Healthcare Improvement Scotland | SMC Advice on new medicines

SMC2310

brentuximab vedotin 50mg powder for concentrate for solution for infusion (Adcetris®)

Takeda UK Ltd

04 December 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

brentuximab vedotin (Adcetris®) is accepted for use within NHSScotland.

Indication under review: in combination with cyclophosphamide, doxorubicin and prednisone (CHP) for adult patients with previously untreated systemic anaplastic large cell lymphoma (sALCL).

In a phase III study, brentuximab vedotin in combination with CHP was associated with a significant improvement in progression-free survival compared with CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) chemotherapy.

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

Chairman
Scottish Medicines Consortium

Indication

Brentuximab vedotin in combination with cyclophosphamide, doxorubicin and prednisone (CHP) is indicated for adult patients with previously untreated systemic anaplastic large cell lymphoma (sALCL).[1]

Dosing Information

The recommended dose in combination with chemotherapy (CHP) is 1.8mg/kg administered as an intravenous infusion over 30 minutes every 3 weeks for 6 to 8 cycles. If the patient's weight is more than 100kg, the dose calculation should use 100kg.

Primary prophylaxis with granulocyte colony-stimulating factor (G-CSF), beginning with the first dose, is recommended for all patients with previously untreated sALCL receiving combination therapy.

Brentuximab vedotin should be administered under the supervision of a physician experienced in the use of anti-cancer agents.

For more information, see Summary of Product Characteristics (SPC).[1]

Product availability date

May 2020. Brentuximab vedotin meets SMC orphan criteria.
Brentuximab vedotin has conditional marketing authorisation from the European Medicines Agency (EMA).

Summary of evidence on comparative efficacy

Brentuximab vedotin is an antibody drug conjugate which is composed of a monoclonal antibody covalently linked via an enzyme-cleavable linker to the antimitotic small molecule monomethyl auristatin E. It delivers an antineoplastic agent to CD30-expressing tumour cells resulting in selective apoptotic cell death. CD30 is a type I transmembrane glycosylated protein and is expressed on cell subsets of non-Hodgkin lymphoma, including sALCL.[1, 2]

ECHELON-2 is a double-blind, randomised, placebo-controlled, phase III study which evaluated the efficacy and safety of brentuximab vedotin plus cyclophosphamide, doxorubicin and prednisone (CHP) versus cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) in patients with newly diagnosed CD30-positive peripheral T-cell lymphoma (PTCL). Patients were aged 18 years or over and had an Eastern Cooperative Oncology Group (ECOG) performance status 0 to 2. Eligible histologies were anaplastic lymphoma kinase (ALK) positive sALCL with an International Prognostic Index (IPI) score ≥2, ALK-negative sALCL, PTCL- not otherwise specified (NOS), angioimmunoblastic T-cell lymphoma, adult T-cell leukaemia/lymphoma, enteropathy-associated T-cell lymphoma, hepatosplenic T-cell lymphoma, and fluorodeoxyglucose (FDG)-avid disease as assessed by the site radiologist.[2, 3]

Patients were randomised equally to receive brentuximab vedotin plus CHP (n= 226) or CHOP (n= 226) for six to eight 21-day cycles as determined by investigator at registration based on patient-specific characteristics. All patients received the CHP components of the CHOP regimen (cyclophosphamide 750mg/m² and doxorubicin 50mg/m² intravenously on day 1 of each cycle and prednisone 100mg once daily orally on days 1 to 5 of each cycle). Patients randomised to the brentuximab vedotin group received 1.8mg/kg intravenously on day 1 of each cycle whilst patients randomised to CHOP received vincristine 1.4mg/m² (maximum dose 2mg); matching placebos were also administered. Consolidative stem cell transplant (SCT) or radiotherapy after treatment was permitted at the investigator's discretion. Randomisation was stratified by histological subtype according to local pathology assessment (ALK-positive sALCL versus all other histologies) and baseline IPI score (0–1 versus 2–3 versus 4–5).[3]

