Scottish Medicines Consortium
Providing advice about the status of all newly licensed medicines
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pemetrexed, 100mg & 500mg, powder for concentrate for solution for infusion (Alimta®) SMC No. (770/12)

Eli Lilly and Company Limited

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

ADVICE: following a full submission assessed under the end of life process

pemetrexed (Alimta®) is accepted for use within NHS Scotland.

Indication under review: monotherapy for the maintenance treatment of locally advanced or metastatic non-small cell lung cancer other than predominantly squamous cell histology in patients whose disease has not progressed immediately following platinum-based chemotherapy.

In patients with locally advanced or metastatic non-squamous non-small cell lung cancer, maintenance treatment with pemetrexed, following completion of first-line platinum-based chemotherapy, was associated with prolonged overall survival and progression-free survival when compared with placebo.

This advice takes account of the views from a Patient and Clinician Engagement (PACE) meeting.

Overleaf is the detailed advice on this product.

Chairman,
Scottish Medicines Consortium

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Indication

Monotherapy for the maintenance treatment of locally advanced or metastatic non-small cell lung cancer other than predominantly squamous cell histology in patients whose disease has not progressed immediately following platinum-based chemotherapy.

Dosing Information

In patients treated for non-small cell lung cancer after prior chemotherapy, the recommended dose is 500mg/m^2 body-surface area administered as an intravenous infusion over 10 minutes on the first day of each 21-day cycle.

To reduce the incidence and severity of skin reactions, a corticosteroid (equivalent to dexamethasone 4mg orally twice daily) should be given the day prior to, on the day of, and the day after pemetrexed administration. To reduce toxicity, patients treated with pemetrexed must also receive vitamin supplementation (folic acid and vitamin B_{12}).

Pemetrexed must only be administered under the supervision of a physician qualified in the use of anti-cancer chemotherapy.

Product availability date

24 October 2011. Pemetrexed monotherapy in this setting meets SMC end of life criteria.

Summary of evidence on comparative efficacy

Pemetrexed is an antifolate antineoplastic agent that exerts its action by disrupting folate-dependent metabolism.[1] SMC has previously issued not recommended advice for pemetrexed monotherapy for the maintenance treatment of non-small cell lung cancer (NSCLC) in patients who have had first line treatment with platinum plus gemcitabine, paclitaxel or docetaxel: "switch" maintenance. The marketing authorisation for pemetrexed was extended in 2011 to allow its use as "continuation" maintenance therapy in patients who have had first-line treatment with cisplatin plus pemetrexed; this indication is also not recommended by SMC due to non-submission. The current submission relates to the maintenance use of pemetrexed in both scenarios: "continuation" and "switch" maintenance.

Two multi-centre, double-blind, randomised phase III studies provide evidence for pemetrexed maintenance: PARAMOUNT[2,3] and JMEN.[4]

The PARAMOUNT study recruited adults with a diagnosis of non-squamous advanced NSCLC (stage IIIB or IV) with an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1. Patients were required to have: at least one measurable lesion as per the Response Evaluation Criteria in Solid Tumours (RECIST 1.0), adequate organ function and no previous systemic chemotherapy for lung cancer. Following a non-randomised induction phase (four cycles of cisplatin-pemetrexed), patients were eligible to proceed to the maintenance phase if they: maintained good performance status (ECOG 0 or 1), had completed four cycles of induction therapy, and had radiographical evidence of stable disease or objective response.[2]

Maintenance therapy was commenced between three and six weeks post day one of the fourth induction cycle. Eligible patients were randomised in a 2:1 ratio to receive pemetrexed 500mg/m^2 plus best supportive care (BSC) (n=359) or placebo plus BSC (n=180), on day one of a three-week cycle. As per the marketing authorisation for pemetrexed, dose adjustment and cycle delay was used to

manage toxicity. All patients received folic acid, vitamin B_{12} and prophylactic dexamethasone. Supportive colony-stimulating factors and erythropoietic agents were permitted if used in accordance with European or American guidelines. Maintenance therapy was continued until disease progression, unacceptable toxicity or individual decision, with follow-up until death or study closure.[2]

