Healthcare Improvement Scotland | SMC Advice on new medicines

SMC2272

brolucizumab 120mg/mL solution for injection in pre-filled syringe (Beovu®)

Novartis Pharmaceutical UK Ltd

07 August 2020

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 Therapeutics Committees (ADTCs) on its use in NHSScotland. The advice is summarised as follows:

ADVICE: following a full submission

brolucizumab (Beovu®) is accepted for use within NHSScotland.

Indication under review: in adults for the treatment of neovascular (wet) age-related macular degeneration (AMD).

Non-inferiority of brolucizumab versus another anti-vascular endothelial growth factor medicine was demonstrated for mean change in best corrected visual acuity from baseline to week 48 in two phase III studies in patients with neovascular AMD.

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

Brolucizumab is indicated in adults for the treatment of neovascular (wet) age-related macular degeneration (AMD).[1]

Dosing Information

The recommended dose is 6mg brolucizumab (0.05mL solution) administered by intravitreal injection every 4 weeks (monthly) for the first 3 doses. Thereafter, the physician may individualise treatment intervals based on disease activity as assessed by visual acuity and/or anatomical parameters.

A disease activity assessment is suggested 16 weeks (4 months) after treatment start. In patients without disease activity, treatment every 12 weeks (3 months) should be considered. In patients with disease activity, treatment every 8 weeks (2 months) should be considered. The physician may further individualise treatment intervals based on disease activity.

If visual and anatomical outcomes indicate that the patient is not benefiting from continued treatment, brolucizumab should be discontinued.

Brolucizumab must be administered by a qualified ophthalmologist experienced in intravitreal injections. Further details including the method of administration and monitoring requirements are included in the Summary of product characteristics (SPC).[1]

Product availability date

April 2020

Summary of evidence on comparative efficacy

Choroidal neovascularisation (CNV) is the formation of abnormal, leaky blood vessels under the macula and is the defining feature in neovascular (wet) age-related macular degeneration (AMD). Abnormally high levels of vascular endothelial growth factor (VEGF) play a role in this process. Brolucizumab is a humanised monoclonal single chain Fv antibody fragment. It inhibits binding of vascular endothelial growth factor A (VEGF-A) to its receptors which suppresses endothelial cell proliferation, leading to reduced pathological neovascularisation and reduced retinal oedema.[1-3]

Key evidence for this indication is from the HAWK and HARRIER studies. These studies were similar, international, multicentre, randomised, double-masked, phase III studies that evaluated the efficacy and safety of brolucizumab compared with aflibercept in patients with neovascular AMD.

HAWK and HARRIER recruited patients ≥50 years old at screening with active CNV lesions secondary to AMD that affected the central subfield in the study eye. The total area of CNV (including both classic and occult components) had to comprise greater than 50% of the total lesion area in the study eye. Patients were required to have intraretinal fluid (IRF) and/or

subretinal fluid (SRF) affecting the central subfield of the study eye, and best corrected visual acuity (BCVA) between 78 and 23 letters, inclusive, in the study eye at screening and baseline using Early Treatment Diabetic Retinopathy Study (ETDRS) testing. In patients where both eyes were eligible, the eye with the worse BCVA at baseline was selected as the study eye. If both eyes had the same BCVA, it was recommended that the right eye was selected as the study eye. Patients had not previously been treated for neovascular AMD in the study eye. [3, 4]

Patients were randomised in a 1:1:1 ratio in HAWK to receive brolucizumab 3mg (dose not licensed), brolucizumab 6mg, or aflibercept 2mg or 1:1 in HARRIER to receive brolucizumab 6mg or aflibercept 2mg. In all treatment arms injections were given at weeks 0, 4, and 8 for the loading phase. Thereafter brolucizumab was given every 12 weeks unless disease activity was identified, and in this case 8 weekly administration was used (for the remaining study duration), and aflibercept was given every 8 weeks for the total study duration of 96 weeks.[3, 4]

Efficacy analyses were performed in the full analysis set, which included all patients who had received at least one dose of study medicine. Non-inferiority of brolucizumab 6mg versus aflibercept was demonstrated in both studies for the primary outcome of least squares (LS) mean BCVA change from baseline to week 48. The lower limits of the 95% confidence interval (CI) of the difference of the LS mean change in mean BCVA from baseline between brolucizumab and aflibercept were greater than -4 letters as specified in the statistical plan for non-inferiority testing.[3, 4] Primary and selected secondary outcomes are included in table 1 below. Brolucizumab is not licensed at the 3mg dose therefore efficacy results for this dose are not presented.

