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

Resubmission

pomalidomide 1mg, 2mg, 3mg and 4mg hard capsules (Imnovid®)

SMC No. (972/14)

Celgene Ltd.

07 November 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 resubmission

pomalidomide (Imnovid®) is accepted for use within NHS Scotland.

Indication under review: in combination with dexamethasone for the treatment of adult patients with relapsed and refractory multiple myeloma who have received at least two prior treatment regimens, including lenalidomide and bortezomib, and have demonstrated disease progression on the last therapy.

Pomalidomide plus dexamethasone significantly increased progression-free survival compared with high-dose dexamethasone in patients with refractory or relapsed and refractory multiple myeloma.

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

Overleaf is the detailed advice on this product.

Chairman,
Scottish Medicines Consortium

Indication

In combination with dexamethasone for the treatment of adult patients with relapsed and refractory multiple myeloma who have received at least two prior treatment regimens, including lenalidomide and bortezomib, and have demonstrated disease progression on the last therapy.

Dosing Information

Recommended starting dose is 4mg once daily taken orally on days 1 to 21 of repeated 28-day cycles. The recommended dose of dexamethasone is 40mg orally once daily on days 1, 8, 15 and 22 of each 28-day treatment cycle.

Dosing should be continued or modified based upon clinical and laboratory findings. Treatment should be discontinued upon progression of disease. The summary of product characteristics (SPC) gives dose modification instructions.

Pomalidomide treatment must be initiated and monitored under the supervision of physicians experienced in the management of multiple myeloma.

Product availability date

4 October 2013. Pomalidomide was designated an orphan medicine for the treatment of multiple myeloma in October 2009.

Summary of evidence on comparative efficacy

Pomalidomide is an immunomodulating agent, similar to thalidomide and lenalidomide. It has been designated an orphan medicine for multiple myeloma. The exact mechanism of action of pomalidomide is unknown but it has direct anti-myeloma tumouricidal activity, immunomodulatory and anti-angiogenic activity and it inhibits stromal cell support for multiple myeloma tumour cell growth. It inhibits proliferation and induces apoptosis of haematopoietic tumour cells. It also inhibits the proliferation of lenalidomide-resistant multiple myeloma cell lines and synergises with dexamethasone in lenalidomide-sensitive and -resistant cell lines to induce tumour cell apoptosis.[1]

The key evidence to support the use of pomalidomide in patients with relapsed and refractory multiple myeloma comes from one pivotal study (MM-003).[1,2] This randomised, open-label, phase 3 study was designed to compare the efficacy and safety of pomalidomide plus low-dose dexamethasone with high-dose dexamethasone in patients with refractory or relapsed and refractory multiple myeloma. The study enrolled patients from 93 centres in Europe, Russia, Australia, Canada and the USA between March 2011 and August 2012. Eligible patients were aged ≥18 years with a documented diagnosis of multiple myeloma and measurable disease. They had received at least two previous consecutive cycles of bortezomib and lenalidomide treatment, alone or in combination, as well as adequate alkylator treatment, and were considered to have refractory or relapsed and refractory disease.

Patients were considered to be refractory if they had progressed on or within 60 days of treatment with bortezomib and lenalidomide (after completing last treatment). Patients were considered relapsed and refractory if they had achieved at least a partial response to previous treatment with bortezomib or lenalidomide, or both, but progressed within 6 months (developing progressive disease on or within 60 days after completing their last treatment). Patients with bortezomib intolerance after at least two cycles of bortezomib who developed progressive disease on or before 60 days after completing their last treatment were also eligible for enrolment. Eligible patients were randomised in a ratio of 2:1 to receive pomalidomide (4mg orally daily on days 1 to 21) plus low-dose dexamethasone (40mg orally daily on days 1, 8, 15 and 22) of a 28-day cycle (n=302) or high-dose dexamethasone (40mg orally daily on days 1 to 4, 9 to 12 and 17 to 20) for a 28-day cycle (n=153). In all patients aged >75 years, the dexamethasone dose was reduced to 20mg daily. Treatment was continued until disease progression or unacceptable toxicity. Randomisation was stratified by age (≤75 years or >75 years), disease status (refractory or relapsed and refractory or bortezomib intolerant) and number of previous treatments (two or at least three). Concomitant thromboprophylaxis was required for patients in the pomalidomide group and for patients considered to be at risk of thrombosis. The choice of thromboprophylaxis and myeloid and erythroid growth factor use was at the physician's discretion.