The primary outcome was investigator-assessed progression-free survival (PFS) analysed in the intention-to-treat (ITT) population. PFS was the time from randomisation to the first date of objectively determined progressive disease or death from any cause. At the time of the primary data cut-off, median patient follow-up was 5.0 months. Maintenance pemetrexed significantly improved investigator-assessed median PFS compared with placebo: 4.1 months for the pemetrexed group, compared with 2.8 months for the placebo group, HR = 0.62 (95% confidence interval [CI]: 0.49 to 0.79), p<0.0001. Data censoring was required for 49% of pemetrexed-treated patients and for 34% of placebo-treated patients. Independent, blinded, central review conducted on scans from 88% of the patients reported similar results: pemetrexed group PFS of 3.9 months, placebo group PFS of 2.6 months and HR = 0.64 (95% CI: 0.51 to 0.81), p=0.0002.[2]

The study was also designed to compare overall survival after 390 deaths. At the final data cut-off, at a median follow-up of 12.5 months, the proportion of patients who had discontinued treatment was 97% and 99% for pemetrexed and placebo respectively, and there had been 397 deaths: 256 (71%) in the pemetrexed group and 141 (78%) in the placebo group. Median maintenance treatment duration was four cycles in each group; however, 37% of pemetrexed patients received at least six maintenance cycles, compared with 18% of placebo patients. The dose intensity achieved in the pemetrexed group was 94% of planned. Patients treated with pemetrexed had statistically significantly longer overall survival compared with placebo: 13.9 months versus 11.0 months HR of 0.78 (95% CI: 0.64 to 0.96), p=0.0195.[3] The survival rates at one and two years were significantly greater in pemetrexed patients (58% and 32%) compared with placebo (45% and 21%).[3]

The proportion of patients receiving post-discontinuation therapy was 64% (231/359) and 72% (129/180) in the pemetrexed and placebo groups respectively: the most frequently employed options were erlotinib (40% and 43% of pemetrexed and placebo patients) and docetaxel (32% and 43% respectively). Apart from docetaxel, the treatment choices were balanced between the groups.[3]

The treatment effect of maintenance therapy (overall survival and PFS) was consistent across pre-specified sub-group analyses: tumour staging (IIIB or IV), induction response (stable disease or objective response), ECOG performance status (0 or 1), gender, smoking status, age, and histology.[2,3] Health-related quality of life was measured using the EQ-5D questionnaire. No significant treatment differences or treatment-by-time interaction were observed during maintenance therapy.[2]

The JMEN study recruited adults with advanced NSCLC (stage IIIB or IV) and ECOG performance status 0 or 1 who had not progressed following four induction cycles of platinum-doublet chemotherapy (cisplatin or carboplatin in combination with gemcitabine, paclitaxel or docetaxel). Induction doublet therapy with pemetrexed was not permitted. Similarly to the PARAMOUNT study, maintenance therapy was randomised in a 2:1 ratio: pemetrexed 500mg/m^2 plus best supportive care (n=441) or placebo plus best supportive care (n=222), in three-weekly cycles.

The primary outcome was investigator-assessed PFS. Pre-specified sub-group analyses were conducted on patients with non-squamous NSCLC, comprising 73% of the ITT population. In these patients with non-squamous NSCLC, PFS was significantly longer for the pemetrexed group (4.5 months) compared with the placebo group (2.6 months), HR = 0.44 (95% CI: 0.36 to 0.55), p<0.0001. Overall survival was also significantly longer for the pemetrexed group than the placebo group (15.5 months versus 10.3 months; HR=0.70 [95% CI: 0.56 to 0.88], p=0.002). One-year survival rates were 60% and 42% for pemetrexed and placebo-treated patients respectively.

