National Cancer Medicines Advisory Group (NCMAG) Programme

NCMAG117 Dasatinib | Advice Document v1.0 | July 2024

Dasatinib for the treatment of adult patients with Philadelphia chromosome positive (Ph+) acute lymphoblastic leukaemia (ALL) with resistance or intolerance to prior therapy [A]

NCMAG Decision | this on-label, off-patent use is **supported**

This advice applies only in the context of the confidential pricing agreements in NHSScotland, upon which the decision was based, or confidential pricing agreements or list prices that are equivalent or lower.

[A] NCMAG considers proposals submitted by clinicians for use of cancer medicines outwith SMC remit. For more detail on NCMAG remit please see our website.

Decision rationale

After consideration of all the available evidence regarding the clinical benefits and harms, the Council were satisfied with the clinical effectiveness case for dasatinib in the proposed population. After consideration of all relevant information under the decision-making framework for value judgements the Council made a decision to support this use.

Governance Arrangements

Each NHS board must ensure all internal governance arrangements are completed before medicines are prescribed. The benefits and risks of the use of a medicine should be clearly stated and discussed with the patient to allow informed consent.

Proposal Details	
Proposers	NHSScotland Haematologists
Medicine Name	Dasatinib
Cancer type	Acute Lymphoblastic Leukaemia (ALL)
Proposed off-patent and on-label indication	Philadelphia chromosome positive (Ph+) ALL with resistance or intolerance to prior therapy.
Medicine Details	Form: Film coated tablets Dose: 140mg once daily

Treatment Marketing Authorisation	Adult patients with Ph+ acute lymphoblastic leukaemia (ALL) and lymphoid blast chronic myelogenous leukaemia (CML) with resistance or intolerance to prior therapy.
Advice eligibility criteria	Confirmed Ph+ ALL with demonstrated resistance or intolerance to prior therapy

1. Current Management Context

Acute Lymphoblastic Leukaemia incidence and symptoms

Acute lymphoblastic leukaemia (ALL) is a blood cancer that develops rapidly with the overproduction of immature B-cells or T-cells. The vast majority of Philadelphia-positive (Ph+) ALL cases are of B-cell lineage[1]. Ph+ ALL is caused by a translocation of parts of chromosomes 9 and 22 which creates the BCR-ABL1 driver mutation oncogene.

In 2021, there were 30 cases of ALL registered in Scotland among individuals aged 20 years and older[2]. Philadelphia-positive ALL is more common in older patients, representing 25% of adult cases of ALL and rising to over 50% in patients over 50 years old[3]. It is estimated that approximately 20 to 40% of patients treated with imatinib in the front-line setting will relapse[4, 5].

Common symptoms of ALL include spontaneous bleeding, fatigue, infections, fever, weight loss, and swollen lymph nodes[6].

Efficacy outcomes used in Ph+ ALL

In general, older studies measured efficacy using outcomes like Major Haematological Response (MaHR), which is either complete bone marrow recovery or the absence of leukaemia cells, to determine remission. A Complete Cytogenetic Response (CCyR), a more sensitive genetic analysis of bone marrow, is defined as the absence of Ph+ leukaemia cells. Minimal residual disease (MRD), a more recently developed highly sensitive measure of response, can be used to predict patient outcomes and guide treatment decisions[7].

Ph+ ALL treatment pathway and prognosis

First line therapy usually includes a targeted tyrosine kinase inhibitor (TKI) such as imatinib. When disease relapses on/after this, the primary goal of therapy is to induce complete remission and achieve disease control. Relapsed disease has poor overall survival and has been reported to range from 6 to 9 months with treatment and under 2 months with best supportive care only[8, 9]. Curative options are usually limited to a stem cell transplant (SCT) or chimeric antigen receptor (CAR)-T cell therapy, but outcomes remain poor. A SCT requires a complete remission to be achieved, or for CAR-T therapy, the leukaemia to be controlled long enough until infusion of the CAR-T therapy[6,8]. The option of a SCT or CAR-T is considered based on the patient's age and co-morbidities, and in the case of SCT, the availability of a suitable donor.

Pharmacology of dasatinib

Dasatinib is a TKI that inhibits the BCR-ABL protein, along with other signalling pathways in leukaemia cells, leading to leukaemia cell death. It is a second-generation TKI that can overcome leukaemia cell resistance to imatinib (excluding resistance due to T315I mutation) as well as being able to cross the blood-brain barrier[13].

National and international context for proposed on-label use

Dasatinib and other TKIs are not routinely accessible either as monotherapy or in combination with other treatments, for patients with Ph+ ALL who are resistant or intolerant to prior therapy in Scotland. Chemotherapy is routinely accessible to all but has limited efficacy on its own. Inotuzumab ozogamicin is only approved for those intended to proceed to STC and who have a specific disease type[10]. Ponatinib is only routinely accessible for patients who are resistant or intolerant to dasatinib, or for those with the T315I mutation (which is inherently resistant to dasatinib)[11]. This effectively makes ponatinib only available in the third-line setting, following the failure of dasatinib, which is currently only accessible through individual patient requests. Dasatinib is anticipated to be used on its own or in combination with other treatments. It is not anticipated that dasatinib would displace other treatments.

