Scottish Medicines Consortium
Providing advice about the status of all newly licensed medicines
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idelalisib, 100mg and 150mg film-coated tablets (Zydelig®) SMC No. (1039/15)

Gilead Sciences Limited

10 April 2015

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 NHS Scotland. The advice is summarised as follows:

ADVICE: following a full submission assessed under the end of life and ultra-orphan processes

idelalisib (Zydelig®) is accepted for use within NHS Scotland.

Indication under review: Monotherapy for the treatment of adult patients with follicular lymphoma (FL) that is refractory to two prior lines of treatment.

Idelalisib demonstrated clinical activity, measured by overall response rate, in a phase II non-comparative study.

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

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

Published 11 May 2015

Indication

Monotherapy for the treatment of adult patients with follicular lymphoma (FL) that is refractory to two prior lines of treatment.

Dosing Information

150mg orally twice daily. Treatment should be continued until disease progression or unacceptable toxicity. Patients should be instructed to swallow the tablet whole. The film-coated tablet should not be chewed or crushed and can be taken with or without food. Dose reductions, as specified in the summary of product characteristics, may be required if adverse events occur.

Treatment with idelalisib should be conducted by a physician experienced in the use of anticancer therapies.

Product availability date

22 September 2014
Idelalisib meets SMC ultra-orphan and end of life criteria for this indication

Summary of evidence on comparative efficacy

Idelalisib is the first in a new class of medicines that inhibit phosphatidylinositol 3 kinase p110δ (PI3Kδ), which is overactive in B-cell malignancies and is key within several signalling pathways that drive proliferation, survival, homing, and retention of malignant cells in lymphoid tissues and bone marrow.[1] Idelalisib is also licensed in combination with rituximab for the treatment of adult patients with chronic lymphocytic leukaemia (CLL) who have received at least one prior therapy or as first line treatment in the presence of 17p deletion or *TP53* mutation in patients unsuitable for chemo-immunotherapy.[1] Idelalisib is accepted for restricted use by SMC for this indication.

The key evidence to support idelalisib use in follicular lymphoma comes from study 101-09, a phase II, single group, open-label, multi-centre study designed to investigate the clinical activity and safety of idelalisib. Eligible patients were adults (≥18 years) with indolent non-Hodgkin's lymphoma (NHL) and a Karnofsky performance score of ≥60 who had either not had a response to rituximab and an alkylating agent or had relapsed within six months.[2] Between April 2011 and October 2012, all patients were allocated to receive idelalisib 150mg orally twice daily until disease progression, unacceptable toxicity or death.[2] A dose reduction to 100mg twice daily or 75mg twice daily was permitted to manage toxicity.[3] A subgroup of the total study population, patients with follicular lymphoma (72/125, 58%), represents the indication under review.

The primary endpoint was the overall rate of response assessed by the independent review committee. At the data cut-off in June 2013, 32% of patients (40/125) were still receiving treatment. Mean duration of treatment was 8.1 months. After a median follow-up of 9.7 months, the response rate in the overall study population was 57% (71/125; 95% confidence interval [CI]: 42 to 66). Seven patients (5.6%) had a complete response, 63 patients (50%) had a partial response and one patient (1%) with Waldenström's macroglobinaemia had a minor response.[2] The median duration of response was 12.5 months (range 0.03 to 14.8), median

progression free survival was 11.0 months (range 0.03 to 16.6 months) and 47% of patients remained progression free at 48 weeks. Median overall survival was 20.3 months (range 0.7 to 22.0 months).[2] Updated results have recently been presented at the American Society of Haematology Conference.[4] At this data cut-off in June 2014, after a median exposure of 11 months (range 0.7 to 35 months), the overall response rate was 56% (95% CI: 47 to 65), 9.6% of patients had a complete response and 46% of patients had a partial response. The median duration of response was 13.9 months (range 0.03 to 31.3) and median progression free survival was 11.0 months. Median overall survival of all patients was 30.8 months.[4]