Quality of life was assessed with the Lung Cancer Symptom Scale (LCSS), completed once per cycle during study treatment and within 30 days of discontinuation. Patients treated with pemetrexed had similar improvement in LCSS scores compared with those receiving placebo. Time to worsening (TWS) of patient-reported symptoms from date of randomisation to the first date of worsening for each symptom were measured. Due to a high rate of censoring, median TWS of haemoptysis was not calculated. Time to worsening of pain and haemoptysis was significantly longer for the pemetrexed than the placebo arm. There were no differences in any of the other TWS variables.[5]

Summary of evidence on comparative safety

No comparative safety data are available. Refer to the summary of product characteristics for details.[1]

The European Medicines Agency noted in its assessment that the safety results observed in the PARAMOUNT and JMEN studies were consistent with the established safety profile of pemetrexed.[5,6]

Summary of clinical effectiveness issues

In NHS Scotland, patients with advanced or metastatic NSCLC who are epidermal growth factor receptor (EGFR) mutation negative are eligible for platinum-based chemotherapy provided they are fit enough. Following first-line platinum-based chemotherapy, supportive care is provided, and second-line anti-cancer therapy offered upon disease progression.[7] Although in the UK erlotinib and pemetrexed are licensed for use as maintenance therapy following the completion of first-line platinum-based chemotherapy, neither has been accepted for use by SMC so maintenance therapy is not standard practice in NHS Scotland. Clinical experts consulted by SMC considered that this is an unmet need in this therapeutic area. Pemetrexed meets SMC end of life criteria for this indication.

The PARAMOUNT study provides robust evidence for pemetrexed "continuation" maintenance therapy. Treatment benefits were consistent across pre-specified sub-groups analysed. In the full study population, when compared with placebo, there was a statistically significantly prolonged PFS. Overall survival was extended by 2.9 months.

When used as "switch" maintenance in the JMEN study, pemetrexed was also associated with statistically significantly longer PFS and overall survival compared with placebo. Median overall survival was prolonged by 5.2 months in patients taking pemetrexed compared with placebo. The sub-population of 73% of patients with non-squamous histology has been used to support efficacy in the licensed population.

The PARAMOUNT and JMEN studies compared pemetrexed with placebo and BSC, the most relevant comparator for patients in NHS Scotland. The primary outcome measure in both pivotal studies was PFS, although the studies were also powered to compare overall survival.

The PARAMOUNT study population had predominantly stage IV disease (91%), which may be in greater proportion than seen in practice. They were also generally younger (mean age 61) and fitter (ECOG performance status 0 or 1 in >99% of patients) than patients likely to be treated in NHS Scotland.

Recent guidelines recommend the use of pemetrexed plus cisplatin as the first-line chemotherapy option in patients with non-squamous locally advanced or metastatic NSCLC.[7] Therefore, in the majority, pemetrexed maintenance will be categorised as "continuation" maintenance. The non-

pemetrexed-based induction regimen utilised in the JMEN study is likely to be less relevant to current practice.

SMC clinical experts have identified an unmet need for maintenance therapy in NSCLC and that the current treatment strategy is to watch and wait. They also advised that the introduction of pemetrexed maintenance therapy would have implications for patients and the service to accommodate the additional three-weekly 10-minute intravenous infusion plus the prophylactic oral corticosteroids and vitamins (oral folic acid and B_{12} injection) required for each cycle. Furthermore, patients may require more frequent follow-up to monitor tumour response to maintenance treatment compared with current practice.

Summary of patient and clinician engagement

A patient and clinician engagement (PACE) meeting with patient group representatives and clinical specialists was held to consider the 'added value' of pemetrexed (Alimta®), as an end of life medicine, in the context of treatments currently available in NHS Scotland.

The key points expressed by the group were:

- Lung cancer is highly unpleasant with symptoms including anorexia, weight loss, debilitating respiratory symptoms, haemoptysis, pain and depression.

- No curative treatment exists at this stage of lung cancer so giving patients the choice of receiving maintenance treatment or a 'watch and wait' approach allows patients to take a more active role in their treatment. The benefit of empowering patients with this choice should not be underestimated.

- Maintenance therapy can be associated with less troubling disease symptoms, improved survival and increased capacity for daily activities, and it can act as a bridge to second line therapy in some patients.

- Carers for those with lung cancer struggle with the rapid decline of their loved ones, and maintenance therapy can ease this pressure both physically and psychologically, allowing patients and their families to have a normal life for longer, undertaking physical activities, going on holiday and looking after grandchildren.

- The PACE group stressed that this treatment gives hope where currently there is none and a survival benefit of greater than 3 months is considered significant by clinicians and patients and their families.

