Healthcare Improvement Scotland | SMC Advice on new medicines

SMC2461

roxadustat 20mg, 50mg, 70mg, 100mg and 150mg film-coated tablets (Evrenzo®)

Astellas Pharma Ltd

08 July 2022

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 NHSScotland. The advice is summarised as follows:

ADVICE: following a full submission

roxadustat (Evrenzo®) is accepted for restricted use within NHSScotland.

Indication under review: treatment of adult patients with symptomatic anaemia associated with chronic kidney disease (CKD).

SMC restriction: for use in patients who are non-dialysis dependent (NDD) at the time of treatment initiation.

Roxadustat was non-inferior to an erythropoiesis stimulating agent (ESA) and superior to placebo for improving haemoglobin (Hb) levels in adults with anaemia in CKD who were NDD.

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

Treatment of adult patients with symptomatic anaemia associated with chronic kidney disease (CKD).[1]

Dosing Information

The appropriate dose of roxadustat is taken orally three times per week and not on consecutive days. The dose should be individualised to achieve and maintain Hb levels of 10 to 12 g/dL as described in the Summary of Product Characteristics (SPC). Adequate iron stores should be ensured prior to initiating treatment.

For patients not previously treated with an ESA the recommended starting dose of roxadustat is 70mg three times per week in patients weighing <100kg and 100mg three times per week in patients weighing ≥100kg. Patients currently treated with an ESA can be converted to roxadustat, however, conversion of dialysis patients otherwise stable on ESA treatment is only to be considered when there is a valid clinical reason. Conversion of NDD patients otherwise stable on ESA treatment has not been investigated. A decision to treat these patients with roxadustat should be based on a benefit-risk consideration for the individual patient. The recommended starting dose of roxadustat is based on the average prescribed ESA dose in the 4 weeks before conversion as described in the SPC. The first roxadustat dose should replace the next scheduled dose of the current ESA.

Roxadustat treatment should not be continued beyond 24 weeks of therapy if a clinically meaningful increase in Hb levels is not achieved. Alternative explanations for an inadequate response should be sought and treated before re-starting roxadustat. Treatment with roxadustat should be initiated by a physician experienced in the management of anaemia. All other causes of anaemia should be evaluated prior to initiating therapy with roxadustat, and when deciding to increase the dose as described in the SPC.[1]

Product availability date

September 2021

Summary of evidence on comparative efficacy

Roxadustat inhibits hypoxia-inducible factor, prolyl hydroxylase (HIF-PH) enzymes, which regulate genes involved in erythropoiesis during the adaptive response to hypoxia. By inhibition of HIF-PH, roxadustat stimulates a coordinated erythropoietic response that includes an increase of plasma endogenous erythropoietin, regulation of iron transporter proteins and reduction of hepcidin (an iron regulator protein that is increased during inflammation in CKD). This results in improved iron bioavailability, increased Hb production and increased red cell mass.[1] Roxadustat is indicated for treatment of symptomatic anaemia in adults with CKD and the submitting company has requested

that SMC considers roxadustat when positioned for use in patients who are NDD at the time of treatment initiation.

Four phase 3 studies (DOLOMITES, ALPS, ANDES and OLYMPUS) recruited adults with stage 3, 4 or 5 CKD (with an estimated glomerular filtration rate [eGFR] <60mL/min/1.73m^2) not receiving dialysis and anaemia defined by Hb ≤10g/dL (≤10.5g/dL in DOLOMITES). Patients had normal folate and vitamin B12 and, in DOLOMITES, were suitable for ESA on Kidney Disease Improving Global Outcomes (KDIGO) 2012 recommendations. Randomisation was stratified by region, baseline Hb (≤8 or > 8g/dL), history of cardiovascular, cerebrovascular or thromboembolic disease (yes or no) and eGFR (<30 or ≥30 mL/min/1.73 m^2), except in OLYMPUS where country was the only stratification factor. In DOLOMITES, patients were equally assigned to open-label roxadustat (70mg if ≤70kg and 100mg if >70kg) orally three times per week or darbepoetin-alfa subcutaneous (SC) or intravenous (IV) (0.45 microgram/kg weekly or 0.75 microgram/kg every two weeks based on weight). In ALPS and ANDES, patients were assigned in a 2:1 ratio to double-blind roxadustat (70mg if ≤70kg and 100mg if >70kg) orally three times per week or placebo. In OLYMPUS, patients were assigned equally to double-blind roxadustat 70mg orally three times per week or placebo. Across the studies, doses were adjusted during the initial correction phase to achieve Hb ≥11g/dL and Hb increase from baseline ≥1g/dL, then in the subsequent maintenance phase to achieve Hb between 10 and 12g/dL. Study duration was up to two years in DOLOMITES and ALPS, 3 years in ANDES and until a required number of cardiovascular events were reached in OLYMPUS.[2-7]

