Healthcare Improvement Scotland | SMC Advice on new medicines

SMC2282

polatuzumab vedotin 140mg powder for concentrate for solution for infusion (Polivy®)

Roche Products 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 on its use in NHSScotland. The advice is summarised as follows:

ADVICE: following a full submission for an end of life and orphan medicine

polatuzumab vedotin (Polivy®) is accepted for use within NHSScotland on an interim basis subject to ongoing evaluation and future reassessment.

Indication under review: in combination with bendamustine and rituximab for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma who are not candidates for haematopoietic stem cell transplant.

In a phase Ib/II study polatuzumab vedotin in combination with bendamustine and rituximab significantly increased complete response rate compared to bendamustine and rituximab alone.

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

Polatuzumab vedotin in combination with bendamustine and rituximab for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma who are not candidates for haematopoietic stem cell transplant.[1]

Dosing Information

The recommended dose of polatuzumab vedotin is 1.8mg/kg, given as an intravenous (IV) infusion every 21 days in combination with bendamustine and rituximab for six cycles. Polatuzumab vedotin, bendamustine and rituximab can be administered in any order on Day 1 of each cycle. When administered with polatuzumab vedotin, the recommended dose of bendamustine is 90mg/m^2/day on Day 1 and Day 2 of each cycle and the recommended dose of rituximab is 375mg/m^2 on Day 1 of each cycle. Due to limited clinical experience in patients treated with 1.8mg/kg polatuzumab vedotin at a total dose >240mg, it is recommended not to exceed the dose 240mg/cycle.

If not already premedicated, premedication with an antihistamine and anti-pyretic should be administered to patients prior to polatuzumab vedotin.

If a planned dose of polatuzumab vedotin is missed, it should be administered as soon as possible and the schedule of administration should be adjusted to maintain a 21-day interval between doses. Information regarding dose modifications for patients who experience peripheral neuropathy, myelosuppression or infusion-related reactions can be found in the Summary of product characteristics (SPC).

Polatuzumab vedotin must only be administered under the supervision of a healthcare professional experienced in the diagnosis and treatment of cancer patients.

Please refer to the SPC for further information.[1]

Product availability date

March 2020

Polatuzumab vedotin received a positive scientific opinion for the above indication under the Early Access to Medicines Scheme with the Medicines and Healthcare Products Regulatory Agency on 25 June 2019.

Polatuzumab vedotin has conditional marketing authorisation from the European Medicines Agency (EMA). It has been designated an orphan medicine by the EMA and also meets SMC end of life criteria for this indication.

Summary of evidence on comparative efficacy

Polatuzumab vedotin (hereafter referred to as polatuzumab) is a CD79b targeted antibody-drug conjugate that preferentially delivers a potent anti-mitotic agent (monomethyl auristatin E) which results in the killing of malignant B-cells. It is licensed in combination with bendamustine and rituximab for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) who are not candidates for haematopoietic stem cell transplant (HSCT).[2, 3]

The key evidence presented is from GO29365, an ongoing randomised, open-label phase Ib/II study of polatuzumab in combination with bendamustine plus rituximab in patients with relapsed or refractory DLBLC, and polatuzumab in combination with bendamustine plus obinutuzumab in patients with relapsed or refractory follicular lymphoma. The DLBCL component of the study recruited adults (aged ≥18 years) with histologically confirmed relapsed or refractory DLBCL following at least one prior line of therapy. This included patients who were ineligible for second-line HSCT, with progressive disease or no response <6 months from start of initial therapy (second line refractory) or with disease relapse after initial response ≥6 months from start of initial therapy (second line relapsed). Also included were patients who were ineligible for third-line (or beyond) HSCT, with progressive disease or no response <6 months from start of prior therapy (third line refractory) or with disease relapse after initial response ≥6 months from start of prior therapy (third line relapsed). If the patient had received prior bendamustine, response duration must have been at least 1 year (for patients who have relapsed disease after a prior regimen). In addition, eligible patients had an Eastern Cooperative Oncology Group (ECOG) performance status of 0 to 2 and a peripheral neuropathy grade ≤1. Double- and triple-hit lymphomas were not excluded.[2, 4]

