Scottish Medicines Consortium
Providing advice about the status of all newly licensed medicines
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dasatinib 20mg, 50mg, 80mg, 100mg and 140mg film-coated tablets (Sprycel®)
SMC No. (1170/16)

Bristol-Myers Squibb Pharmaceuticals Ltd

05 August 2016

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

dasatinib (Sprycel®) is accepted for use within NHS Scotland.

Indication under review: for the treatment of adult patients with newly diagnosed Philadelphia chromosome positive (Ph+) chronic myelogenous leukaemia (CML) in the chronic phase.

In an open-label, phase III study, dasatinib was associated with significantly higher cytogenetic and molecular response rates at 12 months compared with another tyrosine kinase inhibitor. There were no differences in progression-free or overall survival.

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

Overleaf is the detailed advice on this product.

Chairman,
Scottish Medicines Consortium

Published 12 September 2016

Indication

For the treatment of adult patients with newly diagnosed Philadelphia chromosome positive (Ph+) chronic myelogenous leukaemia (CML) in the chronic phase.

Dosing Information

The recommended starting dose of dasatinib for chronic phase CML is 100mg once daily, administered orally. Film-coated tablets must not be crushed or cut in order to minimise the risk of dermal exposure, they must be swallowed whole. They can be taken with or without a meal and should be taken consistently either in the morning or in the evening. Dose increase or reduction is recommended based on patient response and tolerability. In clinical studies, treatment was continued until disease progression or until no longer tolerated by the patient. The effect of stopping treatment on long-term disease outcome after the achievement of a cytogenetic or molecular response (including complete cytogenetic response [CcyR], major molecular response [MMR] and complete molecular response [MR4.5: decrease of 4.5 log below the standard baseline]) has not been investigated.

Therapy should be initiated by a physician experienced in the diagnosis and treatment of patients with leukaemia.

Product availability date

6 December 2010 for this indication. Dasatinib meets SMC orphan criteria.

Summary of evidence on comparative efficacy

Chronic myeloid leukaemia (CML) results in proliferation of abnormal stem cells that compromise normal white blood cell (WBC) production. It progresses through a chronic phase, which may last several years, to an accelerated phase and then a blast phase which has a very poor prognosis. Ninety-five percent of people with CML have a chromosomal abnormality resulting in an oncogene called the 'Philadelphia chromosome' or BCR-ABL. This gene codes for proteins with high tyrosine phosphokinase activity. Dasatinib is a competitive inhibitor at the binding site for BCR-ABL kinase (or other protein kinases) and prevents activation or over-expression of pathways responsible for malignant cells.[1,2]

This submission considers dasatinib for the treatment of adult patients with newly diagnosed Philadelphia chromosome positive (Ph+) chronic myelogenous leukaemia (CML) in the chronic phase. This received marketing authorisation in December 2010 but has not been reviewed by SMC. In April 2012, the National Institute for Health and Care Excellence (NICE) published multiple technology appraisal guidance on dasatinib, nilotinib and standard-dose imatinib for the first-line treatment of CML and did not recommend the use of dasatinib.[3] This guidance takes account of a patient access scheme for nilotinib but not for dasatinib. Healthcare Improvement Scotland has advised that this guidance is valid for Scotland.

The key evidence in newly diagnosed CML patients comes from one pivotal, open-label, randomised, phase III study (DASISION).[2,4,6] Eligible patients were adults diagnosed with Ph+ chronic phase CML by bone marrow cytogenetics within the previous three months. Chronic phase CML was defined as presence of <15% blasts, <20% basophils and <30% blasts plus promyelocytes in the peripheral blood and bone marrow, platelet count of ≥100x10^9/L with absence of extramedullary disease except

for hepatosplenomegaly. They had received no previous treatment for CML except for anagrelide or hydroxyurea and had Eastern Co-operative Oncology Group (ECOG) performance status of 0 to 2. Patients were randomised equally to receive dasatinib 100mg orally once daily with or without food (n=259) or imatinib 400mg orally once daily with food (n=260). Study treatment was continued until disease progression or unacceptable toxicities. Randomisation was stratified by the Hasford risk score (low risk versus intermediate risk versus high risk). During the study, patients were allowed to receive treatment with hydroxyurea to keep the WBC count <50,000/mm^3. Anagrelide could also be used at the investigator's discretion to control platelet counts (>1,000,000/mm^3). Use of granulocyte colony-stimulating factors (G-CSF), granulocyte macrophage colony-stimulating factors (GM-CSF), epoetin or darbepoetin was allowed during the study.

