Healthcare Improvement Scotland | SMC Advice on new medicines

SMC2313

galcanezumab 120mg solution for injection in pre-filled pen (Emgality®)

Eli Lilly and Company Limited

05 March 2021

The Scottish Medicines Consortium (SMC) has completed its assessment of the above product and, following review by the SMC executive, advises NHS Boards and Area Drug and Therapeutic Committees (ADTCs) on its use in NHSScotland. The advice is summarised as follows:

ADVICE: following a full submission

galcanezumab (Emgality®) is accepted for restricted use within NHSScotland.

Indication under review: prophylaxis of migraine in adults who have at least 4 migraine days per month.

SMC restriction: for the treatment of patients with chronic and episodic migraine who have had prior failure on three or more migraine preventive treatments.

In studies in patients with episodic and chronic migraine, galcanezumab significantly reduced the number of migraine days per month compared with placebo.

This advice applies only in the context of an approved NHSScotland Patient Access Scheme (PAS) arrangement delivering the cost-effectiveness results upon which the decision was based, or a PAS/ list price that is equivalent or lower.

Chairman
Scottish Medicines Consortium

Indication

Prophylaxis of migraine in adults who have at least 4 migraine days per month.[1]

Dosing Information

120mg galcanezumab injected subcutaneously (SC) once monthly, with a 240mg loading dose as the initial dose. After training, patients may self-inject galcanezumab if a healthcare professional determines that it is appropriate.

The treatment benefit should be assessed within 3 months after initiation of treatment. Any further decision to continue treatment should be taken on an individual patient basis. Evaluation of the need to continue treatment is recommended regularly thereafter.

Treatment should be initiated by physicians experienced in the diagnosis and treatment of migraine.[1]

Product availability date

August 2019

Summary of evidence on comparative efficacy

Galcanezumab is a monoclonal antibody that binds to calcitonin gene-related peptide (CGRP) and prevents its biological activity. Elevated blood concentrations of CGRP have been associated with migraine attacks. Galcanezumab is licensed for prophylaxis of migraine in adults who have at least 4 migraine days per month[1,2] and the submitting company has requested that SMC considers it when positioned for use in patients with chronic migraine (CM) or episodic migraine (EM) who have failed on at least three prior migraine prevention medicines. In this submission it has been categorised by the frequency of attacks: EM, defined as less than 15 headache days per month and CM, defined as 15 or more headache days per month.

Double-blind phase III studies recruited adults with CM (REGAIN), EM (EVOLVE-1 and -2) and CM or EM (CONQUER), with the latter study only recruiting those who had failed 2 to 4 migraine prevention therapies. Patients in REGAIN had at least one headache-free day per month and during the 4-week baseline period had at least 15 headache days with at least 8 having features of migraine. Patients in EVOLVE-1 and -2 had at least 4 to 14 migraine headache days (MHD) per month prior to screening and at least 2 during the 4-week baseline period. Patients in CONQUER had at least 4 MHD and at least 1 headache-free day per month before and during the 4-week baseline period. After screening patients discontinued any preventative medicines, except in REGAIN, where they could continue propranolol or topiramate at stable doses. Patients who met the inclusion criteria during baseline were randomised in a 1:1:2 ratio to once monthly SC injections of galcanezumab 120mg, galcanezumab 240mg or placebo, except in CONQUER, where they were randomised equally to galcanezumab 120mg or placebo. Patients in the galcanezumab

120mg groups received 240mg as an initial loading dose. Treatment was continued for 6 months in the EVOLVE-1 and -2 studies and for 3 months in the other studies. Randomisation was stratified by country or region in all studies, except EVOLVE-2 and also by baseline migraine frequency (low, high or chronic) in CONQUER; by MHD frequency (<8 or ≥8) in EVOLVE-1 and -2; and by acute headache medication overuse (yes or no) and concurrent migraine prophylaxis (yes or no) in REGAIN. In all studies the primary outcome was overall mean change from baseline in monthly MHD during the double-blind treatment period. This was assessed within patients who had non-missing data for MHD in the intention-to-treat (ITT) population, which comprised all those randomised who received at least one dose of study drug.[2-5]

Results for the licensed dose (galcanezumab 120mg) only are presented. In all studies the primary outcome, overall mean change from baseline in monthly MHD during the treatment period was significantly improved versus placebo with galcanezumab 120mg in the ITT population.[2,3] Results are detailed in Table 1 below for the ITT population. The company also provided results for the subgroup representative of the proposed positioning, SMC is unable to publish these due to commercial confidentiality issues.