In the follicular lymphoma subgroup, the response rate at the data cut-off in June 2013 was 54% (95% CI: 42 to 66); 8.3% of patients had a complete response and 46% of patients had a partial response.[3] Median duration of response was not reached and median progression free survival was 8.5 months (95% CI: 5.7 to 13.1).[3] The median overall survival had not been reached.[3] At the June 2014 cut-off, the overall response rate in the follicular lymphoma subgroup was 54%, 14% of patients had a complete response. Median duration of response was 11.8 months and median progression free survival was 11 months. Median overall survival was not reported for the follicular lymphoma subgroup separately.[4]

Health-related quality of life was measured using Functional Assessment of Cancer Therapy - Lymphoma (FACT-Lym).[3] The FACT-Lym has five domains: lymphoma sub-scale, physical well-being, social/family well-being, emotional well-being and function well-being. Health related quality of life was generally stable for the overall population during the study and for patients in the follicular lymphoma subgroup.[5]

Summary of evidence on comparative safety

Since the pivotal study was of single-arm design there are no comparative safety data available. Refer to the summary of product characteristics for details.

In the total study population, an adverse event was reported in 82% (103/125) of all patients, with a ≥grade 3 adverse event reported in 54% (68/125). Adverse events led to a dose reduction in 34% of patients and discontinuation of treatment in 20% of patients.[2]

The following adverse events (all grades) occurred in more than 20% of patients: diarrhoea, fatigue, nausea, cough and pyrexia. Adverse events reported at ≥grade 3 were neutropenia, diarrhoea, raised serum alanine or aspartate aminotransferase, pneumonia and dyspnoea.[2]

The most common serious adverse events were pyrexia, pneumonia, diarrhoea, colitis, dehydration, febrile neutropenia, acute renal failure and pneumonitis.[2]

No safety data are available for the follicular lymphoma subgroup.

Summary of clinical effectiveness issues

Follicular lymphoma is the most common form of low grade non-Hodgkin's lymphoma in the UK and approximately 85% of these patients have advanced disease at presentation. Rituximab in combination with chemotherapy has improved outcomes in patients with newly diagnosed follicular lymphoma; however, the majority of patients experience relapse of their disease and

will receive a series of treatments over the years.[6] Patients with advanced or end-stage disease often have systemic symptoms such as fatigue, weakness, fever, night sweats and weight loss.[7] The marketing authorisation for idelalisib is for treatment of adult patients with follicular lymphoma that is refractory to two prior lines of treatment. In the clinical study this was defined as patients who had either not had a response to rituximab and an alkylating agent or had relapsed within six months. Clinical experts consulted by SMC considered that there is unmet need in this therapeutic area. Idelalisib meets SMC ultra-orphan and end of life criteria for this indication.

Just over half of the patients in the follicular lymphoma subgroup of the pivotal study achieved an overall response. In the European Public Assessment Report (EPAR) it is noted that intra-patient progression free survival is longer with idelalisib compared with prior treatment and that the response rate is higher than that reported previously with rituximab in the salvage setting; however, the limitations of these historical comparisons are acknowledged, e.g. there is no randomised controlled comparison available and different definitions of response have been used.[3]

The major limitation to this study is the lack of a comparator; therefore, it is not possible to draw any conclusions about relative efficacy or safety. Due to the absence of a defined standard of care, it would be challenging to conduct a randomised study in this setting. The study population included patients with indolent NHL and the evidence for follicular lymphoma patients comes from a subgroup of 58% (72/125) of patients. The primary outcome of this open-label phase II study was overall response but progression free survival and overall survival are preferred outcomes in confirmatory anti-cancer clinical studies.[8] Although the study was of open-label design, response was assessed independently minimising the potential bias. Study follow up is ongoing.[3,4]

Clinical experts consulted by SMC considered that idelalisib is a therapeutic advancement due to its novel mechanism of action and acceptable toxicity profile. As an oral medicine, idelalisib is unlikely to be associated with any significant service implications. The management of toxicity, in particular diarrhoea/colitis, and full blood count and liver function test monitoring will be required.[1]

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 idelalisib , as an ultra-orphan and end of life medicine, in the context of treatments currently available in NHS Scotland, specifically in the treatment of adult patients with follicular lymphoma (FL) that is refractory to two prior lines of treatment.

