Scottish Medicines Consortium
Providing advice about the status of all newly licensed medicines
www.scottishmedicines.org.uk
Delta House 50 West Nile Street Glasgow G1 2NP Tel 0141 225 6999 Chairman: Professor Jonathan G Fox

daclizumab 150mg/mL solution for injection in prefilled syringe/pen (Zinbryta®)

SMC No. (1216/17)

Biogen Idec Ltd

10 March 2017

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

ADVICE: following a full submission

daclizumab (Zinbryta®) is accepted for restricted use within NHS Scotland.

Indication under review: In adult patients for the treatment of relapsing forms of multiple sclerosis.

Restriction: for use

- in patients with rapidly evolving severe (RES) relapsing remitting multiple sclerosis (RRMS) or
- in patients with RRMS with an inadequate response to disease modifying therapy

In a phase III study, the adjusted annualised relapse rate (over a period of 144 weeks) was statistically significantly lower for daclizumab than for an interferon beta treatment in patients with RRMS.

This SMC advice takes account of the benefits of a Patient Access Scheme (PAS) that improves the cost-effectiveness of daclizumab. This advice is contingent upon the continuing availability of the PAS in NHS Scotland or a list price that is equivalent or lower.

Overleaf is the detailed advice on this product.

Chairman,
Scottish Medicines Consortium

Published 10 April 2017

Indication

In adult patients for the treatment of relapsing forms of multiple sclerosis.[1]

Dosing Information

Daclizumab 150mg injected subcutaneously once a month. The usual sites for subcutaneous injection include the thigh, abdomen, and back of the upper arm.

Treatment should be initiated by a physician experienced in the management of multiple sclerosis.[1]

Product availability date

March 2017

Summary of evidence on comparative efficacy

Daclizumab is a monoclonal antibody that binds to CD25 (IL-2Rα) and prevents interleukin-2 (IL-2) binding to CD25. Immunomodulatory effects are thought to reduce CNS pathology in multiple sclerosis (MS), reducing the occurrence of relapses and disability progression.[1]

Current UK guidance recommends that patients with relapsing remitting multiple sclerosis (RRMS) who have at least two relapses in the previous two years and have active disease should be considered for treatment with disease modifying therapy (DMT).[2] The marketing authorisation of daclizumab includes relapsing forms of secondary progressive MS and the submitting company initially requested that SMC considers daclizumab when positioned for use in patients with RRMS. However, during the assessment the company noted that the two subpopulations of specific interest to be considered by SMC were patients with rapidly evolving severe (RES) RRMS and patients with RRMS with an inadequate response to DMT.

Evidence of efficacy was from a multicentre, randomised, double-blind, active-controlled phase III study (DECIDE) conducted in patients aged 18 to 55 years with a confirmed diagnosis of RRMS (2005 McDonald criteria). Patients were eligible if they had cranial magnetic resonance imaging (MRI) showing lesions that were consistent with a diagnosis of MS, and a score of 0 to 5 on the Expanded Disability Status Scale (EDSS). Patients were also required to have one of the following: at least two clinical relapses within the previous three years, with at least one clinical relapse occurring in the 12 months before randomisation; or at least one clinical relapse and at least one new lesion on MRI that was not associated with the clinical relapse within the previous two years, with at least one of these events occurring in the 12 months before randomisation. Patients with progressive forms of MS were excluded.[3]

Patients were randomised equally to treatment with daclizumab 150mg by subcutaneous injection every four weeks (n=919) or interferon beta-1a 30 micrograms by intramuscular injection once weekly (n=922) for 96 weeks to 144 weeks. Stratification was according to study site and prior use of interferon beta. Patients received placebo injections to maintain blinding and prophylactic treatment for influenza-like symptoms during the first 24 weeks of therapy in order to reduce potential for unblinding.[3]

The primary outcome was the adjusted annualised relapse rate over a period of 144 weeks, where relapses were defined as new or recurrent neurologic symptoms that were not associated with fever or infection and that lasted at least 24 hours. The symptoms had to be accompanied by new objective neurologic findings by the examining neurologist that were confirmed by the independent neurologic evaluation committee.[3] The adjusted annualised relapse rate was 0.22 for daclizumab and 0.39 for interferon beta-1a; rate ratio 0.55 (95% confidence interval [CI]: 0.47 to 0.64), p<0.001.[3,4] In analyses conducted in the RES RRMS and RRMS with an inadequate response to DMT subpopulations, the adjusted annualised relapse rate was significantly lower for daclizumab versus interferon beta-1a.[5]

Secondary endpoints were ranked and if a comparison was not significant (at the 0.05 significance level), all lower-ranked endpoints were not considered to be statistically significant within the closed-testing procedure. Table 1, below, includes results of secondary endpoints.