The primary outcome was a confirmed complete cytogenetic response (cCCyR) by 12 months. This was defined as a complete cytogenetic response (CCyR: absence of Ph+ in at least 20 bone marrow metaphases) documented on at least two consecutive assessments at least 28 days apart.[2,4] After a minimum follow-up of 12 months, a significantly higher proportion of patients in the dasatinib than imatinib group achieved a cCCyR by 12 months: 77% (199/259) versus 66% (172/260) patients respectively, p=0.007. Respective cCCyR rates were also numerically higher with dasatinib at subsequent assessments: 80% versus 74% at 24 months; 83% versus 77% at 36 months; 83% versus 78% at 48 and 60 months.[1,2,4]

Secondary outcomes included time in cCCyR (durability), major molecular response (MMR) at any time, median time to cCCyR, median time to MMR, CCyR, MMR by 12 months, progression-free survival (PFS) and overall survival. Interim analyses of secondary outcomes were performed after 12 months follow-up and mature analysis after 5-years. However, since there was no significant difference between groups in the cCCyR at 5-years, according to the study protocol, subsequent statistical testing of sequential secondary outcomes was not performed. Details of primary and secondary outcomes are summarised in table 1.

Table 1: primary and secondary outcomes in the DASISION study[1,2,4,5,6]

	After 12 months follow-up		**After 5-years follow-up**	
	Dasatinib (n=259)	**Imatinib (n=260)**	**Dasatinib (n=259)**	**Imatinib (n=260)**
Primary outcome				
cCCyR by 12 months	77%*	66%	-	-
Secondary outcomes				
Time in cCCyR; between group HR (99.99% CI)	0.7 (0.4 to 1.4), p<0.035		0.79 (0.55 to 1.13)	
MMR at any time	52%**	34%	76%	64%
Median time to cCCyR	3.1 months	5.6 months	3.1 months	5.8 months
Median time to cCCyR: between group HR (99.99% CI)	1.55 (1.0 to 2.3), p<0.0001		1.46 (1.20 to 1.77)	
MMR by 12 months	46%**	28%	-	-
Median time to MMR	6.3 months	9.2 months	9.3 months	15.0 months
Median time to MMR: between group HR (99.99% CI)	2.01 (1.2 to 3.4), p<0.0001		1.54 (1.25 to 1.89)	
CCyR	83%***	72%	88%	84%
Progression-free survival	96%	97%	85%	86%
Overall survival	97%	99%	91%	90%

*p=0.007 versus imatinib; **p<0.0001 versus imatinib; *** p=0.001 versus imatinib

cCCYR: confirmed complete cytogenetic response; HR: hazard ratio; CI: confidence interval; MMR: major molecular response (defined as BCR-ABL transcript level of ≤0.1% on the International Scale which corresponds to a reduction in BCR-ABL transcript level by ≥3 log from the standardised baseline level); CCyR: complete cytogenetic response based on a single bone marrow cytogenetic evaluation

After a minimum of five years follow-up, transformations to accelerated and blast phase CML were reported in numerically fewer dasatinib patients (4.6% [12/259]) than imatinib patients (7.3% [19/260]).[5,6] Additional analyses after five years indicated that dasatinib induced more rapid and deeper responses at early time-points compared to imatinib [1,5] At three months, a higher proportion of dasatinib than imatinib patients achieved BCR-ABL ≤10% (84% versus 64%). In the dasatinib group, of the 84% of patients achieving early molecular response, 3.0% (6/198) experienced transformation compared to 14% (5/37) of those who did not achieve an early molecular response. Estimated PFS and overall survival rates at five years were also higher in those with an early response than not: PFS (89% versus 72%) and overall survival (94% versus 81%). When dasatinib patients who had an early response were compared with those who had not, there were higher rates of CCyR (94% versus 41%), MMR (87% versus 38%) and MR4.5 (54% versus 5%) at five years.[1,6]