Patients in the phase II part of the study were randomised equally (n=40 in each group) to receive bendamustine and rituximab alone or in combination with polatuzumab. Bendamustine 90mg/m^2 was administered on Days 2 and 3 of Cycle 1, then Days 1 and 2 of subsequent Cycles 2 to 6 and rituximab 375mg/m^2 on Day 1 of Cycles 1 to 6. Polatuzumab 1.8mg/kg was administered on Day 2 of Cycle 1 and then on Day 1 of subsequent cycles. Randomisation was stratified according to duration of response to prior therapy (≤12 months versus >12 months).[2, 4]

The primary outcome was complete response (CR) rate as measured at the primary response assessment (6 to 8 weeks after Day 1 of cycle 6 or last dose of study medication) by positron emission tomography-computed tomography (PET-CT) scan and as determined by independent review committee (IRC). The CR rate was defined as the percentage of participants with a complete response according to Modified Lugano Criteria. Results are presented in Table 1 below for the data cut-off 30 April 2018. At this point the primary analysis was possible for the full study population as all treated patients had a one-year follow-up after preliminary response assessment. The median duration of follow-up was 22.3 months. The primary outcome, IRC assessed CR rate was significantly higher in the polatuzumab group. Investigator-assessed CR rate followed a similar trend to the IRC. Progression-free survival (PFS) as determined by independent review committee was a secondary outcome and overall survival was an exploratory outcome. A median absolute

improvement of 5.8 months in IRC assessed PFS and a median absolute survival benefit of 7.7 months was considered clinically meaningful.[2, 4]

Table 1: Outcome results for GO29365.[2, 4, 5]

	Polatuzumab plus bendamustine plus rituximab n=40	Bendamustine plus rituximab n=40
Primary outcome: IRC assessed complete response rate (data cut-off: 30 April 2018)		
IRC assessed CR rate % (n)	40% (16)	18% (7)
Difference (95% CI), p-value	22% (2.6 to 40) p=0.026	
Secondary outcome: IRC assessed objective response rate and progression-free survival (data cut-off: 30 April 2018)		
Objective response rate, % (n)	45% (18)	18% (7)
PFS event, n	25	32
Median PFS (95% CI), months	9.5	3.7
HR (95% CI)	0.36 (0.21 to 0.63)	
Exploratory outcome: Overall survival (updated data cut-off: 15 March 2019)		
Overall survival event, n	NR	NR
Median overall survival, months	12.4	4.7
HR (95% CI)	0.41 (0.24 to 0.71)	

IRC = independent review committee, CR = complete response, CI=confidence interval, PFS=progression-free survival, HR=hazard ratio.

There was an imbalance in baseline prognostic factors including International Prognostic Index (IPI) 4-5, refractoriness to last prior therapy, ECOG performance status and bulky disease that favoured the polatuzumab group. To address this imbalance three types of analyses were explored for the EMA marketing authorisation application via multivariate regression, backward selection and propensity score weighted regression models. Four key outcomes were assessed: IRC assessed CR at end of treatment, IRC assessed best objective response, IRC assessed PFS, investigator assessed PFS and overall survival.[2] The results confirmed the favourable trend in PFS and overall survival for the polatuzumab plus bendamustine plus rituximab group.

Patient reported outcomes for the severity of neuropathy symptoms was assessed using Therapy-Induced Neuropathy Assessment Scale (TINAS) v1.0 questionnaires. This instrument asks patients to rate the severity of their neuropathy-related symptoms in the last 24 hours, 11 items are scored on a scale of 0 to 10, with 0= the symptom is not present and 10= the symptom is as bad as you can imagine. No significant change from baseline was identified from pooled polatuzumab plus bendamustine plus rituximab or obinutuzumab data from the phase Ib and II groups.[2]

Summary of evidence on comparative safety

The EMA concluded that the safety profile of polatuzumab vedotin is not negligible however, it is still manageable in the context of a severe condition like relapsed or refractory DLBCL in those not eligible for HSCT. As part of the specific obligations for the conditional marketing authorisation further safety data from the ongoing GO29365 study (using the licensed formulation) will be provided. Further safety data will also be provided within a randomised study GO39942 due to enrol 875 patients with previously untreated DLBCL, with an estimated follow up of up to 65 months.