Table 1: results of secondary endpoints from DECIDE[3, 4]

	Daclizumab	**Interferon beta -1a**	**Comparison**
Adjusted mean number of new or newly enlarged hyperintense lesions on T2-weighted MRI scans of the brain over 96 weeks	4.3	9.4	lesion mean ratio: 0.46 (95% CI: 0.39 to 0.53), p<0.0001
Estimated proportion of patients with confirmed disability progression sustained for 3 months at 144 weeks*	16%	20%	hazard ratio 0.84 (95% CI: 0.66 to 1.07), p=0.16
Estimated proportion of patients who were relapse-free at 144 weeks	67%	51%	hazard ratio 0.59 (95% CI: 0.50 to 0.69)
Proportion of patients with clinically meaningful worsening on the MSIS-29 physical subscale at week 96**	19%	23%	odds ratio 0.76 (95% CI: 0.60 to 0.95)

* defined as an increase of ≥1 point from a baseline score of ≥1 or an increase of ≥1.5 points from a baseline score of 0 on the EDSS, that was confirmed at 12 weeks (Kaplan-Meier method)
** defined as increase from baseline of ≥7.5 points
CI=confidence interval; MSIS-29=multiple sclerosis impact scale-29

Results for the European Quality of Life, 5 dimensions (EQ-5D) visual analogue scale and utility score indicate some improvement for daclizumab and remained unchanged in the interferon beta-1a group. The differences between groups were (nominally) statistically significant for EQ-5D visual analogue scale by week 72 and EQ-5D utility score by week 96, in favour of daclizumab.

Supportive data are available from SELECT, SELECTION and SELECTED studies. The SELECT study was a randomised, placebo-controlled, dose-ranging phase II study conducted to assess the safety and efficacy of daclizumab in 621 patients with RRMS. The study had similar inclusion criteria to DECIDE except that patients were required to have had at least one confirmed multiple sclerosis relapse in the 12 months before randomisation, or at least one new gadolinium-enhancing lesion on brain MRI done within the six weeks before randomisation. Patients were randomised equally (without stratification) to daclizumab 150mg (n=208), daclizumab 300mg (n=209) or placebo (n=204) administered by subcutaneous injection once every four weeks for 52 weeks. The 300mg dose is unlicensed. The primary endpoint, adjusted annualised relapse rate over 52 weeks, was 0.21 for daclizumab 150mg and 0.46 for placebo; rate ratio 0.46 (95%

CI: 0.32 to 0.67), p<0.0001.[6] Daclizumab 150mg was superior to placebo for most secondary endpoints.

Patients who completed the study could enter a 12 month extension study (SELECTION). In patients who received daclizumab (150mg or 300mg) for an additional 12 months, the annualised relapse rate was 0.16 (95% CI: 0.10 to 0.26).[7] SELECTED is an ongoing open-label extension study in patients who have completed the SELECT and SELECTION studies and has recruited 410 patients. At an interim analysis the median duration of daclizumab treatment was 25 months (range <1 to 45). The adjusted annual relapse rate at six-month intervals from the first dose of daclizumab was 0.21 (95% CI: 0.16 to 0.29) for weeks 0 to 24 and decreased to 0.15 (95% CI: 0.10 to 0.21) by weeks 121 to 144.[8]

Summary of evidence on comparative safety

In DECIDE, the proportion of adverse events (excluding MS relapse) was 90% in the daclizumab group and 89% in the interferon beta-1a group and serious adverse events (excluding MS relapse) was 15% and 9.5% in respective groups. The proportion of patients who discontinued from the study due to an adverse event (excluding MS relapse) was 14% and 9.1%.[3]