The primary outcome was progression-free survival (PFS) according to Blinded Independent Central Review (BICR), defined as the time from the date of randomisation to the date of first documentation of relapse or progressive disease, death due to any cause, or receipt of subsequent systemic chemotherapy to treat residual or progressive PTCL as determined by the investigator, whichever came first. Efficacy analyses were performed in the intention-to-treat (ITT) population, which included all patients who underwent randomisation, and the sALCL population, which included all patients with centrally confirmed sALCL. A hierarchical statistical testing strategy was applied in the study with no formal testing of outcomes after the first non-significant outcome in the hierarchy. Outcomes were tested in the following order: PFS according to BICR (primary outcome), PFS according to BICR (sALCL population), complete remission (CR) according to BICR, overall survival, and objective response rate (ORR) according to BICR.[2, 3]

Brentuximab vedotin plus CHP was associated with a statistically significant improvement in PFS compared with CHOP, in both the ITT population (primary outcome) and the sALCL population (key secondary outcome). Sensitivity analyses of PFS that used alternate censoring rules were supportive. Furthermore, all key alpha-controlled secondary outcomes were met. For details of the primary outcome and secondary outcome results, see Table 1.

Table 1. Primary and secondary outcome results of ECHELON-2 (data cut-off August 2018).[1-3]

	ITT population		**sALCL population**	
	brentuximab vedotin plus CHP (n= 226)	**CHOP (n= 226)**	**brentuximab vedotin plus CHP (n= 163)**	**CHOP (n= 154)**
Progression-free survival (BICR)				
Median follow-up	35.9 months	41.8 months	-	-
Number of events	95	124	56	73
Stratified Hazard Ratio (95% CI)	0.71 (0.54 to 0.93) p= 0.01		0.59 (0.42 to 0.84) p= 0.003	
Median time to event	48.2 months	20.8 months	55.7 months	54.2 months
1 year event-free estimate	72%	58%	79%	60%

Objective response rate (BICR)				
Objective response rate	83%	72%	88%	71%
- p-value	p<0.001		-	
Complete remission	68%	56%	71%	53%
- p-value	p<0.001		-	
Overall survival				
Number of patients	n= 226	n= 226	n= 162	n= 154
Median follow-up	42.1 months		NE	
Number of events	51	73	34	44
Hazard Ratio (95% CI)	0.66 (0.46 to 0.95) p= 0.02		0.63 (0.40 to 0.99)*	
Median time to event	NR	NR	NR	NR

P-values presented for primary and key alpha-controlled secondary outcomes only; * Updated overall survival analysis (25 September 2019); BICR = Blinded Independent Central Review; CHP = cyclophosphamide, doxorubicin and prednisone; CHOP = cyclophosphamide, doxorubicin, vincristine, and prednisone; CI = confidence interval; ITT = intention to treat; NE = not estimable; NR = not reached; sALCL = systemic anaplastic large cell lymphoma.

Health Related Quality of Life (HRQoL) was assessed using 3 questionnaires: the European Quality of Life 5-Dimensions Questionnaire (EQ-5D-3L), the European Organisation for Research and Treatment of Cancer (EORTC) Core Quality of Life Questionnaire- Core 30 (QLQ C30), and the Functional Assessment of Cancer Treatment Gynecologic Oncology Group - Neurotoxicity (FACT/GOG-NTX) subscale. There were no differences between brentuximab vedotin plus CHP and CHOP treatment groups in overall scores of EORTC QLQ C30 or EQ-5D-3L. Neurotoxicity scores for the FACT/GOG-NTX subscale were not meaningfully different between the treatment groups, except for at end of treatment, where it favoured CHOP.[2]

Summary of evidence on comparative safety

Overall, the European Medicines Agency (EMA) concluded that the safety profile of brentuximab vedotin plus CHP observed in ECHELON-2 was consistent with the known safety profile; no new safety signals were identified. The safety profile in the sALCL population was similar to that of the full study population.[2]