In GO29365 at data cut-off 30 April 2018, the median duration of treatment in the polatuzumab plus bendamustine plus rituximab group was 5 cycles and in the bendamustine plus rituximab group was 3 cycles. Any treatment-emergent adverse event (AE) was reported by 100% (39/39) of patients in the polatuzumab plus bendamustine plus rituximab group and 97% (38/39) in the bendamustine plus rituximab group. In each group respectively, patients reporting a grade 3 or 4 AE were 85% versus 72%, patients with a reported serious AE were 64% versus 62%, the proportion of AEs that led to dose interruptions were 54% versus 38% and patients discontinuing therapy (any medicine) due to an AE was 33% versus 10%.[3, 4]

The most frequently reported treatment-emergent AEs of any grade with an incidence ≥20% in the polatuzumab plus bendamustine plus rituximab group versus the bendamustine plus rituximab group were: neutropenia (54% versus 38%), anaemia (54% versus 26%), thrombocytopenia (49% versus 28%), peripheral neuropathy (44% versus 7.7%), diarrhoea (38% versus 28%), fatigue (36% versus 36%), pyrexia (33% versus 23%), nausea (31% versus 41%), decreased appetite (26% versus 20%), constipation (18% versus 20%), lymphopenia (13% versus 0%), febrile neutropenia (10% versus 13%).[4]

Peripheral neuropathy was more frequently reported in the polatuzumab plus bendamustine plus rituximab group, all events were grade 1 or 2 in both arms and most events resolved. Neutropenia of grade 3 or 4 affected 46% and 33% of patients in the respective groups and led to treatment discontinuation in <10% of patients. Grade 3 or 4 thrombocytopenia affected more patients in the polatuzumab treatment group (41% versus 23%) however, the numbers of patients requiring platelet transfusions were comparable between groups (8.9% versus 13%).[2, 4]

Fatal adverse events were reported in nine patients in the polatuzumab plus bendamustine plus rituximab group, including two assessed as treatment-related (meningoencephalitis herpetic and pulmonary oedema). Eleven fatal adverse events were reported in the bendamustine plus rituximab group and one was assessed as related to study drug (septic shock). A fatal case of myelodysplastic syndrome occurred in a patient receiving polatuzumab in combination with bendamustine and obinutuzumab. The risk of carcinogenicity remains closely monitored as part of the important potential risks for polatuzumab. Further evaluation of the risk of carcinogenicity will be provided through post-authorisation long term data.[2]

Among all patients with DLBCL treated with polatuzumab in GO29365, a total of four patients developed anti-drug antibodies. Most patients (n=3) completed 5 to 6 cycles of treatment and duration of response was 21 to 38 months. However, the last patient developed antibodies at cycle 2 and was diagnosed with progressive disease at cycle 3. Further data on anti-drug antibodies and the potential impact on efficacy will be provided as part of the conditional marketing authorisation.[2]

Summary of clinical effectiveness issues

Diffuse large B-cell lymphoma (DLBCL) is the most common non-Hodgkin lymphoma, accounting for approximately 25% of all newly diagnosed cases. The incidence of this aggressive disease increases with age and varies considerably across Europe. Treatment should be stratified according to age, International Prognostic Index (IPI) and feasibility of dose-intensified approaches. Primary refractory disease occurs in 10 to 15% of DLBCL patients and a further 20 to 30% relapse. Higher treatment failure rates are seen in poorer outcome sub-groups, including activated B-cell-like (ABC) and MYC/BCL2 double-expressor lymphomas.[2, 4, 6]