The primary outcome was progression-free survival (PFS) defined according to the International Myeloma Working Group (IMWG) criteria. PFS results assessed by the independent review adjudication committee (IRAC) were presented in the European Public Assessment Report (EPAR) and Summary of Product Characteristics (SPC) and assessed by the investigator in the key publication. At the time of the final PFS analysis (cut-off date 7 September 2012), after a median follow-up of 4.2 months, median PFS, assessed by the IRAC, was 15.7 weeks in the pomalidomide plus low-dose dexamethasone group and 8.0 weeks in the high-dose dexamethasone group: hazard ratio 0.45 (95% CI: 0.35 to 0.59), p<0.001.[1] When assessed by investigator, median PFS was 16.5 weeks and 8.2 weeks respectively: hazard ratio 0.41 (95% CI: 0.32 to 0.53), p<0.001. At this time 29% (45/153) high-dose dexamethasone treated patients had crossed-over to receive pomalidomide +/- dexamethasone.[2]

The key secondary outcome was overall survival (OS) and, at the final OS analysis (cut-off date 1 March 2013), after a median follow-up of 10 months, median OS was 12.7 months in the pomalidomide plus low-dose dexamethasone group and 8.1 months in the high-dose dexamethasone group: hazard ratio 0.74 (95% CI: 0.56 to 0.97), p=0.0285. At this time approximately 50% (76/153) of patients in the high-dose dexamethasone group had crossed over to receive pomalidomide +/- dexamethasone.[2]

Other secondary outcomes were overall response rate (at least a partial response as assessed by investigators) which, at the 1 March 2013 cut-off date, was achieved by 31% (95/302) of patients in the pomalidomide plus low-dose dexamethasone group versus 10% (15/153) of patients in the high-dose dexamethasone group: odds ratio 4.22 (95% CI: 2.35 to 7.58), p<0.0001.This included a complete or stringent complete response in 1.0% (3/302) of patients in the pomalidomide plus low-dose dexamethasone group only.[2] Time to progression (as assessed by the investigator) was a median of 4.7 months versus 2.1 months respectively: HR 0.46 (95% CI: 0.36 to 0.59), p<0.0001. The median duration of response did not differ significantly between treatment groups: 7.0 months versus 6.1 months respectively.[2]

Quality of life was assessed as time to meaningful worsening in five pre-specified European Organisation for Research and Treatment of Cancer (EORTC) quality of life questionnaire for patients with cancer (QLQ-C30) domains: global health status, physical functioning, fatigue,

emotional functioning and pain. Meaningful worsening was defined as a reduction in quality of life ≥minimally important difference for that domain. Results (up to the cut-off data of 7 September 2012) are limited to poster presentations but suggest favourable trends with pomalidomide plus low-dose dexamethasone compared with high-dose dexamethasone.[3,4]

Summary of evidence on comparative safety

During study MM-003 described above, adverse events of any grade reported in more than 10% in the pomalidomide plus low-dose dexamethasone or high-dose dexamethasone groups respectively were anaemia (52% and 51%), neutropenia (51% and 21%), fatigue (34% and 27%), thrombocytopenia (30% and 29%), pyrexia (27% and 23%), diarrhoea (22% and 19%), constipation (22% and 15%), cough (20% and 10%), back pain (20% and 16%), dyspnoea (20% and 14%), bone pain (17% and 13%), peripheral oedema (17% and 11%), upper respiratory tract infection (16% and 8.0%), asthenia (16% and 17%), muscle spasm (16% and 7.3%), pneumonia (15% and 11%), nausea (15% and 11%), leukopenia (13% and 5.3%), dizziness (12% and 8.0%), decreased appetite (12% and 8.0%), insomnia (10% and 20%), bronchitis (10% and 5.3%), febrile neutropenia (10% and 0.7%), epistaxis (9% and 10%), hypercalcaemia (7.0% and 11%), muscle weakness (3.7% and 13%).[2]

The most commonly reported grade 3 or 4 adverse events in the pomalidomide plus low-dose dexamethasone or high-dose dexamethasone groups respectively were haematological in nature and included neutropenia (48% and 16%), anaemia (33% and 37%), thrombocytopenia (22% and 26%), febrile neutropenia (9.3% and 0) and leukopenia (8.6% and 3.3%).[5] Other grade 3 or 4 adverse events were pneumonia (13% and 8.0%), bone pain (7.0% and 4.7%) and fatigue (5.3% and 6.0%).[2]

There were 11 treatment-related deaths in the pomalidomide plus low-dose dexamethasone group (3.6%) and seven in the high-dose dexamethasone group (4.6%). In the pomalidomide plus low-dose dexamethasone group, death was due to infection (n=8), multi-organ failure or sudden death (n=2) and nervous system disorder (n=1). In the high-dose dexamethasone group, deaths were all due to infection (n=7).[2]

Since pomalidomide 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.