In the safety analysis set, any adverse event (AE) was reported by 99% (221/223) of patients in the brentuximab vedotin plus CHP group and 98% (221/226) in the CHOP group; patients reporting a grade 3 or higher AE were 66% versus 65%; patients with a reported serious AE were 39% versus 38%, and patients discontinuing therapy due to an AE was 6.3% versus 6.6%.[3]

The most frequently reported AEs of any grade with an incidence >20% in the brentuximab vedotin plus CHP group versus the CHOP group were: nausea (46% versus 38%), peripheral sensory neuropathy (45% versus 41%), neutropenia (38% versus 38%), diarrhoea (38% versus 20%), constipation (29% versus 30%), alopecia (26% versus 25%), pyrexia (26% versus 19%), vomiting (26% versus 17%), fatigue (24% versus 20%), and anaemia (21% versus 16%).[3]

Summary of clinical effectiveness issues

sALCL is a subtype of PTCL, which is a subset of non-Hodgkin's lymphoma. It is a rare condition with an annual incidence rate in the UK of 0.3 cases per 100,000. Symptoms can include B-symptoms (fever, night sweats, and weight loss), eosinophilia, pruritus, haemophagocytosis, thrombocytopenia and anaemia. Prognosis is variable and dependent on prognostic factors such as subtype, age, lactate dehydrogenase (LDH) value, performance status, Ann Arbor stage, and the number of extranodal involvements. Management for newly diagnosed sALCL most commonly consists of CHOP chemotherapy, provided that the patient is not enrolled in a clinical trial. This chemotherapy regimen may also be adapted to include etoposide for younger patients (≤60 years). Patients who achieve partial or complete response to treatment and are transplant eligible may go on to receive autologous SCT, although evidence to support this intervention is limited. The development of effective first-line treatments remains a priority in sALCL as median overall survival in patients who have relapsed after treatment is very poor (5.5 months in patients with PTCL).[2, 4-6] Brentuximab vedotin meets SMC orphan criteria.

In a well conducted, randomised, double-blind, phase III study, brentuximab vedotin plus CHP was associated with a statistically significant advantage over the most relevant comparator (CHOP) in the overall study population, in addition to the more pertinent sALCL subgroup. Median PFS in the sALCL population appears to be similar between treatment groups (55.7 months versus 54.2 months). However this way of presenting the data is not representative, due to the high level of censoring and the very small number of events in each treatment group driving the result. The reported HR and event-free estimates are more informative. The 2-year PFS rates were 68% and 54% in the brentuximab vedotin plus CHP and CHOP groups respectively, and the HR was 0.59 (95% CI: 0.42 to 0.84), suggesting a clinically meaningful treatment benefit in the sALCL population. Other key, alpha-controlled secondary outcomes were also supportive (CR according to BICR, overall survival, and ORR according to BICR [ITT population]), and the benefits from treatment with brentuximab vedotin plus CHP were observed without an increase in toxicity.[2]

Although a strong piece of evidence, there were some limitations to the ECHELON-2 study worth consideration. The population of interest (sALCL population) were a subgroup, albeit the majority of the total study population were diagnosed with sALCL (70%). Consequently, PFS analysis in the relevant population were not powered to detect statistical differences. A further limitation was the immature overall survival data; only 124 (27%) overall survival events were observed, and median overall survival was not reached in either group. Final overall survival analysis results are awaited, although these results will likely be confounded by the notable amount of patients in the CHOP treatment group who subsequently received brentuximab vedotin (22%).[2] A further limitation is that the study excluded patients with ALK-positive sALCL with an IPI score <2. IPI is a common prognostic tool used in nodal PTCL where scores range from 0 to 5, with lower scores signifying better prognosis.[5] Therefore, there is uncertainty in the generalisability of the results to ALK-positive sALCL patients with better prognosis. Lastly, the censoring rules for the primary PFS analysis were not in accordance with EMA guidance, however sensitivity analysis using the correct censoring rules provided consistent results.