The SPIRIT 2 study is an ongoing, open-label, randomised, phase III study in 814 newly diagnosed patients with chronic phase CML comparing dasatinib 100mg daily with imatinib 400mg daily.[7] The primary outcome is 5-year event-free survival and final results are awaited. Interim analysis reported that at 12 months, molecular response (defined as 3-log reduction in BCR-ABL levels) was achieved in 58% (236/406) dasatinib and 43% (173/406) imatinib patients (p<0.001). CCyR was achieved by 51% (207/406) and 40% (163/406) of patients respectively at 12 months. There was no difference between treatments in PFS or overall survival after 34 months of follow-up.[7]

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

Summary of evidence on comparative safety

In the DASISION study, after at least 12 month follow-up, an adverse event was reported in 93% (239/258) of each treatment group and was considered drug-related in 80% (206/258) of dasatinib and 85% (220/258) of imatinib patients. The adverse events were of grade 3 or 4 severity in 30% and 24% of patients respectively, and serious drug-related adverse events were reported in 7.8% and 5.0% of patients respectively. Drug-related adverse events resulted in discontinuation in 5.0% of dasatinib and 4.3% of imatinib patients after 12 months.[1,2,4]

Drug-related adverse events after 12 months in the dasatinib and imatinib groups respectively included: anaemia (90% and 84%), thrombocytopenia (70% and 62%), neutropenia (65% and 58%), fluid retention (19% and 42% including pleural effusion [10% and 0%]), diarrhoea (17% each), headache (12% and 10%), rash (11% and 17%), musculoskeletal pain (11% and 14%), nausea (7.8% and 20%), vomiting (4.7% and 10%), myalgia (6% and 12%) and muscle inflammation (4% and 17%).[4]

After the 12-month follow-up, there was one treatment-related death in each study group, both due to myocardial infarction.[4]

The summary of product characteristics (SPC) notes that after a minimum of five years follow-up in the dasatinib group, the cumulative rates increased by ≤3% for rash (14%), musculoskeletal pain (14%), headache (13%), fatigue (11%), nausea (10%), myalgia (7%), vomiting (5%), and muscle inflammation or spasms (5%). Cumulative rates of fluid retention and diarrhoea were 39% and 22%, respectively.[1]

After five years, drug-related adverse events resulted in discontinuation in 16% of dasatinib and 6.6% of imatinib patients but no new adverse events were reported. There were higher rates of grade 3 or 4

haematological adverse events in the dasatinib than imatinib group (including neutropenia [29% versus 24%], anaemia [13% versus 9%] and thrombocytopenia [22% versus 14%]) but drug-related non-haematological adverse events were similar or less frequently reported in the dasatinib group with the exception of pleural effusion. At five years, drug-related pleural effusion was reported in 28% of dasatinib and 0.8% of imatinib patients.[6]

Summary of clinical effectiveness issues

The management of CML changed with the development of tyrosine kinase inhibitors, initially imatinib, which became the standard of care, and patients who respond to treatment can expect to have normal life expectancy.[8] The NICE guidance for the first-line treatment of CML recommends imatinib and nilotinib as treatment options, but not dasatinib.[3] The European public assessment reports (EPAR) notes that in newly diagnosed chronic phase CML, eight years of follow-up with imatinib from the IRIS study was associated with a CCyR in 82% of patients and estimated 8-year event-free survival and overall survival of 81% and 85%, respectively. Despite these results, approximately 42% of patients discontinued imatinib during the 8-year follow-up so there is considered to be a need for further treatments.[2] Dasatinib meets SMC orphan criteria.

The pivotal DASISION study compared dasatinib with imatinib. The primary outcome was response assessed cytogenetically (cCCyR at 12 months), which is considered a validated surrogate outcome for PFS by the EMA, based on data with imatinib.[2] The response to tyrosine kinase inhibitors is the most important prognostic factor, and optimal response (cytogenetic and/or molecular response) is considered to be associated with the best long-term outcome, with a duration of life comparable with that of the general population.[7,]

However, results to five years are now also available with dasatinib. There was a significantly higher cCCyR at 12 months with dasatinib compared with imatinib and the treatment difference was considered clinically valuable. The results were supported by a significantly higher MMR with dasatinib than imatinib after 12 months and numerically higher rates after 12 months (formal statistical analysis after 5 years was not performed due to the sequential statistical testing). Although dasatinib appeared to produce a faster and deeper response than imatinib, and patients achieving an early response to dasatinib had better PFS and overall survival than dasatinib patients who did not, the longer term effect on survival versus imatinib remains to be determined. Results to 5 years found no significant difference between dasatinib and imatinib in PFS or overall survival.[1,4,5,6]

The EPAR notes that the safety profiles of both dasatinib and imatinib after the 12-month minimum follow-up in the DASISION study did not indicate any new or unexpected major concerns. There are some differences between the safety profiles of the two medicines.[2]

Quality of life data were not measured during the DASISION study.