Summary of comparative health economic evidence

The economic analysis consisted of a comparison of pemetrexed maintenance therapy in non-squamous NSCLC patients who had received pemetrexed/cisplatin induction therapy and had not progressed with a strategy of watch and wait observation (BSC). A 3 state Markov model (progression free survival, post progression and death) was used with a lifetime time horizon (16 years in the base case). This analysis represents the most relevant one for Scottish clinical practice. However, in addition, an economic analysis using a separate trial based economic model and a lifetime horizon (12 years in the base case) was performed for the use of pemetrexed maintenance vs. watch and wait in patients who had received non-pemetrexed doublet platinum chemotherapy as

induction therapy. Although erlotinib is licensed for maintenance therapy in patients with a stable response to induction therapy, it was not recommended by SMC and the watch and wait/BSC comparator used was considered appropriate, and supported by SMC clinical expert feedback.

The clinical data used were from the PARAMOUNT study for the pemetrexed maintenance post pemetrexed/cisplatin induction therapy analysis, and the JMEN study for the post doublet platinum chemotherapy induction therapy analysis. Extrapolation of overall survival beyond the PARAMOUNT trial was based on fitting a gamma distribution to the observed data at a cut-off of 25% survival probability in each treatment arm. No extrapolation of PFS and treatment discontinuation was deemed necessary as these data were fully mature. A key assumption was that the hazard ratio for pemetrexed survival benefit at the end of the trial was assumed to be maintained during the post progression phase.

For the JMEN analysis, extrapolation was performed from the end of the observed data using an exponential function in the base case. Utility estimates for pre- and post-progression health states stratified according to time prior to death were based on a regression analysis of EQ 5D data obtained from the PARAMOUNT study. A disutility of -0.0248 associated with treatment effect to capture the impact of pemetrexed adverse events was also obtained from the regression analysis.

Costs included the drug acquisition costs and additional resource use associated with administration and monitoring of pemetrexed maintenance treatment. A mean duration of approximately 8 cycles of treatment in both analyses was derived from the trials, with administration assumed to be on a day case basis, and a body surface area for drug costs assumed to be $1.77m^2$ derived from a published UK study in cancer patients. Monitoring requirements were assumed to be 1 hospital visit and a CT scan every 12 weeks based on clinical expert opinion obtained for the NICE STA of pemetrexed maintenance. The costs of second line chemotherapy with docetaxel and erlotinib were included, although no difference was assumed in use between the pemetrexed and watch and wait/BSC arms in the PARAMOUNT analysis. A difference in second line chemotherapy use was assumed for the JMEN analysis, with a greater proportion of watch and wait patients receiving post-progression treatment with docetaxel, erlotinib and (in the watch and wait arm only) second line pemetrexed. Adverse event resource use was based on UK clinical expert opinion, and BSC and terminal care costs were derived from published sources.

The incremental cost-effectiveness ratio (ICER) for pemetrexed maintenance following pemetrexed/cisplatin induction therapy was estimated to be £57,835 per quality-adjusted life-year (QALY) gained, based on incremental cost of £14,342, incremental life years gained of 4.1 months and incremental QALYs of 0.248. Scenario analysis demonstrated that the ICER increased to £64.4k if the survival cut-off applied for extrapolation of the data was changed to a 30% survival probability in each treatment arm, £68.2k/QALY if parametric functions were fitted instead of observed data to estimate PFS, treatment discontinuation and OS, and £67-68k/QALY when no treatment benefit post-progression or a shorter 5 year time horizon was assumed.

The ICER for pemetrexed maintenance following non-pemetrexed doublet platinum induction chemotherapy was estimated to be £37,390/QALY, based on incremental cost of £12,887, incremental life years gained of 6.1 months and incremental QALYs of 0.345. Scenario analysis demonstrated some sensitivity to the use of an alternative Weibull parametric function for OS, with the ICER rising to £45.6k/QALY, to applying a 25% survival probability cut-off for extrapolation with an ICER of £42.1k/QALY, and assuming a 5 year time horizon (£43.3k/QALY). Assuming no difference in use of second line chemotherapy between treatment arms, which may be more plausible than the base case assumption, increased the ICER to ~£40k/QALY.