The key points expressed by the group were:

- Idelalisib with its new mode of action would provide this very small group of patients with a realistic third line treatment option that may prolong life. The psychological benefit for patients and their families of knowing there is a third line treatment option available cannot be under-estimated in this relapsing remitting disease.

- There are data to suggest that idelalisib may improve quality of life through alleviation of disease symptoms and reduced treatment side effects. Patients describe the unrelenting, enduring nature of the FL symptom of severe fatigue as being particularly impactful on their quality of life. Side effects with idelalisib are generally less severe and do not overlap with other treatment options.

- An oral preparation taken at home reduces the costs associated with administration in addition to avoiding the need for an unsightly PICC or Hickman lines which leave patients more prone to infection and with central chest scarring. Patients only need to attend clinic once a month for monitoring, reducing the emotional and social burden on patients and carers compared to alternative treatment options.

- It could be used for a limited period to help bridge to a potentially curative allogeneic transplant. In some transplant patients it could be used as a bridge to a donor lymphocyte infusion.

- Patients generally respond rapidly to treatment making it easy to develop stopping rules and avoiding unnecessary long-term treatment.

Summary of ultra orphan decision-making framework

Idelalisib has been considered by SMC using its decision-making framework for the assessment of ultra-orphan medicines. Relevant factors under each of the criteria are summarised below.

Nature of the condition

Folicular lymphoma is the most common form of low grade non-Hodgkin lymphoma. There is no cure currently available and thus patients will ultimately relapse. The common pattern of disease progression is one of relapse and remission, with each relapse becoming more difficult to treat, and each remission being shorter than the preceding one. As noted above, patients with advanced or end-stage disease often have systemic symptoms such as fatigue, weakness, fever, night sweats and weight loss, all of which can significantly affect a patient's quality of life.

Impact of the new technology

At present there are very limited treatment options for patients who are refractory to two lines of therapy. The phase II clinical study indicated that median progression free survival in the follicular lymphoma subgroup was 8.5 months and just over half of the patients achieved an overall response. At the Patient and Clinician Engagement (PACE) meeting, it was noted that data suggest quality of life may be improved through alleviation of disease symptoms and reduced treatment side-effects. It was also noted at the PACE meeting that idelalisib could be used for a limited period to help bridge to a potentially curative allogeneic transplant, and in some relapsed transplant patients it could be used as a bridge to donor lymphocyte infusion.

Value for money

The submitting company presented a cost-utility analysis of idelalisib compared to current care consisting of retreatment with a range of chemotherapy and/or rituximab regimens in patients with FL who are refractory to at least two prior therapies. In scenario analysis, a comparison was performed against best supportive care (BSC) in refractory FL patients considered too frail for further chemotherapy. A standard 3 state Markov model (pre-progression, post progression

and death, with an indirect health state of palliative care prior to death) was used with a lifetime time horizon of 10 years.

The clinical data used were from the sub-group of 72 patients with refractory FL who received idelalisib from study 101-09. As this was a single arm study, the outcomes for the primary comparator were based on data available for therapy received by the FL patients prior to idelalisib in study 101-09. In total this consisted of 16 chemotherapy and/or rituximab regimens, with outcomes for these assumed to represent a proxy for further chemotherapy and/or rituximab retreatment as a comparator to idelalisib. The analysis consisted of a comparison of time to treatment progression (TTP), and time on treatment (ToT) for idelalisib and the prior therapy proxy. However, as there were no data available for post progression survival (PPS) for the comparator, it was assumed that chemotherapy and/or rituximab regimens (with outcomes for these assumed to represent a proxy for further chemotherapy and/or rituximab retreatment) would have the same PPS as was estimated for idelalisib using study 101-09 data. In each case, TTP and ToT were extrapolated using the Weibull function, and PPS for idelalisib extrapolated using the extreme value function, based on best visual fit and clinical plausibility. The company also assumed (based on expert clinical opinion) that the TTP effectiveness of the comparator regimens would be 0.9 of that estimated from the prior therapy data, on the basis that a further line of re-treatment would be less effective than earlier use. In addition, pre-progression mortality was estimated based on general population life tables, rather than from trial data due to limited deaths. For the comparison with BSC, it was assumed that the estimated TTP for idelalisib would represent the survival benefit for idelalisib (i.e. no PFS and same PPS for BSC is assumed).