Summary of clinical effectiveness issues

Pomalidomide, in combination with dexamethasone, offers an alternative treatment for multiple myeloma in patients who have relapsed and refractory disease after at least two prior treatment regimens, including lenalidomide and bortezomib, and have demonstrated disease progression on the last therapy. Pomalidomide meets SMC end of life and orphan criteria. 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.[5] However, there appears to be no standard of care after progression on these agents for fourth line treatment, the expected positioning of pomalidomide in the company submission. A range of salvage treatment options include retreatment with bortezomib or

lenalidomide, entry into a clinical trial, older agents or palliation. Clinical experts consulted by SMC considered that there is unmet need for patients with relapsed/refractory multiple myeloma. Following multiple technology appraisal, the National Institute for Health and Care Excellence (NICE) guidance for the first-line treatment of multiple myeloma only recommends bortezomib-based therapy if high dose chemotherapy with stem cell transplantation is inappropriate or if thalidomide has not been tolerated or is contra-indicated. SMC has recently accepted lenalidomide for restricted use at first relapse in patients who have received prior bortezomib in whom thalidomide has not been tolerated or is contra-indicated. In this situation, pomalidomide could be used third-line under the licence after bortezomib and lenalidomide.

The primary outcome in the pivotal study was PFS, a validated, surrogate marker for this disease and pomalidomide plus dexamethasone was associated with a significantly longer PFS compared with high-dose dexamethasone.[1,2] High-dose dexamethasone was considered one possible option of the range of salvage treatments used. PFS was reported as assessed by the IRAC and the investigator but, since the study was open-label, the results as assessed by the IRAC would be expected to be more robust with less potential bias. Despite confounding due to patient crossover (50% [76/153] of high-dose dexamethasone patients), pomalidomide plus dexamethasone was also associated with a statistically significant survival advantage compared with high-dose dexamethasone treatment.[1,2] Clinical experts consulted by SMC considered that pomalidomide is a therapeutic advancement due to improvements in PFS and survival.

The BCSH report the median age at presentation of patients with multiple myeloma is 70 years.[5] Patients recruited to the pivotal study were slightly younger (median ages 64 to 65 years). The majority of patients (>80%) also had a performance status of 0 or 1[2], and may be fitter than the population likely to be treated in Scotland. Patients in the pivotal study had received a median of five previous treatments[2] and therefore may have been more heavily pre-treated than patients likely to be treated in Scotland. The subgroup analyses indicated that the treatment effect of pomalidomide plus dexamethasone was consistent with the overall results irrespective of the previous treatment received.[2]

Comparative data are limited to that described with high-dose dexamethasone, and additional available data were not deemed sufficient to perform a mixed treatment comparison with other possible treatment options.

Pomalidomide is administered orally which offers convenience for the patient and the service.

Summary of comparative health economic evidence

The company submitted an economic analysis comparing pomalidomide in combination with dexamethasone (POM+DEX) with bortezomib retreatment in combination with dexamethasone (BOR + DEX) in patients with relapsed and refractory multiple myeloma, with prior treatment consisting at least of bortezomib and lenalidomide but also thalidomide. In scenario analysis, a comparison was also made with retreatment with lenalidomide + dexamethasone (LEN + DEX). The Markov model structure consisted of pre-progression on and off treatment and disease progression health states, with a model cycle length of 1 week. The time horizon in the base case was 25 years.

The primary clinical data for time to treatment failure (TTF), PFS and OS used in the economic model were from the pivotal MM-003 study, which was an assessment of POM+DEX versus

high dose dexamethasone. The high dose DEX arm of the trial was used as a proxy for the efficacy of the comparators in the economic model given the absence of an indirect comparison. In a scenario analysis, an alternative data source for TTF, PFS and OS projection for the comparator arm was used, which was a retrospective single UK centre study consisting of 30 patients receiving a mix of 4th line treatments and prior treatment with bortezomib, lenalidomide (100% of patients) and thalidomide (87% of patients). In this study, 37% of patients were reported as receiving either BOR or LEN as a 4th line treatment. Fifth line treatment was included in the model based on a mix of treatments observed in a real world dataset covering multiple myeloma patients in England (the Haematological Malignancy Research Network Registry). Adverse event (AE) data were derived for pomalidomide from Study MM-003, and for the comparators from previous HTA reports for these drugs.

