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 Angela Timoney FRPharmS
NHS SCOTLAND

# Resubmission:

## lenalidomide, 5mg, 10mg, 15mg and 25mg hard capsules (Revlimid®)

SMC No. (441/08)

## Celgene Limited

07 March 2014

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 second re-submission:

**lenalidomide (Revlimid®)** is accepted for restricted use within NHS Scotland.

**Indication under review:** in combination with dexamethasone, for the treatment of multiple myeloma in adult patients who have received at least one prior therapy. (This resubmission relates to patients who have received only one prior therapy).

**SMC restriction:** to use at first relapse in patients who have received prior therapy with bortezomib in whom thalidomide has not been tolerated or is contraindicated.

Lenalidomide plus dexamethasone significantly increased the time to progression compared with dexamethasone alone in multiple myeloma patients who had been treated with at least one prior therapy.

SMC has previously accepted lenalidomide for use in patients who have received at least two prior lines of therapy i.e. at second relapse. This advice now extends its use to patients at first relapse who received bortezomib as their one prior therapy.

Overleaf is the detailed advice on this product.

**Chairman,**
**Scottish Medicines Consortium**

## Indication

In combination with dexamethasone, for the treatment of multiple myeloma in adult patients who have received at least one prior therapy.

## Dosing Information

The recommended starting dose of lenalidomide is 25mg orally once daily on Days 1 to 21 of repeated 28-day cycles. The recommended dose of dexamethasone is 40mg orally once daily on Days 1 to 4, 9 to 12 and 17 to 20 of each 28-day cycle for the first four cycles of therapy and then 40mg once daily on Days 1 to 4 every 28 days. Dosing is continued or modified based upon clinical and laboratory findings. Prescribing physicians should carefully evaluate which dose of dexamethasone to use, taking into account the condition and disease status of the patient.

Lenalidomide treatment must not be started if the Absolute Neutrophil Counts (ANC) $<1.0x10^9$/L, and/or platelet counts $<75x10^9$/L or, dependent on bone marrow infiltration by plasma cells, platelet counts $<30x10^9$/L.

Treatment should be supervised by a physician experienced in the use of anti-cancer therapies.

## Date of licensing

June 2007.

## Product availability date

June 2007. Lenalidomide was designated an orphan medicine for multiple myeloma in 2003.

## Summary of evidence on comparative efficacy

Lenalidomide is an analogue of thalidomide and has a number of mechanisms of action including anti-neoplastic, anti-angiogenic, pro-erythropoietic and immunomodulatory properties.[1]

SMC has previously restricted lenalidomide, in combination with dexamethasone, for use in patients with multiple myeloma who have received at least two prior lines of therapy. For this resubmission, the submitting company has requested that SMC considers lenalidomide in combination with dexamethasone when positioned for use in adults with multiple myeloma, at first relapse who have received prior therapy with bortezomib.

Two similarly designed multicentre, randomised, double-blind, placebo-controlled phase III studies (MM-09 and MM-010) recruited adults with relapsed or refractory Durie-Salmon stage II or III multiple myeloma (n=704).[2,3] Patients were required to have an Eastern Cooperative Oncology Group (ECOG) performance status 0 to 2 and measurable disease (serum M protein ≥0.5g/dL, or urinary Bence Jones protein ≥0.2g/day). Patients judged to be resistant to dexamethasone were excluded.

Patients received either lenalidomide 25mg daily or placebo on days 1 to 21 of each 28-day cycle in a 1:1 ratio, stratified by: serum $\beta_2$-microglobulin (<2.5mg/L and ≥2.5mg/L), previous stem-cell transplantation (0 versus ≥one), and the number of previous therapies (one versus ≥2). All received oral dexamethasone 40mg on days 1 to 4, 9 to 12, and 17 to 20 of each 28-day cycle for the first four cycles, then on days one to four of subsequent cycles. Treatment continued until disease progression or the occurrence of unacceptable toxic effects. Dose adjustment was permitted to manage adverse events. Allowed concomitant treatments included: granulocyte colony-stimulating factor (G-CSF), erythropoietin, platelet and/or red-cell transfusion, and bisphosphonates.