Table 1: Change from baseline in Migraine Headache Days in CONQUER, REGAIN, EVOLVE-1 and EVOLVE-2 studies.[2,3]

	ITT population		
	N	**Change in MHD**	**Difference (95% CI)**
CONQUER: Chronic and episodic migraine			
Galcanezumab	230	-4.1	-3.1 (-3.9 to -2.3)
Placebo	228	-1.0	
CONQUER: Episodic migraine subgroup			
Galcanezumab	137	-2.9	-2.6 (-3.4 to -1.7)
Placebo	132	-0.3	
CONQUER: Chronic migraine subgroup			
Galcanezumab	95	-6.0	-3.7 (-5.2 to -2.2)
Placebo	98	-2.2	
REGAIN: Chronic migraine			
Galcanezumab	273	4.8	-2.1 (-2.9 to -1.3)
Placebo	538	2.7	
EVOLVE-1: Episodic migraine			
Galcanezumab	210	4.7	-1.9 (-2.5 to -1.4)
Placebo	425	2.8	
EVOLVE-2: Episodic migraine			
Galcanezumab	226	4.3	-2.0 (-2.5 to -1.5)
Placebo	450	2.3	

CI = confidence interval; ITT = intention to treat; MHD = monthly migraine headache days and change is least square mean; Galcanezumab dose = 120mg subcutaneously every month.

In EVOLVE-1, EVOLVE-2 and REGAIN secondary outcomes were tested in the following hierarchical order: 50% and 75% response rate in MHD, MHD with acute medication use, Migraine-Specific

Quality of Life Questionnaire (MSQ) Role-Function Restrictive (RFR), 100% response rate and patient global impression of severity scale (PGI-S), with PGI-S tested before 100% response in the REGAIN study. In CONQUER the hierarchy was: MDH in EM; 50% response in CM and EM; 50% response in EM; MSQ RFR in EM and CM; MQS RFR in EM; 75% response in EM; 100% response in EM; 75% response in CM and EM; and 100% response in CM and EM. In all studies the secondary outcomes were significantly improved with galcanezumab 120mg versus placebo, except in REGAIN, for the second secondary outcome, 75% responder rate, with formal testing in this group being stopped at that point.[2,3,6]

Health Related Quality of Life was assessed using the MSQ total score plus its three domains (role-restrictive, role-preventative and role-emotional) and the Migraine Disability Assessment (MIDAS) questionnaire. In all studies these were improved with galcanezumab compared with placebo.[2,3]

Long-term uncontrolled data were provided by a one-year, open-label phase 3 safety study (CGAJ) that recruited adults (18 to 65 years) with at least 4 MHD and at least one headache-free day per month for the preceding three months. After a wash-out of migraine prevention medicines, patients were randomised to galcanezumab 120mg or 240mg SC monthly for 12 months (with initial 240mg loading dose in the 120mg group). Efficacy was a secondary objective of the study and within the respective groups there was an overall decrease from baseline of 5.6 and 6.5 in monthly MHD.[7]

The company presented Bucher indirect comparisons of galcanezumab 120mg (data from REGAIN,[4,11] CONQUER,[3,6] EVOLVE-1,[5,12] and EVOLVE-2[5,13]) with erenumab (data from Study 295,[14,15] LIBERTY[16] and STRIVE[17]) in patients with CM and EM who had failed on at least three prior migraine prevention medicines for the outcomes: mean change from baseline in MHD and MHD with acute medicine use; ≥50% reduction in MHD and ≥75% reduction in MHD, with supportive analyses in patients who had failed on at least two prior medicines. The company concluded that the indirect comparisons had a number of limitations and should be interpreted with caution. These indirect comparisons were used as a proxy to compare galcanezumab versus fremanezumab.

The company also presented Bucher indirect comparisons of galcanezumab 120mg (data from CONQUER and REGAIN)[3,4] versus botulinum toxin (data from PREEMPT-1 and -2)[8-10] in the total study population and in the subgroup of patients who had failed at least three prior preventative medicines.