Extrapolation of TTF, PFS and OS was performed by fitting parametric functions to the observed data from Study MM-003, or from the single UK centre retrospective data. The selection of base case functions appears to have been performed to accepted standards, and alternative functions were applied in scenario analysis. There was significant patient cross-over to pomalidomide on progression in Study MM-003; the OS estimates were adjusted to account for this using a new technique known as a two stage Weibull approach.

Utilities for the health states and grade 3 or 4 adverse events were derived from regression analysis performed on EQ-5D data from the MM-003 study, and consisted of an estimated 0.75 and 0.65 for response to treatment and stable disease states within PFS, and 0.71, 0.62 and 0.57 for response, stable and progressive disease within the progressive disease state. Costs covered drug acquisition, administration and funded transport, monitoring, adverse event management, terminal care, blood transfusions and concomitant medication. A higher patient monitoring requirement in the first 8 weeks for pomalidomide than the comparator treatments was assumed.

A confidential patient access scheme (PAS) was submitted by the company and assessed by the Patient Access Scheme Assessment Group (PASAG) as acceptable for implementation in NHS Scotland. Under the PAS, a simple discount is given on the list price of the medicine.

With the PAS, the incremental cost effectiveness ratio (ICER) fell to £49,143 given lower incremental costs of £33,716 and incremental quality adjusted life years (QALYs) of 0.69.

The key driver of the incremental costs is the additional drug acquisition costs of pomalidomide. There were also higher patient monitoring and AE costs (the latter due to longer time on treatment estimated with pomalidomide), but lower administration costs as pomalidomide is oral agent compared to BOR which is administered IV or SC. The ICER for the scenario analysis where LEN+DEX was the comparator was estimated to be £53,801/QALY gained with the PAS – no difference in QALYs from the base case was assumed as the same data source was used, but there were higher incremental costs for pomalidomide in this comparison of £36,910 with the PAS. For the scenario using the UK single centre data as a proxy for BOR+DEX outcomes, the ICER was £48,497 with the PAS, though due to the limitations of this data there was high uncertainty in the estimates.

The base case results were sensitive to the choice of parametric function applied, assuming treatment duration is based on PFS rather than TTF, and varying OS curve parameters or the coefficients in the utility regression, with ICERs ranging from £56k to an upper limit of £47k to £83k with PAS. The £83k ICER resulted when a Weibull curve was fitted, but it should be noted that this curve was a poor fit to the available data so this may be viewed as an extreme

scenario. The results were less sensitive to scenarios using alternative utility sources (EORTC 8D from the trial and published utilities). Probabilistic Sensitivity Analysis indicated a 30% probability of POM+DEX being cost-effective at a £50,000/QALY threshold, and a probabilistic ICER of £56.9k/QALY gained.

The main issues in the economic analysis were as follows:

- The use of the high dose DEX arm of the MM-003 trial as a proxy for BOR+DEX and LEN+DEX efficacy is a limitation in terms of knowing the comparative efficacy advantage for pomalidomide. The real world data used as an alternative source of TTF, PFS and OS data are limited for extrapolations, particularly because of the small number of patients in the study.
- SMC clinical experts have indicated there is no standard of care at the 4th line stage and a range of treatments is used dependent on the status of the patient. These include retreating with BOR and LEN (with DEX), but may also include other drugs such as bendamustine, cyclophosphamide, melphalan, or doxorubicin. The UK single centre study used in scenario analysis indicates similar outcomes, based on a mix of treatments, as the DEX arm in MM-003, and regression analysis performed by the company on these data suggests current treatment received at this stage does not have a differential impact on outcomes. However, the average costs of a treatment mix reflecting current practice may differ from the costs when assuming that all patients receive BOR+DEX. The New Drugs Committee requested the results with high dose dexamethasone as the comparator in the analysis as this comparison is based on available trial data and helps to outline the upper bounds on the ICER without the uncertainty associated with the use of proxied evidence. This resulted in a cost per QALY of £71,821 with PAS because of the low cost of high dose dexamethasone.
- The method used for cross-over adjustment is one that has not been used before in submissions. Standard methods previously submitted to SMC include the Rank Preserving Structural Failure Time Model (RPSFTM). In addition, the company provided some supplementary analysis using the RPSFTM. This increased the ICER to £52,715 with PAS versus BOR+DEX). There is high uncertainty in the life year gain estimates which means a large variation in the potential ICER for POM+DEX.
- The time horizon seems implausibly long at 25 years for 4th line MM. A shorter time horizon of 10 years increased the ICER to QALY£55k with PAS.