Table 1: Primary and selected secondary outcomes of HAWK and HARRIER.[3, 4]

	HAWK		HARRIER	
	Brolucizumab 6mg (n=360)	Aflibercept 2mg (n=360)	Brolucizumab 6mg (n=370)	Aflibercept 2mg (n=369)
Primary outcome				
Mean baseline BCVA (letters read)	60.8	60.0	61.5	60.8
LS mean change in BCVA from baseline to Week 48 (letters read)	6.6	6.8	6.9	7.6
LS mean difference versus aflibercept (95% CI), p value for non-inferiority	-0.2 (-2.1 to 1.8) p<0.001	-	-0.7 (-2.4 to 1.0) p<0.001	-
Secondary outcomes				
LS mean average change in BCVA from baseline over the period of Weeks 36 to 48	6.7	6.7	6.5	7.7
LS mean difference versus aflibercept (95% CI), p value for non-inferiority	0 (-1.9 to 1.9) p<0.001	-	-1.2 (-2.8 to 0.5) p<0.001	-

Probability of patients receiving 12 weekly brolucizumab up to Week 48 (KM estimate)	56%	-	51%	-
In patients who received 12 weekly treatment in the initial 12 week cycle, probability of remaining on 12 weekly brolucizumab up to Week 48 (KM estimate)	85%	-	82%	-
Patients with ≥15 letter gain from baseline to Week 48	34%	25%	29%	30%
Patients with disease activity at Week 16	24%	35%	23%	32%
BCVA: best-corrected visual acuity; CI: confidence interval; KM: Kaplan-Meier; LS: least squares				

The European Medicines Agency (EMA) noted that maintenance of the benefit of brolucizumab over time had been addressed through functional outcome (BCVA) as well as anatomical outcomes (changes in CSFT, CNV lesion, retinal fluids) providing positive outcomes at Week 96. The mean change in BCVA from baseline at week 96 in HAWK for brolucizumab 6mg and aflibercept 2mg were 5.6 and 5.6 letters respectively. In HARRIER, the mean change in BCVA from baseline at week 96, was 6.1 letters for brolucizumab 6mg and 6.6 letters for aflibercept 2mg.[3]

Health Related Quality of Life (HRQoL) was assessed using the Visual Function Questionnaire-25 (VFQ-25). In HAWK the mean change from baseline, indicating improvement, in the VFQ-25 composite score at Week 24 and Week 72 respectively was 4.0 and 3.9 in the brolucizumab 6mg group, versus 3.5 and 4.0 in the aflibercept 2mg group.[2, 5] In HARRIER the mean change from baseline at Week 24 and Week 72 was 3.9 and 5.0 in the brolucizumab 6mg group, versus 3.5 and 3.2 in the aflibercept 2mg group.[3]

CRTH258A2301E1 was a 24-week extension of the HAWK study including 150 patients who had enrolled in the US and completed 96 weeks of the study. Patients who received brolucizumab 3mg (n=62) or 6mg (n=45) in the HAWK study received brolucizumab 6mg, the first two doses at 8 weekly intervals and a further dose after 12 or 8 weeks and those who received aflibercept 2mg (n=43) remained on aflibercept. The EMA noted that in patients who initially received brolucizumab 6mg, a trend towards slight decrease in BCVA was observed in the second year of the HAWK study, however the time course during the extension study suggests stabilisation. For those patients initially receiving brolucizumab 3mg, the trend observed during the second year of the HAWK study continued in the extension study.[3]