*Other data were also assessed but remain confidential.**

Summary of evidence on comparative safety

Pooled data from the placebo-controlled double-blind treatment phases of REGAIN, EVOLVE-1 and EVOLVE-2 indicated that treatment-emergent adverse events were reported by 65% (456/705) and 61% (882/1451) of patients in the galcanezumab 120mg and placebo groups; severe adverse events were reported by 7.4% and 7.4%; serious adverse events were reported by 2.3% and 1.3%; and adverse events leading to discontinuation of study drug occurred in 2.4% and 1.7%,

respectively.[18] In the CONQUER study, within the galcanezumab 120mg and placebo groups treatment-emergent adverse events were reported by 51% (119/232) and 53% (122/230), which were treatment-related in 16% and 15% of patients, respectively. Serious adverse events were reported by 0.9% of patients in both groups and only one study patient (from the galcanezumab group) discontinued treatment due to an adverse event.[3] Longer term data, up to one year, were not placebo-controlled. These were provided by the 12-month CGAJ safety study and the 9-month open-label extension to the REGAIN study and were similar to the other phase III studies.[4,7]

Galcanezumab was generally well tolerated. Adverse events associated with galcanezumab included injection site reactions, vertigo, urticaria, pruritus and constipation. Cardiovascular safety was identified as an adverse event of special interest because CGRP is a potent microvascular vasodilator and is hypothesized to play a protective role in cardiovascular health. The phase III studies were of short (three to six months) duration and excluded patients at high risk of cardiovascular events. The European Medicines Agency (EMA) noted that a limited number of patients had been exposed to galcanezumab up to 12 months and none for more than 12 months. Therefore, the effects of long-term CGRP inhibition on cardiovascular risks and safety, especially ischaemic events, cannot be fully assessed yet.[2]

Summary of clinical effectiveness issues

Migraine is a complex and multifaceted brain disorder characterised by recurrent moderate to severe headache typically lasting 4 to 72 hours, which may be accompanied by aura (transient focal neurological symptoms that usually precede or accompany the headache).[2]

Preventative therapies for migraine include propranolol, topiramate, amitriptyline, candesartan and sodium valproate.[19] Patients who fail to respond to these can receive botulinum toxin A, which is indicated for use in CM[20] and has been accepted by SMC (SMC692/11, published February 2017) for restricted use in adults with CM whose condition has failed to respond to at least three prior oral prophylactic treatments, where medication overuse has been appropriately managed. Two monoclonal antibodies (erenumab and fremanezumab) that inhibit CGRP function are licensed for prophylaxis of migraine in adults who have at least four migraine days per month.[21,22] Erenumab (Aimovig®) was accepted by SMC (SMC2134, published April 2019) for restricted use in patients with CM in whom at least three prior prophylactic treatments have failed. Fremanezumab (Ajovy®) was accepted by SMC (SMC2226, published January 2020) for restricted use in the treatment of patients with CM and EM who have had prior failure on three or more migraine preventative treatments. Clinical experts consulted by SMC advised that CGRP inhibitors, erenumab and fremanezumab, would be used after first-line prophylactic therapies and, in areas where it is available, after botulinum toxin.

Galcanezumab is the third medicine (after erenumab and fremanezumab)[21,22] that inhibits the CGRP pathway and is licensed for prophylaxis of migraine in adults who have at least four MHD per month. The submitting company have requested that SMC considers galcanezumab when positioned for use in patients who have failed on at least three prior migraine prevention medicines.

In patients with EM, galcanezumab was associated with a reduction over placebo in monthly MHD of about 2 days in the EVOLVE-1 and -2 studies and about 2.5 days in the EM subgroup of the CONQUER study. The corresponding results in the subgroup of patients who had failed on at least three prior migraine prevention medicines was about 3 days in the CONQUER study. In patients with CM, galcanezumab was associated with a reduction over placebo in monthly MHD of about 2 days in the REGAIN study and about 3.7 days in the CM subgroup of the CONQUER study, with reductions of about 5 days in the subgroup of patients who had failed in at least 3 migraine prevention medicines in both of these populations. The EMA noted that the magnitude of treatment effect in both EM and CM was limited, although it highlighted that there is no agreed minimally relevant effect in terms of MHD reduction and a conclusion on clinical relevance is difficult. The EMA indicated that indirect comparisons, provided by the company to support that galcanezumab's effect appears comparable with other therapies in both EM and CM, were not supported by a sound methodology and have limited usefulness for the evaluation of treatment benefit.[2]