There are no direct data comparing dasatinib with nilotinib in the first-line treatment of chronic phase CML. The submitting company presented results of an updated network meta-analysis (NMA) comparing dasatinib with nilotinib and imatinib. This used Bayesian methods and included a total of six studies. The key outcomes reported were CCyR and partial cytogenetic response (PCyR) by 12 months. Safety was not assessed. The NMA results for cytogenetic responses by 12 months were better with dasatinib and nilotinib than with imatinib, and results with dasatinib and nilotinib were similar. The NMA results were supported by several published indirect comparisons which generally found no or minimal differences between dasatinib and nilotinib.

Nilotinib requires twice daily dosing, approximately 12 hours apart and without food. The SPC recommends that no food is consumed for two hours before and for at least one hour after each dose. Therefore, dasatinib offers an advantage in administration over nilotinib, being taken once daily with or without food. As noted above, there are differences in the adverse events associated with the different tyrosine kinase inhibitors and individual patient characteristics and co-morbidities may make one medicine more suitable for a particular patient than another. Clinical experts consulted by SMC considered that the place in therapy of dasatinib is in high risk patients as an alternative to nilotinib.

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

Summary of comparative health economic evidence

The company submitted a cost-utility analysis of dasatinib for use in the treatment of adult patients with newly diagnosed Ph+ CP CML. The comparators included were imatinib and nilotinib. SMC clinical expert responses confirm the comparators are appropriate, with imatinib being the main first-line treatment used in practice. Clinical experts indicated dasatinib would be used as an alternative to nilotinib in practice. Subsequent treatment lines were also modelled, which included nilotinib, bosutinib, ponatinib and best supportive care.

A 'time in state' model was used consisting of 3 health states: chronic phase (pre-progression), accelerated phase/blast phase (post-progression), and death. A lifetime horizon and monthly cycle length were used. During the chronic phase, patients could receive a number of treatment lines but during accelerated/blast phases, patients were assumed to receive final line therapy based on a weighted average of tyrosine kinase inhibitors, chemotherapy, plus palliative care. Within the chronic phase, patients were categorised according to their level of response to treatment. The response categories were complete response (CCyR at 12 months), partial response (partial cytogenetic response [PCyR] at 12 months) and failure. The nature of the response to treatment at 12 months was used in the model as a surrogate outcome predictor of overall survival. The company noted that the relationship between CCyR (and other surrogate outcomes) and longer term outcomes in CML is well established.

The data source for the response rates used in the model was the NMA, which showed better cytogenetic and molecular responses with dasatinib versus imatinib at 12 months (but note the benefit was not significant at later time points), and similar responses for dasatinib and nilotinib. The CCyR rates at 12 months applied in the model were 82.76%, 69.6% and 78.7% for dasatinib, imatinib, and nilotinib respectively. There were no differences in overall survival between the three treatments reported in the NMA. Overall survival data up to 60 months were available from the DASISION study and used in the model to derive pooled estimates of survival according to response rate at 12 months. The PFS and overall survival curves were then extrapolated using parametric functions, with CCyR at 12 months resulting in the longest survival and longest time in PFS. For overall survival, the log-normal curve was selected to extrapolate survival for patients with CCyR and PCyR, with survival of patients who failed to respond at 12 months extrapolated using the Weibull curve. For PFS, the log-normal curve was selected to extrapolate PFS for all response categories.

Utility values were derived from a published study where the time trade-off technique was used to estimate utility values for CML health states from the general public in Canada, USA, UK and Australia. A utility value of 0.85 was used for responders in the chronic phase, with non-responders assigned a value of 0.68. The utility value for patients with progressed disease (accelerated/blast phase) was estimated to be 0.681. For grade 3/4 adverse events, utility decrements were based on published studies of chemotherapy treatments, with particular focus on previous NICE assessments.

Where utility decrements for a particular adverse event could not be identified from the literature, a 5% utility decrement (-0.05) was assumed.