The submitting company presented Bayesian network meta-analyses (NMA) comparing brolucizumab with aflibercept or ranibizumab in adult patients over 18 with wet AMD. Fourteen studies were included in the NMA and key outcomes were mean change in BCVA, mean change in central retinal thickness (CRT), both at time points of baseline to one year and baseline to 2 years, and treatment discontinuation from baseline to two years. No differences were identified

between brolucizumab (initially given as a loading dose then 12 weekly, changing to 8 weekly if disease progression observed) and the aflibercept or ranibizumab dosing regimens that were included in the NMA for mean change in BCVA, at both time points. For mean difference in CRT the results favoured brolucizumab for the majority of comparisons with aflibercept and ranibizumab. No difference was observed for the treat and extend dose regimens of both comparators in the baseline to 2 years comparison although credible intervals were wide. For treatment discontinuation from baseline to 2 years, no differences were observed between brolucizumab and the available aflibercept and ranibizumab dose comparisons however credible intervals were also wide.

Summary of evidence on comparative safety

The EMA considered that overall the safety profile of brolucizumab appears to be similar to aflibercept, except for intraocular inflammations and ocular occlusive events which were reported more frequently with brolucizumab. Close monitoring is requested by the EMA in the post-marketing setting to further investigate these events.[3]

In the HAWK study at Week 48, ocular adverse events (AEs) were reported by 50% (179/360) of the brolucizumab 6mg group and 47% (170/360) of the aflibercept 2mg group. Non-ocular AEs were reported by 64% (232/360) and 72% (258/360) of the respective groups. In the brolucizumab 6mg and aflibercept 2mg groups respectively ocular serious AEs were reported by 3.1% and 0.8% of the groups and non-ocular serious AEs by 13% and 19% of the groups.[4] The most frequently reported ocular AEs of any grade (with an incidence >2% of eyes in any treatment group) in the brolucizumab 6mg and aflibercept 2mg groups were: Conjunctival haemorrhage (6.4% and 5.6%), visual acuity reduced (5.3% and 6.7%), vitreous floaters (5.0% and 3.1%), and eye pain (4.4% and 4.2%).[4]

In the HARRIER study at Week 48, ocular adverse events (AEs) were reported by 33% (122/370) of the brolucizumab 6mg group and 32% (119/369) of the aflibercept 2mg group. Non-ocular AEs were reported by 59% (219/370) and 57% (211/369) of the respective groups. In the brolucizumab 6mg and aflibercept 2mg groups respectively ocular serious AEs were reported by 2.4% and 1.1% of the groups and non-ocular serious AEs by 9.5% and 12% of the groups.[4] The most frequently reported ocular AEs of any grade (with an incidence >2% of eyes in any treatment group) in the brolucizumab 6mg and aflibercept 2mg groups were: Visual acuity reduced (5.4% in both groups), vitreous floaters (3.0% and 0.8%), eye pain (2.7% and 3.3%), and increased intraocular pressure (3.2% and 2.4%).[4]

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

Summary of clinical effectiveness issues

Neovascular (wet) AMD is a chronic eye condition that generally occurs in patients who are ≥50 years old. Abnormal growth and leakage of blood vessels in the macula causes rapid irreversible vision loss leading to blindness. Neovascular AMD is the main cause of severe vision loss worldwide. Risk factors include smoking, nutritional factors, cardiovascular disease, and genetic predisposition. Intravitreal anti-VEGF treatments are the standard of care in neovascular AMD.[2, 3] Two anti-VEGF medicines, aflibercept (SMC number 857/13) and ranibizumab (NICE MTA 155 considered by Healthcare Improvement Scotland as valid in Scotland) are already accepted for use in NHSScotland.