The primary endpoint in both studies was time-to-progression (TTP) analysed in the intention to treat population. This was defined as the time from randomisation to: first documented progressive disease, based on myeloma response criteria, or discontinuation from the treatment phase due to progression, or death due to progressive disease. Planned interim analyses were conducted when there was at least 50% of the progression events (111/222) required to power the studies. The independent data monitoring committees recommended that the studies be unblinded. Patients in the placebo-dexamethasone groups were given the option of receiving open-label lenalidomide plus dexamethasone. Results of the subsequent analyses of the primary outcome conducted on study unblinding are presented in Table 1.

| | Study 1 (MM-09) | | Study 2 (MM-010) | |
|---|---|---|---|---|
| Data cut-off date | 28 June 2005 | | 03 August 2005 | |
| | Lenalidomide | Placebo | Lenalidomide | Placebo |
| No. of patients | 177 | 176 | 176 | 175 |
| Progressed, n (%) | 92 (52%) | 132 (75%) | 82 (47%) | 142 (81%) |
| Censored, n (%) | 85 (48%) | 44 (25%) | 94 (53%) | 33 (19%) |
| Median TTP, weeks | 48.1 | 20.1 | 48.7 | 20.1 |
| Hazard ratio (95% CI) | 2.82 (2.15 to 3.70) | | 2.85 (2.16 to 3.76) | |
| p-value | <0.001 | | <0.001 | |

Table 1: Primary endpoint for both studies at study unblinding.[2-4] CI = confidence interval

Secondary endpoints included overall survival (OS) and objective response rates.

On study unblinding, there was a significant survival advantage for lenalidomide-treated patients in MM-09. At this point there had been 37 deaths (21%) in the lenalidomide group and 62 deaths (35%) in the placebo group. In MM-010, no significant advantage had been observed at study unblinding, 47 and 59 deaths, respectively.[4] In a later pooled analysis of the two studies, conducted using data up to July 2008, after a median follow-up of 48 months, 56% (199/353) of lenalidomide patients and 62% (219/351) of placebo patients had died. Median OS was 38.0 and 31.6 months, respectively (p=0.045).[5]

On study unblinding, overall response rates (ORR) were significantly higher in the lenalidomide groups compared with placebo. In MM-09 they were 61% and 20%, and in MM-010 they were 60% and 24%, respectively.

A sub-set analysis of the pooled patient populations randomly allocated to lenalidomide explored the efficacy of lenalidomide in patients with one (n=133) versus at least two prior anti-myeloma therapies (n=220). TTP was significantly longer in patients who had received one prior therapy compared to those who had received at least two prior therapies, 17.1 versus 10.6 months (hazard ratio 0.68 [95% CI: 0.48 to 0.97]). There was no significant difference between

the two subgroups for ORR, but the one prior anti-myeloma therapy sub-group had significantly longer OS compared to the other subgroup, when estimated at study unblinding (median not reached versus 30.8 months) and after extended follow-up in 2008 (42.0 versus 35.8 months).[6]

Observational data to support the use of lenalidomide or bortezomib in patients previously treated with bortezomib has been published as part of the follow-up from the VISTA study. VISTA recruited patients with multiple myeloma who were randomised to first-line treatment with bortezomib plus melphalan and prednisolone, or melphalan and prednisolone. In following-up the response to subsequent therapy in those allocated to first-line bortezomib, data were available for 22 patients who received lenalidomide-based regimen and for 22 patients who received bortezomib-based re-treatment. A complete or partial response was observed in 73% (16/22) lenalidomide patients and in 41% (9/22) of bortezomib re-treated patients.[7]

## Summary of evidence on comparative safety

Pooled safety data for the two studies found serious adverse events were experienced by 57% (202/353) of lenalidomide patients and 47% (163/350) placebo patients. Adverse events leading to discontinuation of study drug occurred in 25% of lenalidomide patients and 18% of placebo patients.

Grade 3 or 4 haematological adverse events were reported in a greater proportion of lenalidomide patients than placebo patients: neutropenia (35% versus 3.4%), anaemia (11% versus 6.0%), and thrombocytopenia (13% versus 6.3%).

Common adverse events reported in more lenalidomide patients than placebo patients included: constipation (42% versus 22%), pneumonia (14% versus 8.6%), weight loss (19% versus 15%), tremor (21% versus 7.4%), and rash (22% versus 10%).