In all studies, the European Medicines Agency (EMA) specified primary outcome was Hb response, defined as Hb ≥11g/dL and Hb increase from baseline ≥1g/dL in patients with baseline Hb >8g/dL or ≥2g/dL in patients with baseline Hb ≤8g/dL at two consecutive study visits separated by at least 5 days during the first 24 weeks and without receiving rescue therapy. In the placebo-controlled studies, this was primarily assessed in the full analysis set (FAS), which comprised all randomised patients who received at least one dose of study drug and had at least one post-baseline Hb assessment. In the active-controlled study (DOLOMITES), this was primarily assessed in the per protocol (PP) set which included patients in the FAS who did not meet any criteria for exclusion and a non-inferiority margin of -15% was used.[2-7]

For the primary outcome, Hb response, roxadustat was non-inferior to darbepoetin-alfa in DOLOMITES (as the lower bound of 95% confidence interval [CI] was greater than -15%) and roxadustat was significantly superior to placebo as detailed in Table 1 below.[2-6]

Table 1: Primary outcome of DOLOMITES, ALPS, ANDES, OLYMPUS.[2-6]

Study	Hb response		Outcome (95% CI)
	Roxadustat	Control#	
DOLOMITES	90% (256/286)	78% (213/273)	Difference: 12% (5.7 to 17)
ALPS	79% (308/389)	9.9% (20/203)	Difference: 69% (64 to 75)*
ANDES	86% (523/608)	6.6% (20/305)	Difference: 80% (76 to 83)*
OLYMPUS	77% (1,055/1371)	8.5% (112/1,357)	Relative risk: 9.1 (7.6 to 10.9)*

CI = confidence interval; * p<0.001; # control = darbepoetin-alfa in DOLOMITES and placebo in ALPS, ANDES and OLYMPUS.

In all studies there was a hierarchical testing strategy for key secondary outcomes. In DOLOMITES, there was a significant difference in time to IV iron between roxadustat and darbepoetin-alfa over weeks 1 to 36 (a key secondary outcome), with hazard ratio (HR) of 0.45 (95% confidence interval [CI]: 0.26 to 0.78). This can be interpreted in the context of differences between groups in rescue therapy as noted in the clinical effectiveness issues below. Roxadustat demonstrated benefits compared with darbepoetin-alfa and placebo in another key secondary outcome, change from baseline to average over weeks 12 to 28 in low-density-lipoprotein (LDL)-cholesterol as detailed in Table 2 below. Across the studies, roxadustat was also associated with reductions in HDL, with minimal changes in LDL/HDL ratios.[2-6]

Table 2: Change in low-density lipoprotein cholesterol in DOLOMITES, ALPS, ANDES, OLYMPUS[2-6]

Study	LSM change in LDL-cholesterol from baseline to week 12 to 28 (mmol/L)		Difference (95% CI)
	Roxadustat	Control[#]	
DOLOMITES	-0.36	0.05	-0.40 (-0.51 to -0.3)*
ALPS	-0.60	0.15	-0.70 (-0.83 to -0.57)*
ANDES	-0.48	0.006	-0.45 (-0.53 to, -0.36)*
OLYMPUS	-0.38	-0.02	-0.36 (-0.42 to -0.29)*

CI = confidence interval; * p<0.001; # control = darbepoetin-alfa in DOLOMITES and placebo in ALPS, ANDES and OLYMPUS.