Both HAWK and HARRIER studies demonstrated non-inferiority of brolucizumab 6mg versus aflibercept for the primary outcome, mean change in BCVA from baseline to week 48.[3, 4] The results were statistically significant and the EMA considered that overall brolucizumab demonstrated a similar benefit profile to aflibercept. The EMA also noted that data for 2 years of treatment provided an acceptable level of evidence on the maintenance of the benefit over the time.[3]

Treatment-naïve patients only were recruited to HAWK and HARRIER. This could affect the generalisability to the Scottish population as some patients in clinical practice may have received prior treatment with anti-VEGF therapy and lost benefit over time. The licensed indication for brolucizumab is not limited to first-line treatment. It is unclear whether the treatment effect will be the same in patients with pre-treated disease.

Disease activity criteria were more stringent at week 16 than later assessments. The reason for this is unclear and whether it might have had an effect on the estimation of the probability for a patient to remain on 12 weekly dosing of brolucizumab is also unclear. Patients who switched to 8 weekly dosing could not change back to 12 weekly dosing for the remainder of the study. This may not reflect real-life conditions where dosing intervals could be extended again. A fixed dose regimen of aflibercept was used in the HAWK and HARRIER studies, with maintenance treatment given every 8 weeks. In practice, and within the marketing authorisation for aflibercept, the treatment interval may be maintained at 2 months or further extended using a 'treat-and-extend' dosing regimen where injection intervals are increased in 2- or 4-weekly increments to maintain stable visual and/or anatomic outcomes.[6] Therefore, currently available evidence does not allow any conclusions to be made on differences in injection frequency as no data for brolucizumab versus the 'treat-and-extend' regimen of aflibercept are available.

In HARRIER there was no hierarchical testing procedure for the additional secondary outcomes or the superiority outcomes and no alpha control therefore superiority outcomes can only be considered exploratory. Visual acuity was not selected as an outcome for superiority testing despite it being included in the primary and key secondary outcomes. The main studies assessed the efficacy and safety of brolucizumab in one eye and the study durations were 96 weeks. Data from a 24-week extension study to HAWK, that included 150 patients are also available. There are

no data for bilateral use and efficacy and safety data beyond 2 years are not known. HRQoL data are limited.

No direct data are available versus the other relevant comparator for patients in NHSScotland, ranibizumab. The submitting company presented NMA comparing brolucizumab with aflibercept and ranibizumab. These were associated with some limitations including lack of meta-regression results due to the absence of information within the networks to allow the models to converge, variation in time points reported, and the majority of comparisons only included one study. Further limitations included heterogeneity between studies, not all dosing regimens were able to be included in the comparisons, and no patient reported quality of life outcomes were included. Overall, despite the limitations, the results of the NMA suggest that brolucizumab is likely to be comparable to aflibercept and ranibizumab.

Clinical experts consulted by SMC highlighted how a treatment that allows reduced frequency of injections and visits to clinic would be a therapeutic advancement. The introduction of brolucizumab provides an additional anti-VEGF medicine for the treatment of neovascular AMD. Patients without disease activity may be maintained on 12 weekly dosing immediately after the loading dose, 12 weekly dosing is also possible for the key comparators within a 'treat-and extend' regimen.

Summary of comparative health economic evidence

The submitting company presented a cost-minimisation analysis. The analysis compared brolucizumab with aflibercept and ranibizumab over a 30 year time horizon. A three state Markov model was employed with states of on-treatment, off-treatment, and death. The on-treatment state related to either study eye or bilateral study and fellow-eye treatment. Patients enter the model with either unilateral or bilateral disease. Patients with unilateral disease could develop bilateral disease over time according to an annual probability of neovascularisation. Once patients develop bilateral disease, they do not revert to having unilateral disease.

The NMA described above was used as the evidence base to support the use of a cost-minimisation approach. The cost-minimisation model distinguishes between treatment options based on injection and monitoring frequency (and medicines acquisition costs), and discontinuation. Frequencies and discontinuation rates were based on random-effects network meta-analyses. Frequencies reflected planned intervals for injection (e.g. monthly, bi-monthly, quarterly). A weighted average regimen was used for both aflibercept and ranibizumab in the base case analysis. The weighted average excluded quarterly (12-weekly dosing) regimens, however, due to lack of data reported in relevant clinical studies included in the supporting systematic literature review. Excluded regimens amounted to 7% of the expected distributions and the exclusions were judged by the company not to substantially impact results. Scenario analyses considered single treatment regimens for each of the comparators.