Cardiac adverse events were reported in 18% lenalidomide patients and in 11% placebo patients. The majority of lenalidomide patients experiencing cardiac events had underlying predisposing conditions or were receiving cardiac medication.

There was an increased risk of developing thrombo-embolic adverse events in lenalidomide-treated patients compared with placebo: deep vein thrombosis (9.1% versus 4.3%) and pulmonary embolism (4.0% versus 0.9%).[4]

The European Medicines Agency considered data from studies of lenalidomide in relapsing or refractory multiple myeloma and post-marketing surveillance. There was an increased risk of secondary primary malignancies in patients treated with lenalidomide compared with placebo (3.98 versus 1.38 per 100 patient-years). The main contributor to the lenalidomide risk was non-invasive skin cancers. “The incidence rates for invasive secondary primary malignancies (excluding non-melanoma skin cancers) were consistent with the background rates of the general patient population.”[8]

Since lenalidomide is structurally-related to thalidomide, part of the risk management associated with the marketing authorisation is a pregnancy-prevention programme which is detailed in the summary of product characteristics.[1]

## Summary of clinical effectiveness issues

Lenalidomide, in combination with dexamethasone, is currently used at second-relapse in the multiple myeloma treatment pathway. For this resubmission, the submitting company has requested that SMC considers lenalidomide in combination with dexamethasone when positioned for use in adults with multiple myeloma, at first relapse who have received prior therapy with bortezomib i.e. a shift to use at an earlier stage in the course of the disease. The National Institute for Health and Care Excellence (NICE) guidance for the first-line treatment of multiple myeloma only recommends bortezomib-based therapy in situations where thalidomide has not been tolerated or is contraindicated.[9] The British Committee for Standards in Haematology (BCSH) in their guidance for the diagnosis and management of multiple myeloma consider an individual patient tailored approach to choosing treatment for relapse but note that thalidomide, bortezomib and lenalidomide are the three most commonly used agents at this stage in the disease.[10] The company suggested that for the proposed positioning the relevant comparator would be re-treatment with bortezomib. Clinical experts consulted by SMC advised that bortezomib may be appropriate for this small patient group, but this would depend upon the duration of remission following initial therapy.

The primary outcome in both studies was TTP, a validated, surrogate marker for the disease. Lenalidomide plus dexamethasone treatment was associated with a significantly longer TTP in both studies, when compared with placebo plus dexamethasone.[2,3] Sub-group analysis suggests that those treated with lenalidomide following one anti-myeloma therapy had prolonged TTP compared with those who had at least two prior anti-myeloma therapies.[6] Despite confounding due to patient crossover upon study unblinding (170/351 placebo patients) lenalidomide plus dexamethasone was associated with a significant survival advantage compared with placebo plus dexamethasone treatment.

The BCSH report the median age at presentation of patients with multiple myeloma is 70 years.[3] Patients recruited to the studies were slightly younger (median ages 62 to 64 years). The majority of patients in the studies had a performance status of 0 or 1, and may be fitter than the population likely to be treated in Scotland.

While baseline characteristics of the pooled Phase III studies' populations indicate that only two patients randomised to lenalidomide fall into the patient population proposed by the company,[6] sub-group analysis of TTP by prior treatment (available as a conference poster only) suggests that the type of therapy had no impact on the efficacy of lenalidomide plus dexamethasone.[11] Observational efficacy data have also been presented to support use of lenalidomide and dexamethasone in patients at first relapse who had prior treatment with bortezomib.[7]

As an oral chemotherapeutic agent, lenalidomide offers a more convenient treatment option for patients and the service, avoiding the need for regular injections to administer bortezomib.

## Summary of comparative health economic evidence

A cost-utility analysis of lenalidomide plus dexamethasone compared to re-treatment with bortezomib in multiple myeloma patients treated first line with bortezomib who were unable to tolerate or contraindicated to thalidomide was submitted. The comparator may be reasonable, although the precise circumstances by which re-treatment is considered in practice is uncertain.