The estimated base case ICER for POM+DEX is above usual acceptable thresholds for cost-effectiveness, and uncertainty in survival estimates means the with-PAS ICER is uncertain and could be higher.

As pomalidomide meets the SMC criteria for an orphan medicine, SMC can accept greater uncertainty in the economic case. The Committee considered the benefits of pomalidomide in the context of its decision modifiers that can be applied when encountering high cost-effectiveness ratios or where there is increased uncertainty. The committee concluded that the criteria for a substantial improvement in life expectancy and absence of other treatment options of proven benefit were met.

After application of the appropriate modifiers, the Committee accepted pomalidomide for use in NHS Scotland.

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

Summary of patient and public involvement

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

- A submission was received from Myeloma UK which is a registered charity.
- Myeloma UK has received funding from several pharmaceutical companies in the past two years, including from the submitting company.
- Myeloma is a disease with currently no cure but treatment can halt its progress for periods of time and improve quality of life. Complications of myeloma include severe bone pain, bone fractures, fatigue, frequent infection and kidney damage, all of which can substantially impact on patients' quality of life.
- Myeloma is a relapsing and remitting cancer and patients need to have effective treatments available at each relapse. Relapsing can have a major impact on emotional wellbeing. Pomalidomide is an additional treatment option for patients once they have exhausted treatments already available on the NHS and it will allow clinicians to use a new and innovative oral treatment in patients who they think will benefit.
- There is an absence of routinely available treatments in this group of patients. Pomalidomide may significantly help patients live longer, and with a better quality of life, in a way that may not be achieved currently.

Additional information: guidelines and protocols

The BCSH published "Guidelines for the diagnosis and management of multiple myeloma 2014" in February 2014.[5] For patients with relapsed myeloma, these guidelines recommend that the most appropriate management should be determined on an individual basis depending on the timing of relapse, age, prior therapy, bone marrow function, co-morbidities, and patient preference. There are extensive trial data support the use of thalidomide, bortezomib and lenalidomide-based regimens as treatment modalities at first and subsequent relapse and the clinical effectiveness of thalidomide, bortezomib and lenalidomide is not dependent on the number of previous lines of therapy, or type of therapy previously received. Unless contraindicated, treatment with thalidomide, bortezomib or lenalidomide treatment should be administered with dexamethasone and/or chemotherapy to increase the response rate. A second ASCT may be considered in patients who had a good response to the initial transplant procedure (≥ 18 months to disease progression). Where possible, patients should be treated in the context of a clinical trial and phase I/II trials are appropriate for patients with relapsed/refractory myeloma. Good supportive therapy is essential. These guidelines do not make any recommendations on pomalidomide which is noted as a drug in development.

The European Society of Medical Oncology (ESMO) published "Multiple myeloma: ESMO clinical practice guidelines for diagnosis, treatment and follow-up" in August 2013.[6] These guidelines note that the choice of therapy for relapsed disease depends on several factors including age, performance status, co-morbidities, the type, efficacy and tolerance of previous

treatment, the number of prior lines of treatment, the available remaining treatment options and the time since the last treatment. These guidelines note that the EMA has approved lenalidomide plus dexamethasone and bortezomib alone or plus pegylated doxorubicin but that bortezomib is mostly used in combination with dexamethasone in relapsed disease. Thalidomide and bendamustine are effective drugs, often used, [but not approved at the time of publication]. A second ASCT may be considered in young patients who responded well to previous ASCT with PFS >24 months. Patients should be offered participation in clinical trials when possible. Pomalidomide and carfilzomib, approved in the US, [are not available at the time of publication in Europe outside clinical trials].