Adverse events (excluding MS relapse) that occurred in at least 10% of patients in either group were: nasopharyngitis (25% and 21%), headache (17% and 19%), upper respiratory tract infection (16% and 13%), pyrexia (11% and 15%), injection site pain (10% and 11%), urinary tract infection (10% and 11%) and influenza-like illness (10% and 38%) in the daclizumab and interferon beta-1a groups respectively.[3]

Infections were reported in 65% versus 57% of patients in the daclizumab and interferon beta-1a groups respectively. Serious infections occurred in 4.4% and 1.6% of patients in respective groups and included urinary tract infection (8 versus 2 patients), pneumonia (5 versus 2 patients) cellulitis (2 versus no patients) and viral infection (2 versus 1 patient). Within the adverse events of special interest, cutaneous events occurred in 37% (344/919) of the daclizumab group and 19% (176/922) of the interferon beta-1a group. Cutaneous events led to treatment discontinuation in 4.7% and 0.8% of patients in the daclizumab and interferon beta-1a groups respectively. Any serious cutaneous event occurred in 1.5% and <1% of patients in respective groups. In the daclizumab group serious cutaneous events included dermatitis (n=3) and angioedema (n=2).[3]

Hepatic laboratory abnormalities generally occurred in similar proportions of patients except for alanine aminotransferase or aspartate aminotransferase greater than 5 times upper limit of normal which occurred in 6.4% and 3.4% of patients in the daclizumab and interferon beta-1a groups respectively. There were no between-group differences noted in the incidences of potentially clinically significant haematologic laboratory abnormalities.[3]

The adverse event profile for daclizumab was similar in the SELECT, SELECTION and SELECTED studies.[6-8]

Summary of clinical effectiveness issues

RRMS is the most common clinical presentation of the disease, with the diagnosis usually made on the basis of clinical and radiographic criteria requiring that a patient experiences at least two neurologic events, consistent with demyelination separated both in time and in location in the CNS. Relapses can last days to weeks, occur intermittently over many years, and symptoms include weakness, sensory loss, visual loss, and imbalance. Physical symptoms subside completely after relapse in early stages of the disease but, over time, the clinical recovery from relapses tends to be incomplete, leading to the accumulation of functional disability and the frequent onset of secondary progressive multiple sclerosis.[4]

A number of DMTs are licensed and have been accepted for use by SMC for the treatment of MS. Their licensed indications vary, with some being more specific than for daclizumab.

The submitting company has requested that SMC considers daclizumab when positioned for use in patients with RRMS. However, during the assessment the company noted that two subpopulations of interest were patients with RES RRMS and patients with RRMS with an inadequate response to DMT.

In DECIDE, the adjusted annualised relapse rate was statistically significantly lower for daclizumab than interferon beta-1a. The proportion of patients with confirmed progression of disability sustained for three months over 144 weeks did not reach statistical significance, though confirmed progression of disability sustained for six months did reach statistical significance. However, due to the closed-testing procedure all subsequent endpoints were not considered statistically significant.[3] The European Medicines Agency (EMA) noted that use of interferon beta-1a in DECIDE was acceptable, although they commented that it was probably the least effective form of interferon beta treatment for RRMS.[4] Supportive data are available from the SELECT study where daclizumab was superior to placebo for annualised relapse rate at 12 months and secondary endpoints demonstrating effects on MRI and disability outcomes.[6]

The DECIDE study included a broad patient population; 41% had received prior treatment with a DMT, around one third had previously received interferon beta (although did not have intolerance to it) and 46% met the definition for highly active RRMS.[1,3,5] The EMA considered the available data from the pivotal studies provided evidence that daclizumab has efficacy across an extensive range of multiple sclerosis patients. Consequently, the EMA licensed daclizumab for use in relapsing forms of multiple sclerosis.[4] The submitting company provided subgroup analyses of DECIDE and SELECT for the two sub populations of interest (RES RRMS and RRMS with an inadequate response to DMT). Daclizumab was superior to interferon beta-1a (DECIDE) for annualised relapse rate in these subpopulations.[1,5,9] The analysis performed in the RRMS with an inadequate response to DMT subpopulation was conducted post hoc. Furthermore, for both of the subpopulations the relevant comparator is unlikely to be interferon beta and therefore will have limited applicability.