The Markov model structure consisted of pre-progression on and off treatment and disease progression health states, with a model cycle length of 28 days, and due to the treatment sequences considered, primarily reflects an assessment of the cost-effectiveness of a transition to second line use from current SMC accepted third line use of lenalidomide. The clinical data for time to treatment failure (TTF), progression-free survival (PFS) and overall survival (OS) for lenalidomide plus dexamethasone was from the MM-010 study, and in the base case for bortezomib re-treatment derived from a published retrospective study in 42 patients with multiple myeloma.

Due to a lack of data on patients receiving 2nd line lenalidomide plus dexamethasone after prior bortezomib in MM-010, the company fitted parametric functions for TTF, PFS and OS based on regression analysis using data for all patients in the lenalidomide plus dexamethasone arm of this trial. Using the regression analysis the MM-010 data was adjusted so the patient characteristics better matched those of the comparator study. After this adjustment, hazard ratios were estimated using predicted median PFS and OS outcomes in the bortezomib retreatment retrospective study compared to the predicted median PFS and OS outcomes for lenalidomide + dexamethasone based on the fitted parametric functions. The HR for PFS and OS for bortezomib re-treatment vs. lenalidomide + dexamethasone was estimated to be 0.90 (95%CI: 0.60 to 1.75) and 1.70 (95%CI: 1.52 to 2.28) respectively. Data on TTF was not available for the comparator, but was assumed to have the same HR as for PFS due to the similar pattern for predicted TTF and PFS for lenalidomide + dexamethasone.

Utility values for health states were taken from a published study in multiple myeloma based on the EQ- 5D, with pre-progression utility for multiple myeloma duration of <2 years, >2 years and progressive disease estimated to be 0.81, 0.77 and 0.64 respectively. Disutilities for selected grade 3 and 4 AEs derived from published studies were included.

Costs included drug acquisition costs and administration costs, including an estimate that 50% of patients would require NHS transportation for hospital appointments for drug administration. A complex patient access scheme (PAS) is in place in NHS Scotland for bortezomib whereby the NHS receives a rebate for patients who are deemed non-responders to treatment. The company used the bortezomib list price in their submission base case, however the estimated PAS adjusted cost for bortezomib represents the appropriate base case value. The company has estimated this to be equivalent to a 15% reduction in the cost of bortezomib based on the expected rebate cited in a NICE summary report on the bortezomib response scheme. Other costs relating to adverse events including use of G-CSF in lenalidomide + dexamethasone patients, patient monitoring and terminal care were estimated.

The model included the use and costs of third and fourth line treatments (including administration and transport at third line). Third line treatment after lenalidomide + dexamethasone consisted of a mix of treatments observed in a real world dataset covering multiple myeloma patients in England (the Haematological Malignancy Research Network dataset), whereas in the base case bortezomib retreatment patients were all assumed to receive lenalidomide + dexamethasone in line with the existing SMC recommendation for its third line use. The estimated third line treatment cost per model cycle was £3,800 for the comparator compared to £207 for the lenalidomide + dexamethasone arm. The third line use of lenalidomide + dexamethasone was assumed to have the same TTF and OS hazards as estimated for second line use.

The results show an incremental cost-effectiveness ratio (ICER) of £2,373 per quality-adjusted life-year (QALY) gained based on an incremental cost of £1,343 and incremental QALYs of 0.57 (0.85 life years). However, the cost reduction for bortezomib when the complex PAS is included may be underestimated and, based on information on responder rates reported in the 2009 SMC guidance for bortezomib, a cost reduction of 36% less than the list price can be estimated. As this estimate is based on information in SMC guidance this represents a preferred base case, hence the company was requested to apply this cost reduction which resulted in an ICER of £23,824/QALY gained with an incremental cost of £13,488.

In sensitivity and scenario analysis the results were highly sensitive to variation in the estimates and HRs for PFS and OS. A scenario in which an alternative comparator study was used for source of bortezomib PFS and OS data produced estimated HRs of 1.76 and 1.42 respectively, and resulted in ICERs of £47.4k/QALY (15% cost reduction for bortezomib) or £66.3k/QALY gained (36% cost reduction for bortezomib). A limitation of this study was only 19% of patients received bortezomib re-treatment. A further scenario assuming no difference in PFS (as the difference was non-significant) but applying a third line treatment mix post bortezomib retreatment based on an English registry of multiple myeloma patients which consisted of 44% use of lenalidomide – increased the ICER to £37.2k/QALY (15% bortezomib cost reduction) or £53.8k/QALY (36% bortezomib cost reduction). However, the company also reduced the cost of third line use of lenalidomide based on a scheme that is available in England but not approved in Scotland, on the grounds that the company have made it available to hospitals in Scotland. Removing this increases the cost of the comparator and improves the cost-effectiveness of lenalidomide.