The National Institute for Health and Clinical Excellence (NICE) published a multiple technology appraisal (No. 228): Bortezomib and thalidomide for the first-line treatment of multiple myeloma in July 2011.[7] This guidance states that thalidomide in combination with an alkylating agent and a corticosteroid is recommended as an option for the first-line treatment of multiple myeloma in people for whom high-dose chemotherapy with stem cell transplantation is considered inappropriate. Bortezomib in combination with an alkylating agent and a corticosteroid is recommended as an option for the first-line treatment of multiple myeloma if high-dose chemotherapy with stem cell transplantation is considered inappropriate and the person is unable to tolerate or has contraindications to thalidomide.

These guidelines predate the approval and availability of pomalidomide in the UK.

Additional information: comparators

There is no standard of care for patients with relapsed or refractory multiple myeloma after at least two other treatments. Possible options include retreatment with bortezomib or lenalidomide, clinical trials, older agents, bendamustine (not accepted by SMC) or palliation.

Cost of relevant comparators

Drug	Dose Regimen	Cost per cycle (£)
Pomalidomide plus dexamethasone	**28-day cycle** **Pomalidomide: 4mg orally on days 1 to 21** **Dexamethasone: 40mg orally on days 1, 8, 15 and 22**	**8,946**
Dexamethasone	40mg daily on days 1 to 4, 9 to 12 and 17 to 20 of a 28-day cycle.	62
Lenalidomide plus dexamethasone	28-day cycle Lenalidomide: 25mg orally on days 1 to 21 Dexamethasone 1st four cycles: 40mg orally on days 1 to 4, 9 to 12, and 17 to 20 Subsequent cycles: 40mg orally on days 1 to 4	1st four cycles: 4,555 Subsequent cycles: 4,430
Bortezomib	1.3mg/m^2 subcutaneously or intravenously on days 1, 4, 8 and 11 of a 21-day cycle	3,050

Doses are for general comparison and do not imply therapeutic equivalence. Cost of bortezomib based on surface area of 1.8m^2. Costs from www.mims.co.uk on 1 September 2014 except dexamethasone which is from eVadis in September 2014.

Additional information: budget impact

The submitting company estimated the number of patients expected to be treated with pomalidomide + DEX to be 132 in year 1, rising to 299 in year 5, based on an assumed market share of 55% in year 1, rising to 75% in year 5. These calculations assume a high number of prevalent patients in year 1, some of whom continue to receive some treatment in subsequent years, plus smaller numbers of new incident patients (36-48 per year) flowing into the analysis in years 2 to 5.

Without PAS:
The gross impact on the medicines budget was estimated to be £6.03 million in year 1 and £2.32 million in year 5. The net cost after displacement of bortezomib or lenalidomide was estimated to be £4.25m in year 1 and £1.67m in year 5.

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

References

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

1. European Medicines Agency. Public Assessment Report: pomalidomide, procedure number EMEA/H/C/002682. www.ema.europa.eu [accessed 11 March 2014]

2. San Miguel J, Weisel K, Moreau P et al. Pomalidomide plus low-dose dexamethasone versus high-dose dexamethasone alone for patients with relapsed and refractory multiple myeloma (MM-003): a randomised, open-label, phase 3 trial. Lancet Oncology 2013;14:1055-66.

3. Song KW, Dimopoulos MA, Weisel K et al. Pomalidomide (POM) plus low-dose dexamethasone (LoDEX) improves health-related quality of life (HRQoL) vs high-dose dexamethasone (HiDEX) in relapsed refractory multiple myeloma (RRMM) patients enrolled in MM-003 phase 3 randomised trial. Blood 2013:122 (21)

4. Song KW, Meletios A, Dimopoulos MA et al. Quality of life (QOL) improvements for pomalidomide plus low-dose dexamethasone (POM + LoDEX) in relapsed and refractory multiple myeloma (RRMM) patients (pts) enrolled in MM-003. J Clin Oncol 2013;31 no 15 suppl:8583.

5. Bird JM, Owen RG, D'Sa S et al. Guidelines for the diagnosis and management of multiple myeloma 2014. Available at http://www.bcshguidelines.com/4_HAEMATOLOGY_GUIDELINES.html

6. Moreau P, San Miguel J, Ludwig H et al. Multiple myeloma: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Ann Oncol 2013;24 (suppl 6):vi133-vi137.

7. National Institute for Health and Clinical Excellence (NICE) published a multiple technology appraisal (No. 228): Bortezomib and thalidomide for the first-line treatment of multiple myeloma in July 2011.

This assessment is based on data submitted by the applicant company up to and including 17 October 2014.

**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.