Results of an on-going extension study (EXTEND) will provide more data on the effect of daclizumab on disability progression, given that the pivotal randomised studies were of one to three years duration and insufficient to assess long-term treatment.[10] The study is expected to be completed in August 2019.

In order to provide additional comparative efficacy data, the submitting company undertook Bayesian mixed treatment comparisons (MTC) for daclizumab versus a range of DMTs in the overall population. The efficacy endpoints assessed were annualised relapse rate, confirmed disability progression sustained for three months and for six months. Daclizumab data for the MTC came from DECIDE (and also SELECT for annualised relapse rate). MTC or Bucher adjusted indirect comparisons (when data did not permit a MTC) were also conducted for the RES RRMS and RRMS with an inadequate response to DMT subpopulations.

Limitations of these analyses include: heterogeneity between studies in terms of a number of baseline characteristics and outcomes in some common control arms and a wide variation in the years when the studies were conducted. Analyses of safety endpoints were not possible. For the subpopulation analyses there were limited comparators for RES RRMS (fingolimod and natalizumab) and RRMS with an inadequate response to DMT (fingolimod). Clinical experts consulted by SMC reported use of fingolimod, natalizumab or alemtuzumab in these subpopulations. Other limitations of the subpopulation analyses were use of daclizumab data for from the SELECT study only, which comprised small patient numbers and studies of variable length (12 and 24 months) were included for all endpoints. Additional analyses were provided by the submitting company to address some of these limitations, including the addition of alemtuzumab as a comparator in the two subpopulations of interest as well as inclusion of data from the DECIDE study.

The availability of daclizumab will provide another DMT with efficacy in a broad population of patients with RRMS. It may provide a treatment option for use in patients requiring high efficacy disease modifying therapy but who have risk factors or contra-indications to other treatments (with superior efficacy to interferon beta-1a). While no cases of progressive multifocal leukoencephalopathy with daclizumab have been reported, some patients did develop severe lymphopenia (though not sustained, this is a known risk factor).[1,4]

Daclizumab is administered by subcutaneous injection monthly and may be self-administered following appropriate training. This compares to other treatments which are administered intravenously once monthly (natalizumab) or for two courses (eight infusions) (alemtuzumab) or orally (fingolimod,). Clinical experts consulted by SMC noted the monthly administration schedule may have advantages compared with some comparators. While on treatment with daclizumab, monitoring of liver enzymes is required monthly and also for up to four months following its discontinuation.[1,11-13]

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

Summary of comparative health economic evidence

The submitting company presented a cost-utility analysis which evaluated the cost-effectiveness of daclizumab in two patient subgroups. The first subpopulation analysis compared daclizumab against fingolimod and natalizumab in patients with RES RRMS. The second subpopulation analysis compared daclizumab against fingolimod in patients with RRMS whose disease has inadequately responded to a prior DMT.

The economic analysis used a Markov model with a lifetime horizon, which equated to 50 years. In terms of model structure, the model consisted of 21 health states which captured various EDSS scores for both RRMS and secondary progressive multiple sclerosis (SPMS), and a death state.

All patients entered the model with RRMS and RRMS patients could progress (worsen), regress (improve) or remain in the same EDSS health state. Patients may transition from RRMS to SPMS and transitions from RRMS to SPMS required an increase in EDSS score of 1, except in the highest EDSS state. SPMS patients can either progress in the model or remain in the same health state. Patients with SPMS were also assumed to cease treatment.

The sources of the clinical data included the DECIDE[3,4] and SELECT[6] studies as well as various published data which generated baseline population characteristics, baseline annualised relapse rates, baseline transition probabilities and mortality rates. Similar sources were also used for adverse event rates and treatment discontinuation for each comparator. Treatment efficacy for each medicine was taken from the indirect comparison which generated hazard ratios for disease progression (confirmed disability progression sustained for 3 months) and rate ratios for annualised relapse rate which were applied to the baseline data used in the model.

The utility values used were broadly consistent with values used in other SMC submissions for MS and the analysis included a disutility for adverse events.

Medicine acquisition costs were included in the analysis as were administration, monitoring, disease management, relapse, and adverse event costs.