Base case utility estimates for the pre- and post-progression disease states (0.81 and 0.62 respectively) were derived from a published UK study reporting EQ 5D values for patients with FL at various disease stages. Disutilities associated with grade 3 or 4 adverse events were based on published estimates used in other advanced cancer health technology appraisals.

Idelalisib drug acquisition costs were estimated. No drug administration costs were estimated for idelalisib as this is an oral therapy, but as most of the comparator regimens were delivered by intravenous infusion, an additional cost for drug administration was estimated for these therapies. The estimated durations of treatment for each chemotherapy and/or rituximab regimen considered were derived from English hospital sources, or published trials. No drug cost was included for BSC in this comparison. Health care resource use for disease management pre and post progression, end of life care and management of the grade 3 and 4 AEs have been based largely on expert clinical opinion from Scotland. End of life health and community care costs over an 8 week period were applied to the palliative care health state based on a Kings Fund report into end of life care.

The base case results for the comparison with further chemotherapy and/or rituximab retreatment was an incremental cost-effectiveness ratio (ICER) of £62,653 per quality-adjusted life-year (QALY) gained based on an incremental cost of £22,217 and a QALY gain of 0.35. The cost difference was driven by the additional drug costs for idelalisib, with some cost offset associated with lower drug administration and disease management costs. A patient access scheme (PAS) was submitted for idelalisib and was assessed by the Patient Access Scheme Assessment Group (PASAG) as acceptable for implementation in NHS Scotland. Under the PAS, a simple discount was offered on the list price. SMC would wish to present the with-PAS cost-effectiveness estimates that informed the SMC decision. However, owing to the commercial in confidence concerns regarding the PAS, SMC is unable to publish these results. As such, only the without-PAS figures can be presented.

Sensitivity analysis demonstrated the ICER was sensitive to uncertainty over the TTP estimate for idelalisib with an ICER range of £33k - £121k/QALY without the PAS based on 95% CIs for the Weibull log (scale) parameter. A scenario removing the assumption of lower TTP for the comparator versus prior therapy increased the ICER to £68.2k/QALY without the PAS, and calculating a pre-progression mortality hazard based on study 101-09 data resulted in an ICER estimate of £71.8k/QALY without the PAS. Scenario assuming 10% lower utility estimates for the health states had a small upward impact on the ICER.

For the comparison against BSC the ICER was estimated to be £40,861/QALY without the PAS based on an incremental cost of £28,381, incremental life years of 0.83 (10 months), and incremental QALYs of 0.69. These results were most sensitive to the uncertainty over the TTP estimate for idelalisib with an ICER range of £28k - £55k/QALY without the PAS.

The main issues with the economic analysis were as follows:

- Limitations in the clinical evidence for idelalisib for the economic analysis, which was from a single arm clinical study in a small sub-group of refractory FL patients. Hence, there is uncertainty over the TTP and survival outcomes estimated for idelalisib. More mature data (June 2014 cut-off) have recently become available for TTP, PPS and OS which are supportive of a clinical benefit for idelalisib, although these data have not been included in the economic model.
- The lack of comparator arm in the trial and lack of a clear standard of care resulted in the company using TTP and ToT data available for the range of prior pre-progression chemotherapy and/or rituximab regimens received by the FL patients in study 101-09. Whilst this is a pragmatic approach, the assumption that this is generalisable to reflect further chemotherapy and/or rituximab retreatment efficacy is uncertain. Feedback from SMC clinical experts was that a range of treatments may be used or re-used in double refractory patients, including rituximab, fludarabine and bendamustine based regimens but it is not clear if the mix of treatments used in practice reflects the mix assumed by the company, which was predominantly rituximab-based.
- Post progression survival was estimated for idelalisib and assumed to be the same for the comparator, which is uncertain. Ideally, in economic models an extrapolation of overall survival is preferable. Overall survival extrapolation was performed for idelalisib and demonstrated high uncertainty across different parametric functions but the company argued this was not used in the economic analysis due to the immaturity of the data (only 40% of patients had died) and a lack of data with which to estimate overall survival for the comparator. However, the estimates of mean overall survival this produced for idelalisib ranged from 1.84 to 3.48 life years (with 2.03 life years with the base case Weibull function), compared to an estimate of 2.56 life years with the TTP +PPS approach used in the economic model. Hence, there is uncertainty over the survival estimate for idelalisib, and the survival outcome for the comparator is not known, meaning the ICER estimate for the comparison with chemotherapy and/or rituximab is highly uncertain.
- The choice of parametric function for TTP, ToT and PPS extrapolation appears reasonable, although scenario analysis was not performed on the best fitting function in each case (which was the log-logistic, although this function is typically associated with a longer tail). The impact of applying the log-logistic function was to improve the ICER to £51.4k/QALY without the PAS, although this should be interpreted in the context of the uncertainty over the survival outcome and benefit for idelalisib, as noted above.