After failure of first line therapy, patients receive salvage chemotherapy followed, in responsive patients, by high dose chemotherapy and HSCT. Many refractory or relapsed patients are ineligible for HSCT due to age, co-morbidities or chemotherapy insensitive disease. For patients who are ineligible for HSCT, second line treatment options include salvage chemotherapy or clinical trials with novel drugs. A median overall survival of 6.3 months and a two-year survival rate of 20% has been observed in patients with refractory DLBCL and a median overall survival of 10 months and one and five-year survival rates of 41% and 27% have been observed in patients with relapsed DLBCL.[7, 8] There is no standard salvage chemotherapy and a number of different regimens may be used including platinum and/or gemcitabine-based regimens. Third line or over treatment options include further lines of salvage chemotherapy, CAR T-cell therapy, clinical trials of novel agents or palliative options. The CAR T-cell therapies represent a treatment option for patients who have had two or more prior lines of systemic therapy, with sufficient disease control to await the manufacturing times, who are able to tolerate the conditioning regimen (usually fludarabine/cyclophosphamide), treatment emergent cytokine-release syndrome and sometimes severe neurotoxicities.[6, 9] Clinical expert opinion has highlighted an unmet need for effective treatments with manageable side effects. Polatuzumab meets SMC end of life and orphan criteria.

The key strengths and uncertainties of the clinical evidence are summarised below:

Key strengths

- The key study GO29365 compared polatuzumab in combination with bendamustine plus rituximab with bendamustine plus rituximab in patients with refractory or relapsed DLBCL. The study reported a significant improvement of 22% for complete response rate assessed by IRC in favour of the polatuzumab group.

- The EMA noted this favourable trend in response rate was supported by secondary outcomes of investigator assessed CR rate and objective response and are reflected in PFS and overall survival outcomes.

Key uncertainties

- GO29365 was a small open label exploratory phase Ib/II trial in a heterogeneous population in terms of prognosis. Evidence for the licensed indication is in a limited population (n=40) who received a liquid formulation of polatuzumab. Additional data to confirm the efficacy and safety in a larger patient population using the licensed lyophilised formulation are awaited.

- Some baseline characteristics within the study were imbalanced suggesting patients in the polatuzumab group may have had a less severe condition. The study excluded patients with an ECOG >2 therefore generalisability to a less fit population is unclear.

- There is a lack of direct or indirect evidence against a relevant comparator. Scottish experts consulted by SMC indicated variation in salvage chemotherapy regimens used for this patient population, however rituximab and bendamustine does not appear to be a regimen widely used in Scottish clinical practice.

- World Health Organisation DLBCL status was balanced between groups however only DLBCL, not otherwise specified (NOS) patients, activated B-cell type (ABC) and germinal centre B-cell type (GCB) were included in each of the study groups. PFS and overall survival were favourable in the polatuzumab group for the ABC subtype but results were less certain for the GCB subtype. Further analyses including more distinct subtypes is required to confirm response.

- Four patients in GO29365 treated with polatuzumab for DLBCL developed anti-drug antibodies. Due to this limited number, no conclusion could be drawn concerning a potential effect of immunogenicity on safety. This has been included in the risk management plan.

- Patient reported outcome data are limited and do not include health related quality of life.

Polatuzumab has an EMA conditional marketing authorisation. To further confirm the safety and efficacy of polatuzumab in combination with bendamustine and rituximab, the company has a specific obligation to provide the primary clinical study report for ongoing study GO29365. This will provide evidence of the size and duration of effect in a larger population (approximately 100 further patients) and using the lyophilised formulation. Furthermore, distinct histology subtypes will be analysed. These data are expected Q4 2020. In addition the company must also submit results from a phase III study GO39942 evaluating polatuzumab in combination with a rituximab regimen in an earlier line of treatment, it is expected that efficacy and safety results (due end 2021) will be confirmative in DLBCL.[2] Outcomes of these studies are likely to address some of the key uncertainties in the clinical evidence.

SMC will consider an updated submission from the company after specific obligations and conditions of the licence have been removed. In the interim, as part of an approach to minimise delay in patient access as a result of the COVID-19 pandemic, polatuzumab is accepted for use in NHSScotland subject to ongoing evaluation and future reassessment.