Medicine costs of TKIs used at first and subsequent treatment lines were included. Post-progression medicines costs were based on a range of chemotherapy and palliative treatment costs. Adverse event treatment costs were also included. A patient access scheme (PAS) is in place for nilotinib, which was included in the model using an estimate of the nilotinib PAS. As a simplifying assumption, subsequent lines of therapies with a PAS in place (ie nilotinib and bosutinib) were included using the list prices. Other resource use included a range of tests and interventions, plus inpatient stays, nurse visits and outpatient haematologist/oncologist visits. For post-progression and adverse events, the resource use estimates were based on a UK costing study assessing resource use during treatment of CML.

A 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 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. For the comparison with imatinib, the base case result without the PAS was an incremental cost-effectiveness ratio (ICER) of £134,527 per quality-adjusted life-year (QALY) gained. With the PAS, dasatinib became a cost-effective treatment option. The results were sensitive to the response rates and discontinuation rates, with the ICER increasing when the dasatinib CCyR rate or imatinib discontinuation rates were reduced by 20%. Similarly, the ICER increased when the dasatinib discontinuation rate was increased by 20%.

For the comparison with nilotinib, in the base case results without the PAS, the ICER was estimated to be £227,449 per QALY. A cost-minimisation analysis was also provided which showed that dasatinib with the PAS was cost-effective versus nilotinib.

The following limitations were noted:

- For the comparison with imatinib, while the DASISION study evidence suggests superiority in terms of response rates with dasatinib at 12 months, the significant benefit was not consistently maintained at later time points. To explore this further, the company was asked to provide a cost-minimisation analysis versus imatinib, which showed that dasatinib with the PAS was cost-effective. SMC clinical expert responses indicate adverse events differ between these treatments and can be important in determining the choice of first-line therapy. Therefore, the company also provided the results of the cost-minimisation analysis with the costs of managing adverse events included, and in this analysis, dasatinib with the PAS remained a cost-effective treatment option.
- The results are sensitive to the response rate, whereby reducing the dasatinib CCyR rate by 20% increased the ICER. In this analysis, the response rate with dasatinib is lower than the response rate with imatinib. However, this is a particularly conservative analysis as the DASISION study data showed dasatinib is likely to be more effective than imatinib in terms of increased CCyR.
- There is some uncertainty associated with the estimation of overall survival in the model. There is no evidence of improved survival with dasatinb and therefore the survival gains are estimated based on the link between CCyR at 12 months and overall survival. The results were sensitive to using alternative parametric functions. However, the company subsequently provided further validation of the base case survival estimates by comparing the model estimates with general population estimates. At year 40 (aged 86) in the model, 17.4% of patients are still alive in the dasatinib arm, compared to 34.5% in the general population. The company also noted that the life year gains estimated in the model were broadly consistent

with those estimated by NICE in the multiple technology appraisal of dasatinib, imatinib and nilotinib.

- For the comparison with nilotinib, the cost-minimisation analysis is the more relevant analysis, rather than the cost-utility analysis presented in the base case. The NMA results suggest comparable efficacy between dasatinib and nilotinib, and with the PAS, dasatinib was estimated to be a cost-effective treatment option. This result was maintained when the impact of adverse events was included. An additional sensitivity analysis was also provided which included adverse events and also assumed the subsequent treatment lines would be the same in both arms. Dasatinib with the PAS remained cost-effective in this scenario.

Overall, dasatinib remained cost-effective in the majority of analyses. Therefore, despite the limitations outlined above, the economic case has been demonstrated.

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

Summary of patient and public involvement

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

- We received patient group submissions from the Leukaemia Care and the Chronic Myeloid Leukaemia Support Group (CMLSG).

- Leukaemia Care has received <10% pharmaceutical company funding in the past two years, including from the submitting company. CMLSG has received 95% pharmaceutical company funding in the past two years, including from the submitting company.

- Chronic myelogenous/myeloid leukaemia (CML) is a rare, chronic form of leukaemia. Patients have to cope with the psychological and emotional side effects of a cancer diagnosis as well as an often profound symptom burden.

- Current first line treatments are imatinib and nilotinib.

- Nilotinib has a twice daily fasting requirement which causes practical difficulties and is an added pressure to remaining adherent for a lifetime on treatment. Regular losses of adherence, even if minor, increase the likelihood of loss of response to treatment.