- It is more appropriate to use study 101-09 data to estimate pre-progression mortality than the general population mortality rate. Using the former increases the ICER to £71.8k/QALY without the PAS. The company provided updated estimates using the latest data cut-off, with an estimated ICER of £70k/QALY without the PAS.
- The comparison with BSC is very simplistic and based on an assumption that there is no progression free survival for the comparator. However, feedback received from one SMC clinical expert was that in double-refractory FL patients receiving BSC there would not be an expectation of any PFS time. BSC could be considered to represent a relevant comparator for patients who are truly refractory to all other treatments and hence, the ICER range of £28k - £55k/QALY without the PAS provides an approximate estimate of the potential cost-effectiveness against BSC. However, this ICER range remains subject to the uncertainties associated with the absolute overall survival estimates for idelalisib, and relative to BSC, noted above.

Impact beyond direct health benefits and on specialist services
As noted, quality of life on treatment with idelalisib may be maintained and side effects manageable. This could allow patients to enjoy days not spent in hospital and days free from infections. At the PACE meeting, it was noted that idelalisib offered patients the benefit and convenience of an oral treatment that could be taken at home, thereby avoiding the need for unsightly PICC or Hickman lines which can leave patients more prone to infection and with central chest scarring. Also, as treatment does not lead to hair loss, it may offer body image benefits. It was also noted that idelalisib may offer a psychological benefit for patients and their carers from knowing that a potential third line treatment option is available. Attention was also drawn to the monitoring schedule on treatment being only once per month and that this may reduce the burden on patients and carers compared to other treatment options.

Patient and Clinician Engagement
A Patient and Clinician Engagement meeting was held for this submission. Participants at the PACE meeting indicated a range of potential impacts of the new technology for the patient and families/carers as referred to above.

Costs to NHS and Personal Social Services
The submitting company has estimated that idelalisib treatment would be associated with a net drug budget impact of £56k in year 1 and £139k in year 5 (without the PAS). The submitting company did not estimate any costs outside of the NHS.

The Committee also considered the benefits of idelalisib in the context of the SMC decision modifiers that can be applied when encountering high cost-effectiveness ratios, and agreed that, as idelalisib is an ultra-orphan medicine, SMC can accept greater uncertainty in the economic case.

After considering all the available evidence, the output from the PACE process, and the application of the appropriate SMC modifier, the Committee accepted idelalisib 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 specified Patient Groups.

- Submissions were received from Leukaemia CARE and Leukaemia & Lymphoma Research, both registered charities.

- Both charities have received pharmaceutical company funding in the past two years with Leukaemia CARE receiving funding from the submitting company.

- Follicular lymphoma is the most common form of non-Hodgkin lymphoma, and with no cure currently available, the patient will ultimately relapse. Symptoms can include: swollen lymph nodes, prolonged fever, unexplained weight loss, severe fatigue, irritated or itchy skin, breathlessness and excessive sweating, especially at night. The relapsing, remitting, relentless nature of the disease is particularly difficult for patients and their families to cope with.

- For patients whose disease has been refractory to two previous treatments the options are extremely limited. One of the main options will be to treat with a drug/ drug combination that has already failed. However, as this is likely to include chemotherapy, some patients will be too frail to tolerate this and will therefore be managed with best supportive care.

- Idelalisib offers a treatment option for this patient group that may extend life and control symptoms. It is an oral tablet and can be monitored with monthly clinic visits which are minimally disruptive to patients and their carers.