Summary of comparative health economic evidence

The submitting company developed a three- state partitioned survival analysis model to assess the cost-effectiveness of polatuzumab in combination with bendamustine plus rituximab versus bendamustine plus rituximab in patients with relapsed or refractory (R/R) DLBCL ineligible for HSCT, in line with the licensed indication.

The economic model used a weekly cycle over a 45 year time horizon. A health and social care perspective was used and a 3.5% discount rate was applied to both costs and outcomes in the base case.

The main clinical evidence utilised in the economic evaluation was derived from the March 2019 data cut of the GO29365 study. The model included three mutually exclusive health states: "progression-Free Survival (PFS)", "progressed Disease (PD)" and "death". All patients entered the model in the PFS health state and remained in this health state until disease progression, following which, patients either transitioned into the PD health state or entered the absorbing health state of death. Patients stayed in the PD health state until death. Patients could not transition to an improved health state (i.e. from PD to PFS). The proportion of patients in each health state at any time was defined by the partitioning of patients into "PFS" and "PD" at discrete time points, based on the PFS and OS survival curves from GO29365 study. The proportion of patients falling into the PD health state was the difference between OS and PFS curves.

Both standard parametric survival models as well as a cure-mixture model were used for extrapolation of PFS and OS. Cure-mixture models represent an approach to modelling cancer therapies for which there is evidence to support that a proportion of treated patients enter long-term remission, and subsequently experience mortality aligned with that of the general population. The submitting company assumed the patient population comprises two subpopulations:

1) A subpopulation who have been 'cured' and considered to be at the same risk of mortality as the age- and sex-matched general population
2) A subpopulation with mortality rate defined by a selected standard parametric survival curve.

The company assumed that patients who were progression free at 2 years were 'cured' from the disease, because it considered that a high complete response rate is associated with improved outcomes. According to the cure mixture generalised-gamma model used in the base case, approximately two-thirds of PFS patients at 2 years were considered cured. At 30 months median follow up, the trial data suggested that a small proportion of patients may have a durable response.

Health related quality of life data was not collected in the primary study and hence, base-case utility values were estimated from the ZUMA-1 trial (for axicabtagene ciloleucel) based on a small sample of patients with mixed histology lymphoma. Values were sourced from EQ-5D-5L data, which was cross-walked to 3L values. Due to the cure-mix model, a separate utility value for PFS over 2 years was needed to represent long-term survival. AE-related disutilities were derived from previous NICE appraisals in R/R DLBCL and R/R large cell lymphoma.

The analysis included acquisition and administration costs for polatuzumab plus bendamustine plus rituximab, all comparators and for any further interventions received by patients in the PD state. Treatment related adverse events and any subsequent treatment costs were also 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. Under the PAS, a discount was offered on the list price. The base-case results of the analysis showed an incremental cost-effectiveness ratio (ICER) of £27,396 with PAS.

One-way sensitivity analysis (OWSA), probabilistic sensitivity analysis (PSA) and scenario analyses was performed to investigate levels of uncertainty in the model.

OWSA was conducted for all parameters with single input values (e.g. discount rate, average patient age, utilities, adverse event management costs, administration costs, supportive care costs). Model parameters were systematically and independently varied over a plausible range determined by either the 95% CI or +/-20% where no estimates of precision were available. With the exception of discount rate for effects, none of the parameters led to a substantial change in ICER relative to base case. It is worth noting however, that sensitivity to the cure rate could not be examined in the OWSA.

The company also presented the results of 17 alternate scenarios. The majority of these scenarios led to slightly lower ICERs relative to base case. The most influential scenarios were those with reduced time horizon and more costly comparators (e.g. CAR-T). Notably, the use of standard parametric survival modelling only led to a 6% increase in ICER. Table 2 presents a selection of results from the sensitivity analysis.

Table 2: selected sensitivity analysis results with PAS

	Scenario/Parameter	**ICER (with PAS)**
	Base Case	*£27,396*
1	6% Discount rate (effects)	£32,756
2	PFS Utility (lower limit)	£27,900
3	PD Utility (upper limit)	£27,751
4	Time Horizon – 20 years	£29,433
5	Cure mixture model – Log Normal OS, PFS	£28,661
6	Cure mixture model – Log Logistic OS, PFS	£24,978
7	Standard parametric distribution – Generalised gamma OS, PFS	£28,969
8	Mean PSA	£34,954

Joint parameter uncertainty was explored through a PSA, in which all parameters were assigned distributions and varied jointly. The mean PSA ICER was approximately £35K (table 2 scenario 8) and the probability of polatuzumab plus bendamustine plus rituximab being cost-effective at a threshold of £50K was 70.8%.