A Patient Access Scheme (PAS) was proposed by the submitting 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 price of the medicine.

The base case results with PAS for daclizumab, expressed as incremental cost effectiveness ratios (ICERs), for the patients with RES RRMS and patients who inadequately responded to prior DMT subgroups are presented in tables 2 and 3 below. A PAS is in place for fingolimod and this was included in the analysis by using an estimate of the relevant PAS price.

Table 2: Results for subgroup of patients with RES RRMS

Comparator	ICER
Natalizumab	£17,409,041**
Fingolimod	Dominant

*quality adjusted life year
**less costly and less effective

Table 3: Results for subgroup of patients inadequately responded to prior DMT

Comparator	ICER
Fingolimod	£51,598*

* less costly and less effective

SMC would wish to present the QALY gain estimates that informed the SMC decision. However, owing to the commercial in confidence concerns regarding the PAS, SMC is unable to publish these results.

Similar results as above were reported versus fingolimod in both subgroups when a range of scenario analyses were explored such as: changing the discontinuation rate to 5% for all treatments, using a time horizon of 20 years and applying treatment waning effects.

For the comparison against natalizumab in the subgroup of patients with RES RRMS, the scenario analyses reported similar results as the base case or daclizumab became dominant (i.e. less

costly and more effective); for example, daclizumab was dominant when changing the discontinuation rate to 5% for all treatments, using a time horizon of 20 year and applying treatment waning effects.

The main weaknesses were:

- The subgroup analyses of patients with RES RRMS and patients with RRMS whose disease has inadequately responded to a prior DMT were limited by lack of comparison against relevant comparators such as alemtuzumab. There were weaknesses with the clinical data used in the model such as the fact that the subgroup analyses were based on small patient numbers, and the patients who have inadequately responded to a prior DMT subgroup represented a post-hoc analysis of the data. The results of the indirect comparisons were also considered uncertain.
- There were limitations with the costs included in the analysis, such as health state and relapse costs being underestimated when compared with other health technology assessments. The company has provided sensitivity analysis which increased the health state costs for EDSS levels above 7 by a factor of 5. These analyses reported similar results as the base case analyses for both primary subgroups.
- The results of the MTC generally suggested that daclizumab was similar to the comparators; however, non-significant differences were included in the base case analysis. The company has provided sensitivity analysis which removed non-significant differences and daclizumab was less costly and less effective than the comparators in the two subgroups.

Despite these uncertainties the economic case has been demonstrated.

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

Summary of patient and public involvement

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

- We received patient group submissions from the MS Society and the MS Trust, both are registered charities.

- The MS Trust has received 1.9% pharmaceutical company funding in the past two years, including from the submitting company. The MS Society has received less than 0.5% pharmaceutical company funding in the past two years, including from the submitting company.

- Multiple sclerosis (MS) is a fluctuating, life-long progressive neurological condition. People with MS may experience issues with mobility, balance, pain, fatigue and visual and cognitive impairment. It is a complex unpredictable condition which has an impact on all aspects of life.

- There is no cure for MS, but it has been proven that disease modifying therapies can have a significant impact on relapse rate and the progression of disability. Self-administered injections are preferable for many people with MS. Daclizumab can be self-injected once a month at home. This has benefits over other self-injected disease modifying drugs which require more frequent injections.

- Some serious side effects have been reported from the clinical trials. Patients will need to be counselled about these risks and adequate monitoring put in place. As with other disease modifying therapies, an individual and their MS team will need to consider the benefits and risks of daclizumab alongside personal treatment goals. People with MS, who are often of working age, need choice in their treatment options to ensure they can live as well as possible and for as long as possible, with MS.

Additional information: guidelines and protocols

The Association of British Neurologists: revised (2015) guidelines for prescribing disease-modifying treatments in multiple sclerosis were published in 2015. These are consensus guidelines for all newly approved or licensed treatments for MS. The guidelines predate the licensing of daclizumab. The guideline groups treatments with moderate efficacy (interferon beta, glatiramer acetate, teriflunomide, dimethyl fumarate, fingolimod) and high efficacy (alemtuzumab, natalizumab). Patients with active disease (at least two relapses in previous two years) should be considered for treatment with DMT and are generally commenced on a moderate efficacy medicine with choice depending on patient and disease factors. Those with more active RRMS (frequent relapse and/or MRI activity whilst untreated or on a moderate efficacy medicine) may be considered for a high efficacy medicine.[2]

The National Institute for Health and Care Excellence (NICE) published clinical guideline 186, Multiple sclerosis in adults: management, in 2014. [14]

Additional information: comparators

Fingolimod, natalizumab and alemtuzumab.