Overall, in addition to the potential for high ICERs the key issues with the economic analysis include:

- Lack of clinical data for patients in the proposed positioning, after prior bortezomib and unable to tolerate thalidomide, for use in the economic analysis, and no use of MM-09 trial data with uncertain implications for the cost-effectiveness results. The submitting company subsequently provided this analysis, which reduced the ICER to £14,195 (36% bortezomib cost reduction) or dominant (cheaper and more effective when a 15% bortezomib cost reduction was used). It should be noted that no sensitivity analysis was given to show potential uncertainty with the results based on the MM-09 trial data.
- A lack of a formal indirect comparison which means that the estimated hazard ratios for TTF, PFS and OS are uncertain, and consequently the ICERs estimated are highly uncertain. Transparency over the calculation and application of the hazard ratios is currently lacking. The evidence supporting a difference in estimated PFS or OS between lenalidomide + dexamethasone and bortezomib re-treatment is limited.
- Uncertainty over the use of lenalidomide + dexamethasone third line after bortezomib retreatment, with the ICERs sensitive to scenarios in which a treatment mix is assumed with less third line use of lenalidomide + dexamethasone. SMC expert clinical feedback has indicated that treatment practice in Scotland is likely to be a higher use than the 44% from the English Registry, but is less than the 100% assumed by the company.
- There are concerns over whether bortezomib re-treatment is the only appropriate comparator second line.

SMC considered the likely range of cost-effectiveness ratios for lenalidomide in this setting and the remaining uncertainties in the economic case. The committee considered the benefits of lenolidomide in the context of the SMC decision modifiers and agreed that the criterion for a substantial improvement in quality of life in the patient population targeted in the submission

was satisfied. Although there were limitations in the economic analysis, the committee agreed that the relatively high cost per QALY was acceptable given the expected benefits of the treatment and in the context of the decision modifiers and the orphan status of the medicine.

## Summary of patient and public involvement

The following information reflects the views of the specified Patient Information Group.

- A Submission was received from Myeloma UK, which is a UK registered charity.
- Myeloma UK has received funding from several pharmaceutical companies in the past two years.
- A diagnosis of myeloma can be devastating news for patients and their families. Symptoms and complications of myeloma include bone destruction, bone pain, fatigue, kidney impairment and a severely depleted immune system. Myeloma has a significant impact on the day to day lives of patients and their families.
- As myeloma is a complex type of cancer, it is important for patients and clinicians to have access to a range of treatments, to allow flexibility and optimal treatment.
- Lenalidomide in combination with dexamethasone is an oral treatment which can be taken at home and therefore reduces the burden on patients and families and avoids trips to hospital for other intravenous therapies that may be necessary with other treatments.

## Additional information: guidelines and protocols

The BCSH updated their guidelines for the diagnosis and management of multiple myeloma in 2013.[10] Treatment aims for patients with relapsed myeloma are: achievement of disease control, amelioration of symptoms, prolong survival and improve quality of life. Choice of treatment should be tailored to the individual patient taking into account: timing of relapse (short remission duration is a strong indication to use an alternative regimen), efficacy and toxicity of prior therapy, age, bone marrow function, co-morbidities and patient preference. Thalidomide, bortezomib and lenalidomide should be given with dexamethasone +/- chemotherapy, unless contraindicated, to increase the response rate.

The European Society for Medical Oncology (ESMO) developed clinical practice guidelines for multiple myeloma in 2010.[12] In the treatment of relapsed or refractory myeloma, a second remission can be induced with the use of regimen used in the initial treatment of the disease. Novel therapies have been noted to dramatically improve OS:

- Thalidomide +/- dexamethasone +/- chemotherapy
- Bortezomib +/- dexamethasone +/- chemotherapy
- Lenalidomide plus dexamethasone

## Additional information: comparators

Novel therapies used in the management of relapsed or refractory multiple myeloma include: bortezomib- and thalidomide-based regimen.