The main areas of uncertainty in the analysis were:

- Cure mixture modelling: Given the choice between applying a standard parametric model or a cure mixture model for long term extrapolation, the latter does indeed seem more appropriate as it captures the potentially curative aspect of this disease. However, it is difficult to establish from the KM curves and hazard plots whether polatuzumab plus

bendamustine plus rituximab does offer a cure. This calls into question the cure rate assumed by the company, which has not been sufficiently justified. The cure rate was also inadequately explored as part of the sensitivity analysis which makes it very challenging to assess its impact on cost-effectiveness. This is likely the cause of the unexplained difference between the OWSA and PSA results.

- Inconsistent mortality modelling: An individual patient-level approach based on the age distribution in the trial was used for modelling background mortality. Using different methods to model disease progression associated mortality (cohort-based) and background mortality (individual patient-level based) within the same analysis is inconsistent with recommended methods for modelling PFS/OS.
- Utility values were not trial-based and were estimated from a trial conducted in a much wider patient population. The impact of using alternate utility values was explored in the sensitivity analysis however, and this was not considered to be a key driver of cost-effectiveness.

The above uncertainties should be viewed in the context of a medicine with a conditional marketing authorisation accepted on an interim basis (as noted in the clinical effectiveness section above) and will be subject to future reassessment by SMC in due course.

*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 British Committee for Standards in Haematology published Guidelines for the management of diffuse large B-cell lymphoma in 2016.[9] This guidance predates the availability of polatuzumab and therefore no specific recommendations were made. The guidance makes recommendations in relapsed / refractory disease, only in patients who are eligible for transplant.[9]

The European Society for Medical Oncology (ESMO) published diffuse large B-cell lymphoma (DLBCL): ESMO clinical practice guidelines for diagnosis, treatment and follow-up in 2002. This guidance was subsequently updated in 2012 and again in 2015. This guideline predates the availability of polatuzumab; therefore no specific recommendations were made. In patients unsuitable for transplant who have experienced a first relapse or progression platinum- and / or gemcitabine-based regimens or enrolment in clinical trials with novel drugs should be considered. In patients who have experienced two or more relapses, the guideline recommends enrolment in clinical trials with novel drugs, allogeneic transplant or palliative care.[6]

The National Comprehensive Cancer Network (NCCN) published Clinical practice guidelines in oncology: B-cell lymphomas in July 2020. The NCCN guidance recommends a number of second

line treatments for patients with DLBCL who are not suitable for HSCT including; gemcitabine-based regimens with rituximab or polatuzumab vedotin with/without bendamustine and with/without rituximab (after ≥2 prior therapies). The guidance also recommends axicabtagene ciloleucel and tisagenlecleucel as treatments for patients with in refractory or relapsed DLBCL who have received two or more prior lines of systemic therapy.[10]

Additional information: comparators

Salvage chemotherapy, novel agents in clinical trials and palliative chemotherapy. CAR T-cell therapy may be used for those who have received two or more prior systemic treatment lines. There is no defined standard of care for patients with relapsed or refractory DLBCL.

Additional information: list price of medicine under review

Medicine	Dose Regimen	Cost per cycle (£)
Polatuzumab	1.8 mg/kg, given as an intravenous (IV) infusion every 21 days for 6 cycles.	11,060

Costs from BNF online on 08/07/20. Costs calculated using the full cost of vials/ampoules assuming wastage. Dose is based on body weight of 70kg. Costs do not take any patient access schemes into consideration.

Additional information: budget impact

The company estimated the number of patients treated 22 in year 1 rising to 38 in year 5.

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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This assessment is based on data submitted by the applicant company up to and including 14 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:

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.