In both patient populations, the results were sensitive to using alternative published NSCLC health state utility values previously used in HTA submissions with higher ICERs of £68k/QALY and

£45k/QALY for the PARAMOUNT and JMEN analyses respectively. However, the EQ 5D based utility values that were used can be considered relatively more robust and in line with SMC methods, and appear to be plausible.

The main issue is that the ICERs estimated are above those normally considered to represent acceptable cost-effectiveness. However, the company requested that pemetrexed be considered under SMC End of Life criteria. Related to this, key issues in the economic analyses are:

- Uncertainty over the extrapolated survival benefit associated with the PARAMOUNT and JMEN analyses, which demonstrated a potentially higher ICER of up to £68k/QALY and £45k/QALY respectively, depending on extrapolation methods used. As the PARAMOUNT observed OS data is mature, an analysis for this patient population using these data with no extrapolation was requested in order to provide an upper ICER estimate; this was calculated to be £108k/QALY. However, this analysis is conservative as it does not allow for any extrapolation beyond the trial period. Further sensitivity analysis varying the OS benefit estimated according to 95% CI's for the estimated survival outcomes in the PARAMOUNT analysis demonstrated an ICER range of £52 - £67k/QALY and, for the JMEN analysis, varying incremental survival by ±20% resulted in an ICER range of £31.5k to £46.2k/QALY.
- It is difficult to assess the relative ICERs for the post non-pemetrexed induction therapy and the post pemetrexed/cisplatin induction analysis due to the use of different economic models for each patient population, and no validation performed. The direction of any bias is unknown. However, this is not a major issue in that the PARAMOUNT analysis is the relevant one to focus on for Scottish clinical practice.

SMC considered the likely range of cost-effectiveness ratios for pemetrexed in the maintenance setting and the remaining uncertainties in the economic case. The committee considered the benefits in the context of the SMC decision modifiers and agreed that the following criteria were satisfied: a substantial improvement in life expectancy in the patient population targeted in the submission; and the absence of other treatments of proven benefit. After considering all the available evidence, the output from the PACE process, and after application of the appropriate modifiers, the Committee accepted pemetrexed maintenance therapy for use in NHS Scotland.

Summary of patient and public involvement

The following information reflects the views of the specified patient group.

- A submission was received from the Roy Castle Lung Cancer Foundation, which is a registered charity.

- The Roy Castle Lung Cancer Foundation has received funding from pharmaceutical companies in the past two years, including from the submitting company.

- Lung cancer is a life limiting disease, often diagnosed in late stages when palliative treatment is the only option. Life expectancy may only be months. Patients are frequently short of breath therefore limiting mobility, often with recurrent chest infections and pleural effusions which require to be drained. Currently available treatments bring limited relief.

- Advantages of the new medicine compared to existing medicines include: reduction in disease progression, improved quality and length of life, and good symptom management with reduced side-effects.

- For the overwhelming majority of NSCLC patients, cure is not a treatment option. Patients most frequently look for effective symptom management and a few more months of life to spend with their families. This medicine can contribute to these goals. Where there is no cure, this drug can offer immeasurable benefit to patients and their families.

Additional information: guidelines and protocols

The Scottish Intercollegiate Guidelines Network (SIGN) updated guidance on the management of lung cancer in February 2014.[7] In patients with good performance status with advanced disease and who have predominantly non-squamous NSCLC and are epidermal growth-factor (EGFR) mutation negative, systemic anticancer therapy consisting of the combination of pemetrexed and cisplatin should be offered. Platinum-doublet therapy should be given in four cycles and should not exceed six cycles. The guideline noted the clinical evidence for the use of erlotinib and pemetrexed as maintenance therapy in patients with locally advanced or metastatic NSCLC but acknowledged that neither agent is accepted for use within NHS Scotland by the SMC.

The National Institute for Health and Care Excellence issued guidance on the diagnosis and treatment of lung cancer in April 2011.[8] With regard to patients with stage III or IV NSCLC, those with good performance status (WHO 0, 1 or Karnofsky score of 80 to 100) should be offered chemotherapy to improve survival, disease control and quality of life. The guideline does not cover maintenance therapy post platinum-based chemotherapy treatment.