Total costs were also dependent on rate of discontinuation and visual decline. Based on the NMA, the rate of discontinuation was assumed to be slightly lower with brolucizumab than either aflibercept or ranibizumab. Scenario analysis included discontinuation assumptions from NICE NG82. While on treatment patients were at risk of moving to bilateral disease with associated increased resource use: medicines acquisition cost of treatment was doubled and the cost of administration was assumed to increase by 50%. A one-off cost of fundus fluorescein angiography (FFA) was applied at the time of any incident neovascularisation, including development of wet AMD in a second eye. Costs of adverse events were not considered in the base case.

Medicines acquisition and administration costs, monitoring, fundus fluorescein angiography and outpatient appointments costs were included. 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.

PAS discounts are in place for aflibercept and ranibizumab and these were included in the results used for decision-making by using estimates of the comparator PAS price for aflibercept and ranibizumab. The base case results and key sensitivity analyses are presented in the tables below at list prices.

The results presented do not take account of the PAS for brolucizumab or the PAS for aflibercept or ranibizumab 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 aflibercept or ranibizumab due to commercial confidentiality and competition law issues.

Table 2: Base case cost-minimisation results at list prices for all medicines

	Aflibercept	Ranibizumab
Incremental cost brolucizumab versus comparator	**-£16,358**	**-£9,638**

Sensitivity analyses highlighted discontinuation, bilateral cost multiplier, and injection frequency as the most important parameters in the comparison against aflibercept and ranibizumab. Scenario analyses showed that under base case settings, brolucizumab remained cost-saving against each of the individual comparator regimens irrespective of delivery schedule (those shown cover range of resulting savings). Brolucizumab was not cost-saving at list prices for all medicines under the extreme scenario in which monitoring visits were assumed equal across all regimens. Additional monitoring for brolucizumab in year one had negligible impact.

Table 3: Scenario analyses results; incremental costs (brolucizumab v comparator) at list prices for all medicines

	List prices	
	Aflibercept	**Ranibizumab**
Scenario		
Base-case	-£16,358	-£9,638
Baseline age: 65 years	-£19,418	-£12,367
Aflibercept 2mg q4w	-£57,230	Not applicable
Aflibercept 2mg LP->q8w	-£3,273	Not applicable
Ranibizumab 0.5mg LP->PRNX	Not applicable	£2,653
Ranibizumab 0.5mg q4w	Not applicable	-£29,588
Discontinuation: NICE NG82 Appendix J	-£23,881	£1,340
Include adverse events	-£16,405	-£9,795
Additional monitoring in Year 1 for brolucizumab included	-£16,275	-£9,555
Year 3+ injection and monitoring frequencies: UK expert opinion	-£3,007	£5,663
Injection and monitoring visits set the same (as ranibizumab)	£4,461	£20,216
Discontinuation rates set the same (as brolucizumab)	-£20,203	-£9,736
q4w: every 4 weeks; LP: loading phase; PRNX: pro re nata and extend dosing regimen		

Minor weaknesses with the economic case included:

- Total cost for aflibercept and ranibizumab is dependent on assumptions as to weights for individual regimens.
- Quarterly dosing regimens for aflibercept and ranibizumab were excluded from weighted average costs for these comparators due to data limitations.
- Progression to bilateral disease amplifies single-eye cost savings. As treatment for bilateral disease requires continued treatment any uncertainty around discontinuation rates contributes to uncertainty around these costs.
- Though uncertainties appear to be capable of having notable effects on total cost estimates, these appear unlikely to suggest that brolucizumab would be more costly.

Despite the minor weaknesses outlined above, the economic case has been demonstrated.

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

Summary of patient and carer involvement

Patient Group Submissions were not required as this submission was assessed through an amended process used during the COVID-19 pandemic.