Across the studies there were generally no consistent differences between roxadustat and placebo or darbepoetin-alfa for quality of life outcomes, including short form 36 (SF-36), Functional Assessment of Cancer Therapy (FACT) anaemia subscale and Euroqol 5 dimension (EQ-5D).[2-10]

Summary of evidence on comparative safety

In DOLOMITES, within the roxadustat and darbepoetin-alfa groups adverse events were reported by 92% (296/323) and 92% (271/293) and these were considered treatment-related in 24% and 22% of patients, respectively. Serious adverse events occurred in 65% and 62% of patients and were treatment-related in 5.6% and 3.1%. Adverse events led to discontinuation of study drug in 7.7% and 3.8% of patients. There were two patients in the roxadustat group (and no patients in the darbepoetin-alfa group) who had an adverse event leading to death that was considered treatment-related by the investigator.[3,10]

Across the placebo-controlled studies in NDD patients (ALPS, ANDES and OLYMPUS), duration of treatment was longer in the roxadustat groups than placebo groups (due to more treatment discontinuations in the placebo group), with pooled data indicating medians of 87 versus 57 weeks, respectively. This difference does not fully account for consistently increased rates of adverse events with roxadustat. Pooled data indicate that within the roxadustat and placebo groups the incidence rate per 100 patient years' exposure for drug-related adverse events were 8.3 and 6.6; for serious adverse events were 45.9 and 43.9; for treatment-related serious adverse events were 1.9 and 0.9; and for adverse events leading to study discontinuation or study drug discontinuation were 3.9 and 3.8, respectively.[2]

Adverse events associated with roxadustat include nausea, diarrhoea, hypertension, peripheral oedema, hyperkalaemia, deep vein thrombosis, convulsions (seizures), sepsis and vascular access thrombosis, as detailed in the SPC.[1,2]

Adverse events of special interest included major adverse cardiovascular events (MACE), defined as death, non-fatal myocardial infarction and/or stroke. Pooled analysis of placebo-controlled studies (ALPS, ANDES and OLYMPUS) suggests that roxadustat, compared with placebo, may be associated with higher rates of MACE, MACE+ (MACE plus hospitalisation for unstable angina or congestive cardiac failure) and all-cause mortality.[1,2]

In DOLOMITES, there appeared to be no substantial differences between the roxadustat and darbepoetin-alfa groups for MACE and MACE+. This was supported by analyses of pooled data from this study and studies in dialysis dependent patients that compared roxadustat with ESA. These did not suggest increased cardiovascular or mortality risks with roxadustat versus ESA.[2,3,10]

Summary of clinical effectiveness issues

A variety of factors can contribute to anaemia in CKD, including issues with the oxygen-sensing mechanism in the kidney that can result in reduced production of erythropoietin from it. Other factors include shorter lifespan of red blood cells (RBC), decrease in erythropoietin response in haematopoietic cells due to inflammation and nutritional deficiency, impaired ability to absorb and use stored iron and blood loss associated with haemodialysis.[2] Patients with CKD are regularly monitored for anaemia and may have long-term requirements for iron supplements.[11] However, iron supplements alone are rarely sufficient to resolve anaemia in CKD, and ESA have been used as standard of care in this setting for many years. These can be short-acting (for example, epoetin-alfa) or long-acting (for example, darbepoetin-alfa), with no evidence to support the superiority of one ESA over another in terms of efficacy, safety or quality-of-life. Iron status should be checked before and during treatment with ESA and iron supplementation used if necessary (for example, when serum ferritin <100 microgram/L or transferrin saturation is <20%). Blood transfusions are usually a last resort as they are associated with risks, including sensitisation that may decrease potential future matches for kidney transplant.[2]

Roxadustat is the first HIF-PH inhibitor licensed in the UK. It may be an alternative treatment option to ESA in patients with anaemia in CKD. The submitting company has requested that SMC considers roxadustat when positioned for use in patients who are NDD at the time of treatment initiation.