The European Society for Medical Oncology (ESMO) updated its guideline on the diagnosis and treatment of NSCLC in 2012.[9] Two types of maintenance treatment strategies were described, "continuation maintenance" and "switch maintenance", referring to "the use of an agent included in the first-line treatment or the introduction of a new agent following the completion of the platinum-based chemotherapy."

- Treatment decisions should take into account: histology, performance status, patient preference, toxicity from first-line chemotherapy, and response to platinum-based chemotherapy.
- In patients with a non-squamous NSCLC, who had four cycles of platinum-based chemotherapy, switch-maintenance with pemetrexed was associated with improvements in PFS and OS when compared with placebo.
- Continuation maintenance with pemetrexed is recommended in patients with non-squamous NSCLC following completion of first-line pemetrexed plus cisplatin.
- In patients with all histologies of NSCLC, switch maintenance with erlotinib was associated with improvements in PFS and OS when compared with placebo, with greatest treatment effect in the sub-group of patients with stable disease (rather than evidence of objective response).
- Patients who have EGFR mutation positive NSCLC should receive a EGFR tyrosine kinase inhibitor (e.g. erlotinib) as their maintenance treatment if not received as first-line therapy.

A consensus meeting of ESMO held in May 2013 considered the use of maintenance therapy in advanced NSCLC.[10] Three recommendations were made:

- Switch maintenance with pemetrexed may be offered to patients with EGFR wild-type advance non-squamous NSCLC who have not been treated with pemetrexed first-line. *(Grade of recommendation = B, strong or moderate evidence for efficacy but with a limited clinical benefit, generally recommended)*
- Switch maintenance with erlotinib is a treatment option for patients with advanced NSCLC who have stable disease after first-line platinum-based therapy. *(Grade of recommendation = B)*
- Continuation maintenance treatment with pemetrexed may be offered to patients with advanced NSCLC not progressing after first-line pemetrexed-cisplatin therapy. *(Grade of*

recommendation = A, strong evidence for efficacy with a substantial clinical benefit, strongly recommended)

Additional information: comparators

Erlotinib is licensed for use as maintenance treatment in patients with locally advanced or metastatic NSCLC with stable disease after 4 cycles of standard platinum-based first-line chemotherapy. SMC has not recommended it for use in NHS Scotland.

Cost of relevant comparators

Drug	Dose Regimen	Cost per 21-day cycle (£)	Cost per course (£)
Pemetrexed	**500mg/m^2 intravenous infusion over 10 minutes on the first day of each 21-day cycle**	**1,440**	**5,760**
Erlotinib	150mg orally daily	1,142	4,568

Doses are for general comparison and do not imply therapeutic equivalence. Costs from MIMS online on 28 July 2014. Pemetrexed cost based on body surface area of 1.8m^2 and a median of four 21-day treatment cycles in the PARAMOUNT study. Erlotinib costs calculated for the same duration for comparison purposes. Costs do not include prophylactic supplements (e.g. vitamin B_{12} injection).

Additional information: budget impact

For the patient population receiving induction therapy with pemetrexed/cisplatin, the submitting company estimated there to be 118 patients in year 1 rising to 122 patients in year 5 eligible for treatment with pemetrexed maintenance therapy, with an estimated uptake rate of 20% in year 1 (24 patients) and 40% in year 5 (49 patients). The gross medicines budget impact was estimated to be £320k in year 1 and £666k in year 5. The company assumed some displacement of the use of second line chemotherapy resulting in a net medicines budget impact of £309k in year 1 and £643k in year 5.

For the patient population receiving induction therapy with doublet platinum chemotherapy, the submitting company estimated there to be 55 patients in year 1 rising to 58 patients in year 5 eligible for treatment with pemetrexed maintenance therapy with an estimated uptake rate of 20% in year 1 (11 patients) and 40% in year 5 (23 patients). The gross medicines budget impact was estimated to be £153k in year 1 and £318k in year 5. The company assumed some displacement of the use of second line chemotherapy, resulting in a net medicines budget impact of £143k in year 1 and £297k in year 5.

The assumption of lower use of second line chemotherapy following pemetrexed maintenance is uncertain and, therefore, the gross budget impact estimates may be more reliable.

References

The undernoted references were supplied with the submission.

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This assessment is based on data submitted by the applicant company up to and including 15 September 2014.

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.

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.