of Botox®.

While providing valuable data on longer-term use of Botox®, the reporting of the real-world observational studies' designs and results was limited. Of most relevance to the company's proposed positioning, the UK-based studies described outcomes in patients who were selected based on some of the eligibility criteria for Botox® outlined by the National Institute for Health and Care Excellence (NICE). While patients had an extensive history of prophylactic treatment for chronic migraine, many fulfilled the definition of analgesic overuse.[11,14]

Clinical experts consulted by SMC considered that the place in therapy of Botox® is in patients whose chronic migraine is not responding to currently available oral treatments.

Botox® injections require to be administered by appropriately trained personnel in hospital specialist centres. This may have implications for service delivery as well as for the patient. The decision to treat with Botox® may require additional consultation time and additional time and resource to administer the treatment. Clinical experts consulted by SMC highlighted these issues in their feedback.

The company proposed that it would be appropriate to implement both a negative stopping rule and a positive stopping rule in practice. The negative stopping rule would be applied when patients failed to achieve a 30% reduction in headache days per month. The positive stopping rule would be applied when Botox® may no longer be required (e.g. when a patient is considered to have episodic migraine, <15 days per month). This positive stopping rule is likely to require continued specialist consultation for a decision to cease, to continue or to re-introduce treatment on relapse. The company's submission reported the difficulties of implementing the positive stopping rule.

Summary of comparative health economic evidence

A cost-utility analysis using a Markov model structure was submitted comparing Botox® injections, given every 12 weeks, to BSC in a subset of patients experiencing chronic migraine, who have previously failed on three or more oral prophylactic therapies, and for whom medication overuse is appropriately managed. BSC was assumed to encompass a range of interventional procedures and unlicensed medications and may consist of acute treatments only (ie no prophylactic medication but rescue medications such as triptans).

Effectiveness data for the model for the sub-group of patients who had failed on ≥3 oral prophylactic therapies were taken from patient level data from the post hoc pooled analysis of the PREEMPT clinical studies. The mean headache days over a 28-day period was used to categorise patients into on-treatment and off-treatment health states in the model. BSC was assumed to be as effective as the placebo saline solution injections arm of the key studies. Clinical study data were available for up to 56 weeks for Botox® treated patients, and 24 weeks for placebo patients. Transition probabilities were generated for each treatment arm from these data based on a model cycle length of 12 weeks. The treatment effect was assumed to be retained for patients remaining on Botox® treatment up to the model time horizon. On discontinuing treatment the patient is assumed to follow transition probabilities for placebo and remain in the off-treatment state for the duration of the model. A 3-year time horizon was used for the analysis.

Negative and positive stopping rules for Botox® were incorporated into the model, based on expert clinical opinion. The negative stopping rule consisted of patients ceasing Botox® treatment if they do not experience a reduction of at least 30% in headache days per 28 days within the first two model cycles (at 24 weeks). The positive stopping rule was also based on expert clinical opinion, whereby if patients transition to an episodic migraine health state (≤15 headache days per 28 days) after one year then treatment could be discontinued. It was estimated that 56% of patients who transition to episodic migraine would discontinue treatment due to this stopping rule based on a study presented as an abstract at a US conference.[24]

Utilities for the headache day health states were based on EQ-5D values from a European observational study of Botox® in patients with chronic migraine. Medicine acquisition costs for Botox® plus associated administration costs were incorporated into the analysis. Administration was assumed to be performed by a specialist nurse, with scenario analysis exploring administration by a consultant. Nurse and consultant appointment costs were based on ISD data. No medication costs were assumed for the comparator arm of the model.

Other resource use, including GP visits, A&E visits, hospitalisation and triptan use, relating to acute episodes was estimated from the International Burden of Migraine Study (IBMS) conducted in a range of countries, hence there may be some issues regarding generalisability to the Scotland setting.

The base case incremental cost per quality adjusted life year (QALY) was £10,816/QALY based on an incremental cost of £1,301 and a QALY gain of 0.12. In scenario analysis, the incremental cost effectiveness ratio (ICER) was most sensitive to the time horizon (1 year was £26.8k/QALY, 10 years was £8.9k/QALY)the use of a medical consultant for drug administration (£17.4k/QALY), use of mapped IBMS to EQ- 5D based utilities increased the ICER to £14k/QALY, and assuming no negative or positive stopping rule increased the ICER to £15.1k/QALY and £14.6K/QALY respectively. Applying negative stopping rule criteria that an increase in headache days will lead to treatment discontinuation (which seems clinically plausible) results in an ICER of £13.1k/QALY. As a significant proportion of patients are estimated to cease treatment due to the stopping rules, the results are reasonably sensitive to a scenario in which no stopping rules are applied, with the ICER increasing to £19.5k/QALY.