In studies of NDD patients, roxadustat was non-inferior to darbepoetin-alfa for the primary outcome, Hb response, which assessed improvement in anaemia and roxadustat was superior to placebo for this outcome.[2-6]

There was a significant difference in time to IV iron between roxadustat and darbepoetin-alfa over the initial 36 weeks (a key secondary outcome). This can be interpreted in the context of differences between groups in rescue therapy: RBC infusions and ESA in the roxadustat group versus RBC infusions only in the darbepoetin-alfa group. During the study, in the roxadustat group compared with darbepoetin-alfa more patients had rescue therapy (14% and 9.6%) and fewer

patients had IV iron (with 6.2% and 13% having had IV iron before week 36 and included in the analysis of the key secondary outcome).[3,10]

Roxadustat was associated with a reduction in LDL-cholesterol that was significantly greater than darbepoetin-alfa and placebo. However, roxadustat was also associated with decreases in HDL-cholesterol, which could counteract the potential benefits of LDL-cholesterol reduction. There were minimal changes in the LDL/HDL ratios and effect on cardiovascular outcomes are unclear.[2]

A pre-specified pooled analysis of placebo-controlled studies in NDD patients (ALPS, ANDES and OLYMPUS) suggests that roxadustat, compared with placebo, may be associated with higher rates of MACE, MACE+ and all-cause mortality.[1,2] The DOLOMITES study did not provide any evidence of difference between roxadustat and darbepoetin-alfa for these outcomes. However, the study was not powered for comparison of these outcomes.[3]

The evaluation of cardiovascular safety in NDD patients was pre-specified and based on MACE and mortality using a-priori analyses of data from the on-treatment period (OT-28; on-treatment or within 28 days of last dose) with censoring for treatment discontinuation. At disclosure of the main studies but before unblinding of adjudicated MACE events, an intention-to-treat (ITT) analysis of MACE and mortality was set and this gave lower HR compared with the OT-28 analyses: 1.10 (95% CI: 0.96 to 1.27) for MACE and 1.08 (95% CI: 0.93 to 1.26) for mortality. Compared with OT-28 analyses, the ITT analyses were considered to have lower sensitivity, as events were less likely due to study treatment and could be affected by background event rates and subsequent therapies (such as ESA after treatment discontinuation), which may confound them.[2]

The active-controlled study, DOLOMITES, was open-label which may limit assessment of subjective outcomes such as quality-of-life and safety. In all of the placebo-controlled studies (ALPS, ANDES and OLYMPUS) the rate of discontinuation from study drug was much lower in the roxadustat groups than in the placebo groups: 38% versus 59% in pooled analysis. This resulted in a longer median duration of treatment in the roxadustat groups compared with placebo.[2] The reason for the difference is unclear and it may impact the quality of the studies. Also, outcomes such as adverse event rates may be best expressed as rates per patient years of exposure.

In all four studies the populations were representative of the positioning of roxadustat for use in patients who are NDD at the time of treatment initiation, but they did not include all patients within the licensed indication as those on dialysis were excluded. The studies also excluded patients who received ESA within 6 or 12 weeks prior to randomisation. Roxadustat has not been assessed in NDD patients currently receiving an ESA, that is, it has not been investigated in conversion from ESA within this group.[2] This SPC notes that conversion of NDD patients otherwise stable on ESA treatment has not been investigated. A decision to treat these patients with roxadustat should be based on a benefit-risk consideration for the individual patient.[1]

Clinical experts noted that darbepoetin-alfa, the active comparator in the DOLOMITES study, is representative of practice in Scotland and the European regulatory review considered that there is no evidence to support the superiority of one ESA over another in terms of efficacy, safety or quality-of-life.

Clinical experts consulted by SMC note that roxadustat in the treatment of anaemia in CKD may be used in place of ESA for selected patients, particularly those with issues related to the parenteral route of administration of ESA.