In all studies, the primary outcome measured days of migraine headache, rather than episodes. The definition of MHD included migraine and probable migraine with a duration of at least 30 minutes, which is shorter than the International Classification of Headache Disorders (ICHD) guideline duration of at least 4 hours. This definition was used to prevent delay in administering acute medication and to capture episodes that did not become full migraine attacks due to the use of acute medications. However, analysis of the secondary outcome, ICHD MHD not including probable migraine and sensitivity analyses of the primary outcome (using varying durations of migraine) confirmed the treatment effects.[2]

The REGAIN study excluded patients who had used opioid or barbiturate-containing analgesics more than three times per month in more than two of the preceding 6 months. This may limit the application of the study results to this group of patients.[4] There is limited data in patients older than 65 years, as they were excluded from all studies, except CONQUER. However, subgroup analyses of efficacy by age groups (18 to 40; 40 to 50; 50 to 55 and >55) demonstrated that age had no clear effect on galcanezumab efficacy, therefore, the EMA noted that the treatment effect of galcanezumab can be extrapolated to older patients (≥65 years).[2,3]

Migraine patients have a higher rate of ischaemic cardiovascular co-morbidities and an increased risk of ischaemic cardiovascular events compared with the population without migraine. The generalisability of cardiovascular safety from the galcanezumab studies to the population with migraine is limited as the studies excluded patients with recent acute cardiovascular events (including myocardial infarction, unstable angina, coronary artery bypass graft (CABG), stroke, deep vein thrombosis) and/or those deemed to be at serious cardiovascular risk.[2]

REGAIN, EVOLVE-1 and EVOLVE-2 studies, excluded patients who had previously failed to have an efficacy response to three or more classes of migraine preventive treatments.[2] The evidence for the proposed positioning (in patients who have failed at least three prior preventative medicines) was derived mainly from post-hoc subgroup analysis of the CONQUER study. However, the submission also provided limited data from the 17% of the REGAIN study population who comprised this subgroup. [11,23]

Double-blind treatment was of six months' duration in the EVOLVE-1 and -2 studies and of three months' duration in the REGAIN and CONQUER studies.[2,3] There are no controlled longer term data and there are no clinical data in patients treated beyond 12 months, which may be a limitation for a chronic condition.

The Bucher indirect comparisons of galcanezumab 120mg versus erenumab 70mg and 140mg, had a number of limitations. There were differences across the studies in design, definition of outcomes and baseline characteristics. Data were derived from post-hoc subgroup analyses, some with small sample size. There was heterogeneity across the studies in design and definition of some outcomes. Due to lack of data, it was not possible to assess baseline differences between studies in the EM analysis and only four baseline characteristics were compared in the CM analyses. The indirect comparison did not assess safety in the subgroup who had failed on three prior preventative medicines (only in those who had failed on two) and it did not assess quality of life outcomes in any subgroup. The rationale supporting the indirect comparison of galcanezumab with erenumab and the use of this comparison as a proxy to compare galcanezumab and fremanezumab was based on opinion rather than data. However, results in the population that had failed at least three prior migraine prevention medicines were supported by scenario analyses in patients who had failed at least two prior migraine prevention medicines.

Clinical experts consulted by SMC consider that the class of CGRP inhibitors are a therapeutic advance in the treatment of CM and EM, although they note that evidence on the relative efficacy of medicines within this class is limited. They suggest that galcanezumab would be used in practice at a similar stage in the treatment pathway to other CGRP inhibitors.

*Other data were also assessed but remain confidential.**

Summary of comparative health economic evidence

The submitting company presented a cost-utility analysis evaluating galcanezumab in its licensed indication, with an additional restriction to patients who have a history of at least three prior pharmacological preventive treatment failures. Two comparators were used within the initial submission: botulinum toxin A (Botox) and best supportive care (comprising non-steroidal anti-inflammatory drugs, paracetamol and paracetamol-containing medicines and triptans). Clinical experts consulted by SMC suggested that erenumab and fremanezumab represent the most likely treatments to be displaced, and comparisons with these medicines were provided upon request in the form of a simple cost-minimisation analysis. Therefore the details presented below focus on the comparisons with erenumab and fremanezumab.