- In comparison with imatinib, dasatinib can enable patients to achieve positive, more durable response rates in a shorter time frame. It has similar side effects to imatinib and these are considered to be manageable. Dasatinib offers patients an alternative treatment option.

Additional information: guidelines and protocols

The National Institute for Health and Care Excellence (NICE) published Technology Appraisal Guidance 251: Dasatinib, nilotinib and standard-dose imatinib for the first-line treatment of chronic myeloid leukaemia in April 2012.[3] This recommended standard-dose imatinib and nilotinib (at the discount agreed as part of patient access scheme), but not dasatinib, as options for the first-line treatment of adults with chronic phase Ph+ CML.

The European LeukemiaNet published their recommendations for the management of chronic myeloid leukemia in 2013.[9] The guideline recommends that patients with newly diagnosed chronic phase CML

receive either imatinib 400mg once daily, nilotinib 300mg twice daily or dasatinib 100mg once daily as a first-line therapy for CML. The choice of the tyrosine kinase inhibitor must take into account tolerability and safety, as well as patient characteristics, particularly age and comorbidities, which may be predictive of particular toxicities with the different medicines.

The European Society for Medical Oncology (ESMO) published: Chronic myeloid leukemia: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up in 2012.[10] The guideline recommends that patients with newly diagnosed chronic phase CML receive either imatinib 400mg once daily, nilotinib 300mg twice daily or dasatinib 100mg once daily as a first-line therapy for CML and notes that there is no strong evidence to make recommendations on choice of medicine.

Additional information: comparators

Imatinib and nilotinib.

Cost of relevant comparators

Drug	Dose Regimen	Cost per year (£)
Dasatinib	**100mg orally once daily**	**30,394**
Nilotinib	300mg orally twice daily	31,627
Imatinib	400mg orally once daily	23,620

Doses are for general comparison and do not imply therapeutic equivalence. Cost for dasatinib from Dictionary of Medicines and Devices (dm&d) on 5 May 2016. Costs for nilotinib and imatinib from eVadis on 3 May 2016.

Additional information: budget impact

The submitting company estimated there would be would be 41 patients eligible for treatment with dasatinib in year 1 and 195 patients in year 5.

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

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

References

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

1. Bristol-Myers Squibb Pharmaceutical Ltd. Sprycel® summary of product characteristics, last updated 2 April 2015.

2. European Medicines Agency. European Public Assessment Report: Sprycel (dasatinib) b, CHMP assessment report, EMA/761358/2010, 29 November 2010. www.ema.europa.eu

3. National Institute for Health and Care Excellence. NICE Technology Appraisal Guidance 251. Dasatinib, nilotinib and standard-dose imatinib for the first-line treatment of chronic myeloid leukaemia (part review of technology appraisal guidance 70). 25 April 2012. Available from: https://www.nice.org.uk/guidance/ta251.

4. Kantarjian H, Shah NP, Hochhaus a et al. Dasatinib versus imatinib in newly diagnosed chronic-phase chronic myeloid leukemia. N Engl J Med 2010;362:2260-70.

5. Cortes J, Saglio G, Baccarani M et al. Final study results of the phase 3 dasatinib versus imatinib in newly diagnosed chronic myeloid leukemia in chronic phase (CML-CP) trial (DASISION, CA180-056) [abstract] Blood 2014;124 (21):152.

6. Cortes JE, Saglio G, Kantarjian HM et al. Final 5-year study results of DASISION: the dasatinib versus imatinib study in treatment-naive chronic myeloid leujemia patients trial. J Clin Oncol 2016 doi:10.1200/JCO.2015.64.8899

7. O'Brien SG, Hedgley CA, Adams S et al. Spirit 2: An NCRI randomised study comparing dasatinib with imatinib in patients with newly-diagnosed CML [oral abstract] Blood;124(21):517

8. Jabbour E, Kantarjian H et al. Chronic myeloid leukemia: 2016 update on diagnosis, therapy and monitoring. Am J Hematol 2016; 91:253-56.

9. Baccarani M, Deininger MW, Rosti G, et al. European LeukemiaNet recommendations for the management of chronic myeloid leukemia: 2013. Blood. 2013;122(6):872-84.

10. Baccarani M, Pileri S, Steegmann J-L, et al. Chronic myeloid leukemia: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Annals of Oncology. 2012;23(suppl 7):vii72-vii7.

This assessment is based on data submitted by the applicant company up to and including 17 June 2016.

*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.