## Cost of relevant comparators

| Drug | Dose Regimen | Cost per cycle (£) |
|---|---|---|
| Lenalidomide plus dexamethasone | 28-day cycle<br>Lenalidomide: 25mg orally on days 1 to 21<br>Dexamethasone<br>1st four cycles: 40mg orally on days 1 to 4, 9 to 12, and 17 to 20<br>Subsequent cycles: 40mg orally on days 1 to 4 | **1st four cycles: 4,402**<br>**Subsequent cycles: 4,379** |
| Bortezomib | 1.3mg/$m^2$ subcutaneously or intravenously on days 1, 4, 8 and 11 of a 21-day cycle | 3,050 |
| Thalidomide | 200mg orally daily for six weeks | 1,791 |

There are various permutations of bortezomib and thalidomide-based regimen, costs for monotherapy presented only. Doses are for general comparison and do not imply therapeutic equivalence. Cost of bortezomib based on surface area of 1.8$m^2$. Thalidomide use for this indication is unlicensed. Costs from www.mims.co.uk on 05 January 2014.

## Additional information: budget impact

The submitting company estimated the population eligible for treatment to be 117 in year 1 and 210 in year 5 with an estimated uptake rate of 55% in year 1 and 72% in year 5, with 58% of patients estimated to discontinue treatment each year (hence, estimated 27 patients treated in year 1, and 63 patients in year 5).

The gross impact on the medicines budget was estimated to be £939k in year 1 and £2.2m in year 5. As bortezomib re-treatment was assumed to be displaced the net medicines budget impact is expected to be a cost of £487k in year 1 and £819k in year 5 (based on applying a 36% cost reduction for bortezomib).

References

The undernoted references were supplied with the submission. Those shaded in grey are additional to those supplied with the submission.


1) Celgene Ltd. Revlimid®. Summary of Product Characteristics. 2013. Available at: http://www.medicines.org.uk/emc/medicine (Last updated 13 June 2013)
2) Weber DM, Chen C, Niesvizky R et al. Lenalidomide plus dexamethasone for relapsed multiple myeloma in North America. N Eng J Med 2007; 357: 2133-42
3) Dimopoulos M, Spencer A, Attal M et al. Lenalidomide plus dexamethasone for relapsed or refractory multiple myeloma. N Eng J Med 2007; 357: 2123-32
4) European Medicines Agency. Public Assessment Report: lenalidomide. www.ema.europa.eu (Last updated 26 June 2007)
5) Dimopoulos MA, Chen C, Spencer A et al. Long-term follow-up on overall survival from the MM-09 and MM-010 phase III trials of lenalidomide plus dexamethasone in patients with relapsed or refractory multiple myeloma. Leukaemia 2009; 23: 2147-52
6) Stadtmauer EA, Weber DM, Niesvizky R et al. Lenalidomide in combination with dexamethasone at first relapse in comparison with its use as later salvage therapy in relapsed or refractory multiple myeloma. European Journal of Haematology 2009; 82: 426-32
7) Mateos MV, Richardson PG, Schlag R et al. Bortezomib plus melphalan and prednisone compared with melphalan and prednisone in previously untreated multiple myeloma: updated follow-up and impact of subsequent therapy in the phase III VISTA trial. J Clin Oncol 2010; 28: 2259-66
8) EMA. Assessment report for Revlimid. 13 January 2012. www.ema.europa.eu
9) National Institute for Health and Care Excellence. Technology Appraisal Guidance 228 – Bortezomib and thalidomide for the first-line treatment of multiple myeloma. July 2011. Available at www.nice.org.uk
10) Bird JM, Owen RG, D'Sa S et al. Guidelines for the diagnosis and management of multiple myeloma 2013. Available at http://www.bcshguidelines.com/4_HAEMATOLOGY_GUIDELINES.html
11) Dimopoulos M, Weber D, Ishak J et al. Consistency of LEN plus DEX efficacy across prior treatments in relapsed or refractory multiple myeloma (RRMM). Poster presented at the 14th International Myeloma Workshop. Kyoto, Japan. 3 to 7 April 2013. P-183.
12) Harousseau JL & Dreyling M. Multiple myeloma: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Annals of Oncology 2010; 21 (suppl. 5): v155-7.


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