In both the cost-utility analysis and cost-minimisation analyses, two populations were modelled separately, covering chronic and episodic migraine. A semi-Markov structure was used, comprising six distinct health states: 'on treatment (up to week 12)', 'responder', 'non-responder', 'on treatment (after response assessment)', 'off treatment' and 'Death'. The 'responder' and 'non-responder' states were used as tunnel states determining the proportion of patients anticipated to continue treatment based on a response assessment at 12 weeks. Response was defined as a

≥50% reduction from baseline in monthly mean MHDs for patients with episodic migraine or HFEM, and as a ≥30% reduction from baseline in monthly MHDs for patients with chronic migraine. A twenty-five year time horizon was used, a monthly cycle length applied and a perspective of NHSScotland and social work used in the base case.

Clinical effectiveness data for galcanezumab, in terms of the mean change from baseline per month and proportion of responders after three months, were derived from the CONQUER study for both chronic and episodic populations. Negative binomial and beta-binomial regression models were used to estimate the monthly MHDs for each treatment in the episodic and chronic populations, respectively. A waning of treatment effect was applied following discontinuation of galcanezumab due to lack of response or adverse events, after which patients reverted to baseline monthly MHDs. An indirect treatment comparison, described in the clinical effectiveness section, was used to justify an assumption of equivalence of erenumab and fremanezumab to galcanezumab. However, unadjusted data for discontinuation due to adverse events were used to assume a difference in discontinuation rates between the biologic medicines.

Cost of medicines acquisition and administration were included, as were the costs of GP visits, A&E visits, hospitalisations, and specialist consultations. The dose and duration of treatment with galcanezumab and comparators was applied according to the relevant summaries of product characteristics, and a stopping rule was applied for patients not meeting the response criteria defined above at 3 months.

A Patient Access Scheme (PAS) was submitted by the company and assessed by the Patient Access Scheme Assessment Group (PASAG) as acceptable for implementation in NHSScotland. Under the PAS, a discount was offered on the list price. PAS discounts are also in place for erenumab and fremanezumab and these were included in the results used for decision-making by using estimates of the comparator PAS price.

As mentioned previously, comparisons with erenumab and fremanezumab were provided upon request and the New Drugs Committee (NDC) felt these were the key analyses for decision-making. The results of the revised base case for the cost-minimisation analysis, where differential discontinuation rates due to adverse events were assumed, are shown below in Table and 3. An alternative scenario, where discontinuation rates were assumed equal, is shown in

Table .

The results presented do not take account of the PAS for erenumab and fremanezumab or the PAS for galcanezumab but these were considered in the results used for decision-making. SMC is unable to present the results provided by the company which used an estimate of the PAS price for erenumab and fremanezumab due to commercial confidentiality and competition law issues.

Table 2: Cost minimisation results: Episodic migraine, at list prices for all medicines

Treatment	Incremental Costs
Galcanezumab 120mg	-
Fremanezumab 225mg	-£390

Fremanezumab 675mg	£13

Table 3: Cost minimisation results: Chronic migraine, at list price for all medicines

Treatment	Incremental Costs
Galcanezumab 120mg	-
Fremanezumab 225mg	-£5,518
Fremanezumab 675mg	-3,355
Erenumab 70mg	-£7,167
Erenumab 140mg	-£3,225

Table 4: Scenario analysis: equal discontinuation rates, at list price for all medicines

Treatment	Incremental Costs
Episodic migraine	
Galcanezumab 120mg	-
Fremanezumab	£450
Chronic migraine	
Galcanezumab 120mg	-
Fremanezumab	£425
Erenumab	£3,052

There are a number of limitations to the economic case:

- Relative effectiveness estimates: both the cost-utility and cost-minimisation analysis relied upon estimates of relative effectiveness derived from Bucher indirect comparisons, the limitations of this approach is discussed above in the 'clinical effectiveness' section. The results of these analyses are therefore subject to some uncertainty, however on balance, NDC felt these provided sufficient justification for use of a cost-minimisation analysis (Tables 2 – 4).
- Cost-minimisation: although an indirect comparison is provided to justify an assumption of clinical equivalence, this does not include adverse events as an outcome. A naive comparison of discontinuation due to adverse events is therefore used to differentiate between galcanezumab, erenumab and fremanezumab. Although unlikely to be a key driver of the results, a separate scenario was obtained where discontinuation rates due to adverse event rates were assumed equal: this results in a reduction in the total costs of fremanezumab and erenumab, with a corresponding change in incremental costs (
- Table).

Despite these uncertainties, the economic case has been demonstrated.

*Other data were also assessed but remain confidential.**

Summary of patient and carer involvement

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

- We received patient group submissions from The Migraine Trust and the National Migraine Centre, which are both registered charities.