At present, there are no direct or indirect data comparing brentuximab vedotin plus CHP with CHOP plus etoposide, which may be a relevant comparator in Scottish clinical practice for younger patients. Retrospective subset analysis of completed prospective studies has shown an event-free survival benefit in patients aged ≤60 years with the addition of etoposide to CHOP, however benefit in terms of overall survival has not been demonstrated.[7]

Where a medicine has conditional marketing authorisation, SMC has the opportunity to issue interim accepted advice subject to re-evaluation where the committee considers that there is uncertainty around the clinical analysis and the requirements for additional evidence that have been specified by the EMA (known as specific obligations) are expected to address key uncertainties in the evidence presented by the submitting company.

Brentuximab was granted a conditional marketing authorisation from the EMA but there are no specific obligations relating to this indication and interim acceptance has not been considered relevant in this instance.

Clinical experts consulted by SMC considered that brentuximab vedotin plus CHP is a therapeutic advancement due to the benefits in PFS and overall survival that were reported in ECHELON-2 without an observed increase in toxicity. Treatment with brentuximab vedotin plus CHP is anticipated to replace CHOP as the first-line option for adult patients with previously untreated sALCL. Clinical experts felt that the impact of the introduction of brentuximab vedotin plus CHP on the service would be low. Infusion times may be modestly longer for brentuximab vedotin plus CHP than CHOP.

Summary of comparative health economic evidence

The economic model presented was a partitioned survival approach to assess the cost-effectiveness of brentuximab vedotin plus CHP versus CHOP for the treatment of adult patients with previously untreated sALCL. The model used a 45 year lifetime horizon and tracked disease progression through three mutually exclusive health states, which were PFS, progressed disease (PD) and death. The mean age applied within the economic model base case was 52 years and was varied in sensitivity analysis.

Clinical evidence informing the economic analysis was obtained from the ECHELON-2 study.[3] Treatment duration in the model was based on observed use of brentuximab vedotin plus CHP and CHOP in ECHELON-2. The proportion of patients in the progression-free state over time was estimated directly from PFS reported in the sALCL population from ECHELON-2. The proportion of patients alive was estimated directly from overall survival (OS) in the sALCL population from ECHELON-2. The proportion of patients in the PD state is estimated as the difference between OS and PFS.

Observed data in ECHELON-2 showed 36% of sALCL patients who progressed following relapse from brentuximab vedotin plus CHP received brentuximab vedotin monotherapy. The company acknowledged that this is unlikely to occur in practice in the Scottish setting and a statistical adjustment was applied in the base case to remove the effect and cost of retreatment with brentuximab vedotin, whilst allowing for it in the CHOP arm.

In the economic model, subsequent brentuximab vedotin re-treatment was applied as the mean number of brentuximab vedotin lines in progressed patients, with estimates taken from ECHELON-2 for CHOP (and removed in the base case for brentuximab vedotin plus CHP). The two-stage estimator (TSE) approach assumes everyone is equal at the start of progression and forms a new baseline for additional brentuximab vedotin treatment. As there can be some bias at this new baseline, re-censoring is recommended and the company carried out both with and without re-censoring and there was little difference between these. Advice from medical statistician confirms that this is not surprising as the trial data (K-M) is relatively short compared to the time horizon.

Extrapolations were presented to UK clinical experts by the submitting company where it was advised that the risk of relapse after front-line treatment was highest in the first two years following treatment, and that patients who have not relapsed within two years have a low likelihood of relapse. This was supported by a retrospective analysis of 775 patients from the US, Sweden and Canada.[9]

The model applies adjusted age- and gender-matched population mortality rates when the implied rate of mortality extrapolated from ECHELON-2 falls below that of the (adjusted) general population. A mortality multiplier of 1.21 has been applied in the base case analysis, representing a 5% reduction in life expectancy. Values of 1.29 and 1.42 were used in sensitivity analyses, reflecting a 7.5% and 10% reduction in life expectancy, respectively.

Quality of life data were collected during study ECHELON-2 and used in the economic model. A time-to-death analysis was used to calculate health-related quality of life (HRQoL) in the base case where HRQoL declined significantly as patients approached death. The company also explored a different approach to analyse quality of life data by the inclusion of an indicator for health state membership (progression-free and progressed disease).