Additional information: guidelines and protocols

The European network for health technology assessment (EUnetHTA) published an assessment report titled 'brolucizumab for the treatment of adults with neovascular (wet) age-related macular degeneration (AMD)' in 2020. The key conclusions in the EUnetHTA assessment of brolucizumab were:

- Noninferiority of brolucizumab compared with aflibercept in terms of visual function measured as BCVA in the treatment of patients with nAMD was demonstrated in two phase III studies.
- Brolucizumab 6mg every 8 or 12 weeks has only been compared with aflibercept 2mg dosed at fixed intervals of every 8 weeks and not to other dosing schedules commonly used in clinical practice. Due to this, the HAWK and HARRIER study design does not allow any conclusions to be drawn about treatment burden (injection frequency) between these two medicines.
- In comparison with aflibercept, the incidence of intraocular inflammation and retinal artery occlusive events were higher for brolucizumab. There are no safety data for brolucizumab beyond 2 years of treatment or in bilateral use.
- Evidence of the efficacy and safety of brolucizumab is based only on data for anti-VEGF treatment–naïve patients.
- Direct comparisons with ranibizumab and bevacizumab [unlicensed] are not available. Indirect comparisons between brolucizumab and ranibizumab showed no differences in mean change in BCVA or most of the other outcomes.[2]

The National Institute for Health and Care Excellence published clinical guidance (NG82) titled 'age related macular degeneration' in 2018. The guideline recommends the use of intravitreal anti-VEGF treatments ranibizumab and aflibercept. The use of pegaptanib is not recommended in patients with wet AMD.

Ranibizumab within its marketing authorisation is recommended when all the following criteria are met (as specified in NICE TA155):

- the best-corrected visual acuity is between 6/12 and 6/96
- there is no permanent structural damage to the central fovea
- the lesion size is less than or equal to 12 disc areas in greatest linear dimension
- there is evidence of recent presumed disease progression (blood vessel growth,
- as indicated by fluorescein angiography, or recent visual acuity changes)

- the manufacturer provides ranibizumab with the discount agreed in the patient access scheme (as revised in 2012).

Aflibercept is also recommended as an option for treating wet age-related macular degeneration only if:

- it is used in accordance with the recommendations for ranibizumab
- the manufacturer provides aflibercept solution for injection with the discount agreed in the patient access scheme (recommendation adapted from NICE TA294).

The guideline notes that no clinically significant differences in the efficacy and safety between different anti-VEGF medications have been observed in the studies reviewed by the guideline committee.[7]

The European Society for Retina Specialists (EURETINA) published guidance on the first line management of wet AMD titled 'guidelines for the management of neovascular age-related macular degeneration' in 2014. EURETINA recommends the use of anti-VEGF therapies including ranibizumab and aflibercept. Treatment with pegaptanib is not recommended.[8]

Additional information: comparators

Aflibercept and ranibizumab.

Additional information: list price of medicine under review

Medicine	Dose Regimen	Cost per year (£)
brolucizumab	6mg by intravitreal injection every 4 weeks for the first 3 doses. Thereafter, the physician may individualise treatment intervals based on disease activity. In patients without disease activity, treatment every 12 weeks should be considered. In patients with disease activity, treatment every 8 weeks should be considered.	Year 1: £4,896 to £6,528 Subsequent years: 3,536 to 5,304

Costs from MIMS online on 01.06.20. Costs do not take patient access schemes into consideration. See SPC for full details of dosing regimen.

Additional information: budget impact

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.

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

References

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5. Novartis Data on File. RTH258-C001 (HAWK) Clinical Study Report.
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8. Schmidt-Erfurth U, Chong V, Loewenstein A, Larsen M, Souied E, Schlingemann R*, et al.* Guidelines for the management of neovascular age-related macular degeneration by the European Society of Retina Specialists (EURETINA). The British journal of ophthalmology. 2014;98(9):1144-67. Epub 2014/08/20.

This assessment is based on data submitted by the applicant company up to and including 27 July 2020.

**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.