There were a number of limitations and issues associated with the analysis:

- There are limitations in the clinical data underpinning the model which were based on a post hoc sub-group analysis comprising 35% of the pooled study population. In addition, the data include medication overuse patients with no evidence showing all of these had been adequately managed or whether this has any impact on the relative efficacy results.
- There is some uncertainty over the relative effectiveness estimates. BSC is assumed to be proxied by placebo efficacy in the pooled clinical study analysis with some uncertainty associated with this. The company state the high placebo response seen in the clinical studies supports its use as a proxy for BSC efficacy. Sensitivity analysis showed that if BSC reduced the number of headache days by one per month more than placebo, the ICER increased to £11.8K/QALY. If Botox® effectiveness was reduced by one headache day per month, the ICER increased to £18.9k/QALY.
- There is uncertainty over the implementation and impact of the positive stopping rule for Botox®, with very limited evidence to support the feasibility of its application in practice. There is some evidence from the use of Botox® in Scotland in chronic migraine via individual patient requests to suggest that patients will continue to be treated despite meeting the criteria for stopping, which will increase the ICER. It was also assumed in the model that, with the positive stopping rule applied, patients would stay in the same episodic migraine health state they were in at the end of year 1, until year 2 after which they would follow the transition probabilities of placebo. There is no clear rationale for this assumption, or for its plausibility in clinical practice. A scenario analysis assuming patients with episodic migraine who cease treatment after 1 year remain in their health state for only 6 months increases the ICER to £14.1k/QALY. Overall, there is high uncertainty over the feasibility of applying a positive stopping rule in clinical practice.
- No account has been taken in the base case economic analysis for the impact of assuming

any disutility associated with the administration of Botox® (31-39 injections per administration). A scenario analysis assuming a 0.05 utility decrement associated with administration whilst on Botox® treatment increased the ICER to £13k/QALY.Training costs for administration of Botox® have not been included, although inclusion of these would not be expected to impact on the ICER significantly.

- The base case cost per QALY was not unduly high, but there are a range of uncertainties in the data and input parameters used in the model which means there is on balance upwards uncertainty in the ICER up to approximately £20k/QALY as a reasonable base case estimate. The company provided additional scenario analyses to explore the cumulative impact of a number of uncertainties. Assuming a 2 year time horizon, 20% of patients adhering to a positive stopping rule and a negative stopping rule based on any increase in headache days resulted in an ICER of £19.8k/ QALY and £21.8k/ QALY if no positive stopping rule was applied. These results did not assume any additional utility decrement associated with Botox® administration.

Despite these uncertainties, the economic case was demonstrated.

Summary of patient and public involvement

The following information reflects the views of the specified Patient Groups.

- We received patient group submissions from Migraine Action and the Migraine Trust which are both registered charities.

- Migraine Action has received 6.1% pharmaceutical company funding in the past two years, including from the submitting company. The Migraine Trust has received 33% pharmaceutical company funding in the past two years, including from the submitting company.

- Chronic migraine is extremely debilitating and highly disabling. Frequent painful attacks and the recovery time that follows can lead to poor quality of life and social isolation. On rare, attack free days, the anxiety of an attack occurring can continue to restrict an individual's activities. Family lives, social lives, education and employment are all adversely affected by the condition.

- Current prophylactic treatments for migraine do not benefit everyone with chronic migraine and have side effects which often make them poorly tolerated.

- Botulinum toxin type A can transform the lives of patients who respond to it with an overall reduction in pain and use of other medications reported.

- Botulinum toxin type A would provide a treatment option for patients with chronic migraine for whom current treatments are not suitable or ineffective. This opens up the possibility of improving their quality of life and reducing the disabling effects of the condition.