The analysis included acquisition and administration costs for brentuximab vedotin, concomitant medication costs, adverse event costs and subsequent brentuximab vedotin costs. Costs for health states pre-progression and post-progression were included, as were stem cell transplant costs for salvage chemotherapies.

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 NHS Scotland. Under the PAS, a discount is offered on the list price of the medicine. In the base case, the company estimated an incremental cost-effectiveness ratio (ICER) of £21,141.

The company's choice of extrapolation distribution was the Gamma distribution. There was a large variation between the different distributions and so the company has provided scenarios with the alternative OS extrapolations. The results and can be seen in Table 2 (scenarios 10-13). The ICERs provided show the choice of distribution is not a key driver of results, and it remains within an acceptable range.

The company provided scenario analyses, deterministic sensitivity analysis (DSA) and probabilistic sensitivity analysis. In the DSA, each variable was increased and decreased by the 95% CI or 15% where no estimates of prevision were available. The most sensitive parameter was the treatment effect of brentuximab vedotin plus CHP vs CHOP on OS as can be seen in scenario 9 in Table 2. The

OS was varied by the 95% CI with OS ranging from 0.273 and 1.967 (the constant being 1.120). The high ICER can therefore be said to be particularly conservative. This sensitivity was expected as the results of the analysis were primarily driven by survival gains. The company also provided scenario analysis to explore uncertainty around key structural assumptions.

A summary of key sensitivity analyses are presented in table 2.

Table 2. Selected sensitivity analyses

Scenario	Change(s) made to model	ICER (with PAS)
	Base case	£21,141
1	Unadjusted analysis as per ECHELON-2 (including costs and effects of subsequent brentuximab vedotin)	£22,659
2	Removing costs and effect of brentuximab vedotin re-treatment in the brentuximab vedotin +CHP arm (TSE, with re-censoring)	£19,369
3	10-year time horizon	£43,286
4	Model entry age of 57.7	£24,215
5	10% mortality rate for patients in long-term remission (base case 5%)	£21,862
6	Progressed utility using alternative published study (Swinburn) utility in progressed disease	£19,637
7	All patients receive 8 cycles (base case 6 .2 cycles)	£27,901
8	No patients receive concomitant medications	£21,028
9	Most sensitive parameter in DSA: OS (TSE), no re-censoring – gamma, treatment effect	£13,473 - £70,206
10	Distributions for OS and PFS - Gompertz	£20,656
11	Distributions for OS and PFS - Log-logistic	£14,501
12	Distributions for OS and PFS - Log-normal	£15,352
13	Distributions for OS and PFS - Weibull	£12,146
14	2x administration costs for BV+CHP (including PAS)	£22,073

Abbreviations: OS, overall survival; PFS, progression-free survival; TSE, two-stage estimator.

Key weaknesses:

- Adjustment of brentuximab vedotin monotherapy retreatment due to observed data on this being unlikely to occur in clinical practice is the main source of uncertainty in the model. The alternative adjustments have been explored in scenarios 1 and 2 in table 2 and show the results are not sensitive to it.
- There appears to be some uncertainty around the appropriate mortality rate. The model applied adjusted age- and gender-matched population mortality rates when the implied rate of mortality extrapolated from ECHELON-2 falls below that of the (adjusted) general

population. There is some uncertainty around the appropriate values, but the company provided ICERs with increased mortality rates that still lie within an acceptable range.

Despite the limitations outlined above, the results are relatively robust to changes in the key parameters. Therefore, the economic case is 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 Group.

- We received a patient group submission from Lymphoma Action, which is a registered charity.

- Lymphoma Action has received 9.8% pharmaceutical company funding in the past two years, including from the submitting company.