Summary of comparative health economic evidence

The submitting company provided a cost-utility analysis assessing roxadustat positioned within a sub-group of its licensed indication as follows: adult patients with symptomatic anaemia associated with CKD who are NDD at the time of treatment initiation. This compared roxadustat to a number of ESA (epoetin alfa, epoetin beta, epoetin zeta, darbepoetin-alfa, and methoxy polyethylene glycol-epoetin beta), which were modelled as a single comparator weighted by their frequency of use as found in the TUNE study.[12]

A *de novo* economic model was built by the company using a proportion-in-state modelling approach (in essence a partitioned survival model allowing bi-directional movement between health states). This included eight-core health states (excluding death) defined on the basis of different ranges of Hb levels. A three-month cycle length was used with a lifetime time horizon (25 years based on a starting age of 63 years).

Clinical effectiveness data used in the economic evaluation were primarily based on a meta-analysis of pooled individual patient data (IPD) from the roxadustat clinical study programme among NDD patients. This dataset was used to fit a number of statistical models to estimate patient outcomes including: changes in Hb levels over time, time to initiation of renal replacement therapy, and overall survival. Transition probabilities between health states defined using Hb ranges were estimated using a multinomial logistic regression analysis, while time to renal replacement therapy and overall survival were extrapolated using a series of parametric survival curves; of the various survival curves fitted by the company, the log-logistic and exponential distributions were selected to model time to initiation of renal replacement therapy and overall survival respectively, on the basis that these functions had the best statistical fit and long-term clinical plausibility.

Baseline utility values were estimated using age- and gender-adjusted UK general population values calculated by Kind *et al*,[13] which were further adjusted for complaints associated with CKD, changes in Hb levels, and treatment-related adverse events (TRAE). Utility decrements due to CKD complaints were sourced from a previous National Institute for Health and Care Excellence (NICE) Technology Appraisal (TA)[14] within autosomal dominant polycystic kidney disease, whereas decrements associated with different Hb ranges were estimated using the pooled IPD from the roxadustat clinical study programme. TRAE utility decrements were set equal to those available from published literature.[15-17]

Medicine acquisition costs for roxadustat and ESA were included in the analysis. The company stated that, given the frequent dose adjustments made in clinical practice, it was difficult to accurately estimate dosages for roxadustat and ESA. To capture this complexity, dosages were also estimated using the pooled IPD from the roxadustat clinical study programme; a generalised linear mixed model was used to predict the mean weekly dose of roxadustat and ESA based on patients'

Hb level after controlling for cardiovascular disease and co-morbid diabetes at baseline. Administration costs were included for the fraction of patients receiving subcutaneous ESA who are unable to self-administer. No administration costs were included for roxadustat given its status as an oral therapy. Resource use associated with different types of renal replacement therapy (for patients in receipt of this) was included, alongside blood transfusion, intravenous iron supplementation, TRAEs, and monitoring costs.

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 simple discount was offered on the list price.

The main economic results, with a PAS applied for roxadustat, show that treatment with roxadustat was estimated to generate greater patient benefit than treatment with ESA at a lower cost; on average, a patient treated with roxadustat was expected to gain additional discounted quality-adjusted life-years (QALYs) with an incremental cost saving compared to a patient treated with ESA. Treatment with roxadustat was therefore predicted to be a dominant strategy (i.e. less costly and more effective) versus treatment with ESA in the company's base case analysis. No difference in life expectancy was assumed across treatments.

Disaggregated analyses indicated that incremental costs associated with ESA stem from the lower medicine acquisition and administration costs associated with roxadustat, plus lower costs for rescue therapy, and for treating stroke and myocardial infarction. The difference in incremental QALYs was principally associated with a greater proportion of patients spending time in target ranges for Hb levels when treated with roxadustat than with ESA.

Key scenario analyses shown in Table 3 indicate that the cost-effectiveness of roxadustat was relatively stable to changes in structural assumptions such as the use of alternative health state utility values, and shorter or longer time horizons.