Additional information: guidelines and protocols

The National Institute of Health and Clinical Excellence Clinical Guideline (NICECG) 150: Headaches. Diagnosis and management of headaches in young people and adults. September 2012 was updated in 2015.[18] This guideline provides guidance on the assessment, diagnosis and management of all types of headache. For prophylaxis of migraine after discussion with the patient the guideline recommended patients should be offered topiramate or propranolol according to comorbidities and risk of adverse events. If both topiramate and propranolol are unsuitable or ineffective, consider a course of up to 10 sessions of acupuncture over 5–8 weeks. The updated guideline states amitriptyline should be considered for the prophylactic treatment of migraine according to the person's preference, comorbidities and risk of adverse events. Gabapentin should not be offered as a treatment option for prophylactic migraine. For people who are already having treatment with another form of prophylaxis and whose migraine is well controlled, continue the current treatment as required. Review the need for continuing migraine prophylaxis 6 months after the start of prophylactic treatment. Advise people with migraine that riboflavin (400 mg once a day) may be effective in reducing migraine frequency and intensity for some people.

The British Association for Study of Headache (BASH) published Guidelines for All Healthcare Professionals in the Diagnosis and Management of Migraine, Tension-Type, Cluster and Medication-Overuse Headache (3rd edition, 1st revisions) in January 2010.[22] The following recommendations are based on this evidence coupled with expert clinical experience. First-line prophylactic drugs include beta-adrenergic blockers without partial agonism (atenolol, metoprolol, propranolol or bisoprolol) or amitriptyline. Second-line prophylactic drugs include topiramate or sodium valproate. Third-line prophylactic drugs include gabapentin or methysergide. The guidelines note that Botox® is licensed for prophylaxis of patients with more than 15 headache days per month, of which at least eight days are with migraine. The difference between active and placebo treatments was small in reported clinical trials, although statistically significant.

The Scottish Intercollegiate Guideline Network (SIGN) published; Diagnosis and management of headache in adults, a national clinical guideline (no. 107) in November 2008.[17] Propranolol is recommended for first-line use for migraine prophylaxis and timolol, atenolol, nadolol and metoprolol can be used as alternatives to propranolol. Topiramate, gabapentin, amitriptyline or venlafaxine are alternative treatment options. Botulinum toxin type A is not recommended for the prophylactic treatment of migraine. Need for updating being considered.

Additional information: comparators

Topiramate and propranolol are licensed for the prophylaxis of migraine. Other medicines used off-label include amitriptyline and venlafaxine.

Cost of relevant comparators

Drug	Dose Regimen	Cost per year (£)
botulinum toxin type A (Botox®)	**155 to 195 units intramuscularly every 12 weeks.**	**1,380**
amitriptyline	25mg to 150mg orally per day	15 to 134
propranolol	80mg to 240mg orally per day	37 to 72
topiramate	50mg to 200mg orally per day	22 to 60
venlafaxine	75mg to 150mg orally per day	20 to 40

Doses are for general comparison and do not imply therapeutic equivalence. Costs from eVadis on 01 November 2016. The cost of Botox® is based on 5 treatments. The dose regimens for comparators are taken from the SIGN 107 guideline (and may be higher than SPC recommendations), and are used off-label for amtriptyline and venlafaxine.

Additional information: budget impact

The submitting company estimated there would be 3,764 patients eligible for treatment with Botox® in all years. The estimated uptake rate was 2.5% in year 1 (83 patients), rising to 7.0% in year 5 (232 patients), with a discontinuation rate of 12.0% applied in all years.

The gross impact on the medicines budget was estimated to be £99k in year 1 rising to £278k in year 5. As no medicines were assumed to be displaced, the net medicines budget impact is equivalent to the gross impact.

The analysis also included additional costs for a specialist nurse to administer the injections. The net total budget impact was £119k in year 1, rising to £335k in year 5.

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This assessment is based on data submitted by the applicant company up to and in 14 December 2016.

Drug prices are those available at the time the papers were issued to SMC for consideration. SMC is aware that for some hospital-only products national or local contracts may be in place for comparator products that can significantly reduce the acquisition cost to Health Boards. These contract prices are commercial in confidence and cannot be put in the public domain, including via the SMC Detailed Advice Document. Area Drug and Therapeutics Committees and NHS Boards are therefore asked to consider contract pricing when reviewing advice on medicines accepted by SMC.

Advice context:

No part of this advice may be used without the whole of the advice being quoted in full.

This advice represents the view of the Scottish Medicines Consortium and was arrived at after careful consideration and evaluation of the available evidence. It is provided to inform the considerations of Area Drug & Therapeutics Committees and NHS Boards in Scotland in determining medicines for local use or local formulary inclusion. This advice does not override the individual responsibility of health professionals to make decisions in the exercise of their clinical judgement in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.