Cost of relevant comparators

Drug	Dose Regimen	Cost per year (£)
daclizumab	**150mg once monthly by SC injection**	**19,164**
alemtuzumab	12mg daily for 5 days by IV infusion (course 1) 12mg daily for 3 days by IV infusion (course 2)	35,225 21,135
fingolimod	500 micrograms once daily, orally	19,100
natalizumab	300mg every 4 weeks by IV infusion	14,690

Doses are for general comparison and do not imply therapeutic equivalence. Costs from eVadisor DM&D on 7 November 2016 and 12 January 2017. Costs do not take any patient access schemes into consideration.
SC=subcutaneous; IV=intravenous

Additional information: budget impact

The submitting company provided budget impact estimates for the two populations considered:

Patients in the RES subgroup
The submitting company estimated there would be 520 patients eligible for treatment with daclizumab in year 1 and 612 patients in year 5, to which confidential estimates of treatment uptake were applied.

Patients in the inadequate response subgroup
The submitting company estimated there would be 1559 patients eligible for treatment with daclizumab in year 1 and 1836 patients in year 5, to which confidential estimates of treatment uptake were applied.

SMC is unable to publish the with PAS budget impact due to commercial in confidence issues. A budget impact template is provided in confidence to NHS health boards to enable them to estimate the predicted budget with the PAS.

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

References

The undernoted references were supplied with the submission.

1. Biogen Idec Ltd. Summary of product characteristics for daclizumab (Zinbryta) 150mg solution for injection in pre-filled pen. 1 July 2016.
2. Scolding N, Barnes D, Cader S et al. Association of British Neurologists: revised (2015) guidelines for prescribing disease-modifying treatments in multiple sclerosis. Pract Neurol. 2015;15(4):273-9.
3. Kappos L, Wiendl H, Selmaj K, Arnold DL, Havrdova E, Boyko A*, et al.* Daclizumab HYP versus interferon beta-1a in relapsing multiple sclerosis. New England Journal of Medicine. 2015;373(15):1418-28.
4. European Medicines Agency. European Public assessment Report for daclizumab (Zinbryta). 2016.
5. **Commercial in Confidence*.
6. Gold R, Giovannoni G, Selmaj K, Havrdova E, Montalban X, Radue E-W*, et al.* Daclizumab high-yield process in relapsing-remitting multiple sclerosis (SELECT): a randomised, double-blind, placebo-controlled trial. Lancet. 2013;381(9884):2167-75.
7. Giovannoni G, Gold R, Selmaj K, Havrdova E, Montalban X, Radue E-W*, et al.* Daclizumab high-yield process in relapsing-remitting multiple sclerosis (SELECTION): a multicentre, randomised, double-blind extension trial. The Lancet Neurology. 2014;13(5):472-81.
8. Gold R, Radue E, Giovannoni G et al. Safety and efficacy of daclizumab in relapsing-remitting multiple sclerosis: 3-year results from the SELECTED open-label extension study. BMC Neurology. 2016;16(17).
9. **Commercial in Confidence*.
10. www.clinicaltrials.gov [NCT01797965].
11. Biogen Idec ltd. Summary of product characteristics for natalizumab (Tysabri) 300mg concentrate for solution for infusion. September 2016.
12. Genzyme Therapeutics. Summary of product characteristics for alemtuzumab (Lemtrada) 12mg concentrate for solution for infusion. June 2016.

13. Novartis. Summary of product characteristics for fingolimod (Gilenya) 0.5mg hard capsules. January 2016.
14. National Institute for Health and Care Excellence. Clinical guideline 186; Multiple sclerosis in adults: management. 2014.

This assessment is based on data submitted by the applicant company up to and including 21 February 2017.

**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_statements/Policy_Statements

Drug 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 drug 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 NHS Scotland 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 NHS Scotland 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.