Additional information: guidelines and protocols

The European Society for Medical Oncology (ESMO) guidelines for follicular lymphoma published in 2014 entitled 'Newly diagnosed and relapsed follicular lymphoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up' provides an outline of consensus-driven recommendations outside clinical studies.[9] For advanced stage III-IV disease, treatment options are as follows. Chemoimmunotherapy such as bendamustine-rituximab (BR), rituximab in combination with chemotherapy such as CHOP (cyclophosphamide, doxorubicin, vincristine and prednisone) (R-CHOP), rituximab in combination with cyclophosphamide, vincristine and prednisone (R-CVP) or in selected cases bendamustine monotherapy.

Antibody monotherapy (rituximab, radioimmunotherapy) or chlorambucil plus rituximab are treatment options in those with a low-risk profile or contraindications for a more intensive chemoimmunotherapy. In younger patients with a high-risk profile or relapse after ASCT, allogeneic stem-cell transplantation may be considered, especially in cases of early relapse or refractory disease.

The guidelines report rituximab maintenance over 2 years has superior results for PFS than alternatives including radioimmunotherapy consolidation and myeloablative consolidation.

The ESMO guidelines state idelalisib has been approved by the European Medicines Agency for treatment in adult patients with double-refractory follicular lymphoma.

The British Committee for Standards in Haematology (BCSH) published guidelines on follicular lymphoma in 2011 entitled 'guidelines on the investigation and management of follicular lymphoma'.[6] For early stage disease, the BCSH recommend radiotherapy, combined modality treatment and observation alone, where no residual disease is present. For advanced stage asymptomatic follicular lymphoma, the BCSH highlight there is no advantage to immediate treatment, particularly so where patients are over 70 years of age and observation may be the most appropriate approach. For patients with relapsed disease, a biopsy procedure is recommended. For relapsed patients requiring treatment, rituximab is the standard therapy for those who have never received rituximab before and for patients who have responded to rituximab, chemotherapy in combination with rituximab is recommended as the standard therapy for relapsed follicular lymphoma patients.

Specific recommendations for older patients with relapsed follicular lymphoma include radioimmunotherapy with Y-Ibritumomab tiuxeten. This treatment is also recommended for patients who are refractory to or intolerant of chemotherapy and rituximab.

Additional information: comparators

Treatment of adult patients with follicular lymphoma that is refractory to two prior lines of treatment depends on a number of patient factors including performance status, duration of disease, histology and duration of response to prior treatment.

Cost of relevant comparators

Drug	Dose Regimen	Cost per course (£)
Idelalisib	**150mg orally twice daily**	**25,229**

Doses are for general comparison and do not imply therapeutic equivalence. Cost from eMIMS on 22/12/14. Cost per course based on mean duration of treatment in the pivotal study of 8.1 months. The cost does not take the patient access scheme into consideration

Additional information: budget impact

The submitting company estimated there to be 24 patients in year 1 rising to 27 patients in year 5 eligible for treatment with idelalisib.

Without the PAS, the submitting company estimated the gross medicines budget impact to be £68k in year 1, £171k in each of years 2-5. It was assumed that there would be displacement of chemotherapy and/or rituximab retreatment resulting in a net medicines budget impact of £56k in year 1, £139k in each of years 2-5.

*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.

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3. The European Medicines Agency CHMP Assessment Report. Idelalisib (Zydelig®) 24/07/2014, EMEA/CHMP/324336/2014 www.ema.europa.eu
4. Gopal AK, Kahl BS, de Vos S, et al. Mature follow up from a phase 2 study of PI3K-delta inhibitor idelalisib in patients with double (rituximab and alkylating agent)-refractory indolent B-cell non-hodgkin lymphoma (INHL). Conference: 56th Annual Meeting of the American Society of Hematology, ASH 2014. Blood 2014;124(21)
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8. European Medicines Agency. Guideline on the evaluation of anticancer medicinal products in man. EMA/CHMP/205/95/Rev.4. 13 December 2012. Available at www.ema.europa.eu
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This assessment is based on data submitted by the applicant company up to and including 13 February 2015.

*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.