- The Migraine Trust has received 8.7% pharmaceutical company funding in the past two years, including from the submitting company. The National Migraine Centre has received 1.7% pharmaceutical company funding in the past two years, with none from the submitting company.

- Migraine is a complex brain disease that greatly impacts day-to-day life. It presents in a diverse number of ways, although principally characterised by headache some can experience other symptoms such as light sensitivity, dizziness and fatigue even more debilitating than the pain of the headache. One of the biggest challenges of living with migraine is its unpredictability as an attack can occur at any time. The impact of migraine is pervasive, as people living with the condition say it impacts their ability to work or progress in their career, and to participate in education and social and family life. It also has a hugely detrimental impact on mental health and wellbeing.

- There are a number of acute and preventative treatments currently available, however many have been repurposed from other conditions with limited efficacy and risk of debilitating side effects. They can also cause additional difficulties for people with migraine (e.g. medication overuse headache).

- For people who have failed a range of other preventative treatments, galcanezumab provides another treatment option to improve symptoms and quality of life. It is a specific preventative treatment designed for migraine and seems to be generally well-tolerated. Many of those who have used galcanezumab report that it has improved their quality of life.

Additional information: guidelines and protocols

In February 2018 the Scottish Intercollegiate Guidelines Network (SIGN) issued publication number 155: Pharmacological management of migraine. It recommends propranolol (80mg to 160mg daily) as a first-line prophylactic treatment for patients with episodic or chronic migraine; topiramate (50mg to 100mg daily), amitriptyline (25mg to 150mg at night), candesartan (16mg daily) and sodium valproate (400mg to 1,500 mg daily) as options for prophylactic treatment for patients with episodic or chronic migraine. Botulinum toxin A is recommended for the prophylactic

treatment of patients with chronic migraine where medication overuse has been addressed and patients have been appropriately treated with three or more oral migraine prophylactic treatments.[19]

In November 2015 the National Institute of Health and Care Excellence (NICE) published an update to the 2012 clinical guideline 150: Headaches in over 12s, diagnosis and management. This recommends topiramate or propranolol for the prophylactic treatment of migraine according to the person's preference, comorbidities and risk of adverse events.[25]

Additional information: comparators

Erenumab, fremanezumab.

Additional information: list price of medicine under review

Medicine	Dose Regimen	Cost per year (£)
Galcanezumab	240mg subcutaneous injection (as loading dose), then 120mg subcutaneously once monthly	5,400* (5,850 in year 1)

Costs from BNF online on 17 November 2020. Costs do not take patient access schemes into consideration. based on 12 doses*

Additional information: budget impact

Chronic migraine

The company estimated there would be approximately 5,224 patients eligible for treatment with galcanezumab in year 1 and 5,351 patients in year 5 to which confidential estimates of uptake were applied.

Episodic migraine

The company estimated there would be approximately 5,558 patients eligible for treatment with galcanezumab in year 1 and 5,693 patients in year 5 to which confidential estimates of uptake were applied.

SMC is unable to publish the with PAS budget impact due to commercial in confidence issues. A budget impact template is provided in confidence to NHS health boards to enable them to estimate the predicted budget with the PAS. This template does not incorporate any PAS discounts associated with comparator medicines or PAS associated with medicines used in a combination regimen.

*Other data were also assessed but remain confidential.**

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This assessment is based on data submitted by the applicant company up to and including 12 February 2021.

**Agreement between the Association of the British Pharmaceutical Industry (ABPI) and the SMC on guidelines for the release of company data into the public domain during a health technology appraisal: http://www.scottishmedicines.org.uk/About_SMC/Policy*

Medicine 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.

Patient access schemes: A patient access scheme is a scheme proposed by a pharmaceutical company in order to improve the cost-effectiveness of a medicine and enable patients to receive access to cost-effective innovative medicines. A Patient Access Scheme Assessment Group (PASAG), established under the auspices of NHS National Services Scotland reviews and advises NHSScotland on the feasibility of proposed schemes for implementation. The PASAG operates separately from SMC in order to maintain the integrity and independence of the assessment process of the SMC. When SMC accepts a medicine for use in NHSScotland on the basis of a patient access scheme that has been considered feasible by PASAG, a set of guidance notes on the operation of the scheme will be circulated to Area Drug and Therapeutics Committees and NHS Boards prior to publication of SMC advice.

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.