Table 3: Key scenario analyses

	Description	**ICER**
0.	*Base case*	Dominant
1.	Alternative values to inform QoL (EQ-5D- 5L)	Dominant
2.	Applying utilities associated with method of administration	Dominant
3.	Shorter time horizon (5 years)	Dominant
4.	100% Epoetin alfa use	Dominant
5.	100% Darbepoetin-alfa use	Dominant
6.	100% Epoetin beta use	Dominant
7.	100% Epoetin zeta use	Dominant
8.	100% Methoxy polyethylene glycol-epoetin beta use	Dominant
9.	DOLOMITES IPD to inform regression model inputs	Dominant

Abbreviations: ESA, erythropoiesis stimulating agents; QALYs, quality-adjusted life-years; ICER, incremental cost-effectiveness ratio; IPD, individual patient data; QoL, quality of life; EQ-5D-5L, EuroQol-5-Dimension-5-Level

The following limitations associated with the economic evaluation were identified:

- Complex statistical modelling was used to estimate dosages of roxadustat and ESA according to Hb level and equivalent dosages among ESA, increasing the uncertainty associated with these figures; if dosages of roxadustat are higher than estimated (or ESA dosages lower than estimated), this would have a large upwards impact on results.
- The DOLOMITES study was not powered to compare the incidence of MACE between roxadustat and darbepoetin-alfa, yet the probability of these events from this particular study were used within the economic evaluation. However, MACE did not appear to have a significant influence on results based on deterministic sensitivity analyses, so this is unlikely to impact on decision-making.
- The relative safety of roxadustat versus darbepoetin-alfa (and other ESA) in terms of mortality is not yet fully understood, making the extrapolation of patient survival over the model time horizon less reliable; however, no difference in overall survival across treatments has been assumed in the economic evaluation, reducing the likelihood of this impacting on decision-making.

After considering all the available evidence, the Committee accepted roxadustat for use in NHSScotland.

Summary of patient and carer involvement

No patient group submission was received.

Additional information: guidelines and protocols

In 2021, the National Institute of Health and Care Excellence (NICE) published a guideline (NG203): Chronic kidney disease: assessment and management. This recommends that when anaemia can't be managed by iron alone, treatment with an ESA should be considered. These should be offered to patients with anaemia of CKD who are likely to benefit in terms of quality of life and physical function, and to avoid blood transfusion in patients considered suitable for transplantation. ESAs need not be administered if the presence of comorbidities, or the prognosis, is likely to negate the benefits of correcting the anaemia. If there is uncertainty over whether comorbidities, or the prognosis, would negate benefit from correcting the anaemia with ESAs, a trial of anaemia correction is recommended.[11]

The Renal Association clinical practice guideline on anaemia of CKD in 2017 reflects earlier NICE guidelines (now replaced by NG203).[18]

The Kidney Disease: Improving Global Outcomes (KDIGO) 2012 Anaemia Work Group' guideline recommends that for adult CKD NDD patients with Hb concentration <10g/dL the decision whether to initiate ESA therapy should be individualised based on the rate of fall of Hb concentration, prior response to iron therapy, the risk of needing a transfusion, the risks related to ESA therapy and the presence of symptoms attributable to anaemia.[19]

Additional information: comparators

Erythropoiesis stimulating agents such as epoetin-alfa (Eprex®), epoetin-beta (NeoRecormon®), epoetin-zeta (Retacrit®), darbepoetin-alfa (Aranesp®) and methoxy polyethylene glycol epoetin-beta (Mircera®).

Additional information: list price of medicine under reveiw

Medicine	Dose Regimen	Cost per year (£)
Roxadustat	70mg to 300mg* orally three times per week	2,696 to 11,552

*Costs from BNF online on 4 May 2022. *Maximum dose in non-dialysis dependent patients is 3mg/kg body weight or 300mg three times per week, whichever is lower. Costs do not take patient access schemes into consideration.*

Additional information: budget impact

The submitting company estimated there would be 1,387 patients eligible for treatment with roxadustat in year 1 and 1,366 year 5 respectively.

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 or other discounts associated with comparator medicines.

*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 17 June 2022.

**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:*https://www.scottishmedicines.org.uk/about-us/policies-publications/

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.