- Symptoms of sALCL include: enlarged lymph nodes, fatigue, weight loss, fevers, night sweats, itching or skin rash. People also might experience shortness of breath, cough, vomiting, diarrhoea or abdominal pain and can develop neutropenia, anaemia and thrombocytopenia. sALCL has a significant impact on the quality of life of patients and their carers. The disease and its current treatments can have harmful effects on their working and social lives. Patients can have prolonged time off work after aggressive treatment regimens which can cause financial hardship. The psychological impact is also severe. As sALCL is a rare disease, patients may feel isolated and unsupported, and are often looked after by staff who have limited experience of treating people with the disease.

- There is no accepted standard of care for sALCL. Treatment pathways frequently involve stem cell transplants. Stem cell transplants have a massive impact on quality of life, typically requiring an extended hospital stay, time off work and a prolonged recovery period. The chemotherapy regimens used to treat sALCL have significant side effects and risk of late effects. They also involve repeated trips to-and-from hospital for outpatient treatment.

- There is a clear unmet need for an effective treatment that improves outcomes, and resulting quality of life, in sALCL. Patients feel that brentuximab vedotin has the potential to improve outcomes and quality of life and is more convenient than current treatment options. Patients also felt that the tolerability profile of brentuximab vedotin would allow them to continue a more normal life than other treatment options

Additional information: guidelines and protocols

The British Society for Haematology (BSH) guideline "Guidelines for the Management of Mature T-cell and NK-cell Neoplasms" (updated August 2013) states that CHOP is the most commonly used first line treatment for non-ALK-positive PTCLs despite the fact that it has never been established as the preferred or most effective treatment. They maintain, however, that there are insufficient data to recommend an alternative and clinical trials are of paramount importance in finding new treatment regimens.[8]

The European Society for Medical Oncology (ESMO) guideline "Peripheral T-cell lymphomas: ESMO clinical practice guidelines" (published in 2015), recommends treatment to be selected according to factors such as age, IPI, and co-morbidities. Whenever possible, patients should be enrolled into clinical trials. The most common treatment for nodal PTCL is cyclophosphamide, hydroxydaunorubicin, vincristine and prednisone (CHOP), or variants of it. The guideline also suggests that etoposide may be added in to CHOP in patients aged <60 years as it has shown benefits in event-free (but not overall) survival.[5]

Additional information: comparators

CHOP, with or without etoposide.

Additional information: list price of medicine under review

Medicine	Dose Regimen	Cost per cycle (£)
brentuximab vedotin*	1.8mg/kg by intravenous (IV) infusion every 3 weeks for 6 to 8 cycles	£7,500

** Cost of brentuximab vedotin only - cost of CHP not included. Costs assume a patient weight of 70kg. Costs from BNF online on 01 October 2020. Costs calculated using the full cost of vials/ampoules assuming wastage. Costs do not take patient access schemes into consideration.*

Additional information: budget impact

The submitting company estimated the population eligible for treatment to be 14 patients in each year to which confidential uptake rates 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.

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

References

1. Takeda UK Ltd. Brentuximab vedotin (Adcetris®) Summary of product characteristics. Electronic Medicines Compendium www.medicines.org.uk Last updated 05 Aug 2020. 2019.

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6. Mak V, Hamm J, Chhanabhai M, Shenkier T, Klasa R, Sehn LH*, et al.* Survival of patients with peripheral T-cell lymphoma after first relapse or progression: spectrum of disease and rare long-term survivors. J Clin Oncol. 2013;31(16):1970-6. Epub 2013/04/24.

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8. Dearden CE, Johnson R, Pettengell R, Devereux S, Cwynarski K, Whittaker S*, et al.* Guidelines for the management of mature T-cell and NK-cell neoplasms (excluding cutaneous T-cell lymphoma). Br J Haematol. 2011;153(4):451-85. Epub 2011/04/13.

9. Maurer MJ, Ellin F, Srour L, *et al*. International Assessment of Event-Free Survival at 24 Months and Subsequent Survival in Peripheral T-Cell Lymphoma. J Clin Oncol. 2017; **35**(36): 4019-26.

This assessment is based on data submitted by the applicant company up to and including 13 October 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.