International guidelines support the use of dasatinib or other TKIs for relapsed Ph+ ALL. The European Leukaemia Network (ELN), the European Society for Medical Oncology (ESMO), and the National Comprehensive Cancer Network (NCCN) guidelines support the use of an alternative TKI in relapsed disease, with or without chemotherapy or immunotherapy (inotozumab ozagamicin or blinatumomab). Treatment decisions are based on identified genetic mutation resistance profiles and comorbidities. These treatments can be used as a bridge to SCT or CAR-T therapy, if appropriate[6, 8, 12]

2. Evidence Review Approach

A literature search to identify clinical and economic evidence was conducted on key electronic databases including MEDLINE, Embase, the Cochrane Database of Systematic Reviews, major international health technology agencies, as well as a focused internet search. The search strategy comprised both Medical Subject Headings and keywords. The main search concepts were dasatinib, Philadelphia chromosome positive and acute lymphoblastic leukaemia. Titles and abstracts were screened by one reviewer with a second opinion sought by another reviewer when required. The included key studies were critically appraised using the Cochrane risk of bias version 2.0 tool and the Risk of Bias in non-randomised studies of interventions (ROBINS-I)[14, 15].

3. Clinical Evidence Review Summary

Clinical Efficacy Evidence

Evidence for the use of dasatinib where resistant or intolerant to prior therapy

Two studies were identified as being relevant to this proposal: one phase III study and one phase II single arm study[16, 17].

Lilly et al[16] conducted a multicenter, open label, international phase III study to compare the efficacy of two dasatinib dosing regimens (140mg once daily versus 70mg twice daily) including patients with Ph+ ALL who were resistant or intolerant to imatinib. The study included patients aged 15 years or older with primary or acquired haematologic resistance or intolerance to imatinib. Patients with adequate hepatic and renal function and an Eastern Cooperative Oncology

Group (ECOG) performance status score of 0-2 were included. Patients received dasatinib at a dose of either 140mg once daily or 70mg twice daily until disease progression, unacceptable toxicity, or withdrawal. The 140mg once daily dose aligns with the proposed, on-label, dosing regimen. The majority of patients received prior treatment with imatinib at doses of either 400-600mg daily (32%) or over 600mg daily (76%). More than half of patients (56%) had a treatment duration of less than 1 year, and 40% had treatment durations between 1 and 3 years. Imatinib status was characterised as; primary resistance (8%), acquired resistance (73%) and intolerance (19%).

The primary outcome was rate of major haematologic response (MaHR) defined as complete haematologic response or no evidence of leukaemia, secondary outcomes included overall haematologic response (OHR) defined as complete haematologic response, no evidence of leukaemia or minor haematologic response. On completion of treatment, patients were followed up for 30 days.

The START-L study[17] was a phase II single arm, open label, multicentre, international study to evaluate the efficacy of dasatinib in patients with Ph+ ALL who were resistant or intolerant to imatinib. The study included patients aged 15 years or older with primary or acquired haematologic resistance or intolerance to imatinib. Patients with adequate hepatic and renal function and ECOG performance status score of 0-2 were included. Patients received dasatinib at a dose of 70mg twice daily, which does not align with the proposed regimen. All patients received prior treatment with imatinib at doses of 400-600mg daily (53%) or over 600mg daily (47%). More than half of patients (53%) had treatment durations ranging from 1 to 3 years, and 44% had treatment durations less than 1 year. Imatinib status was characterised as imatinib resistance (94%) and imatinib intolerance (6%).

The primary outcome was rate of MaHR defined as best haematologic response of complete haematologic response or no evidence of leukaemia and OHR defined as best haematologic response of complete haematologic response, no evidence of leukaemia or minor haematologic response. On completion of treatment, patients were followed up for 30 days.

In the Lilly et al study patient baseline characteristics were generally well balanced between the groups with some differences; the median duration of disease was longer in the 70mg twice daily arm compared to the 140mg once daily arm (19.1 versus 11.5 months) and the median platelet count was higher in the 140mg once daily arm compared to the 70mg twice daily arm (119 versus 73 [$x10^{-3}/mm^3$]).

In the Lilly et al[16] study, the median duration of treatment was 3.4 months in the once daily arm and 2.5 months in the twice daily arm. The median age was 52 years (range 15-80), 48% were male and just over half had a mutation of the BCR-ABL oncogene. The majority of patients had an ECOG status of 0-1 (75%). In the START-L trial the median duration of treatment was 3.2 months (range 0.2 to 11 months), the median age was 46 years (range 15-85), 64% were male, and 78% had the BCR-ABL mutation. In the Lilly et al study haematologic response was similar between the once daily and twice daily doses with slightly greater cytogenic responses in the once daily dose

compared to the twice daily dose (Table 1). Responses in the START-L study[17] were similar to those seen in the Lilly et al study (Table 1).

Table 1: Key outcomes for studies of second line use of dasatinib

	Lilly[16]		START-L[17]
	140mg once daily n=40	70mg twice daily n=44	70mg twice daily n=36
OHR n(%) [95% CI]	19 (48%) [32-64]	18 (41%) [26-57]	18 (50%)
MaHR[a] n(%) [95% CI]	15 (38%) [23-54]	14 (32%) [19-48]	15 (42%)
• CHR[a] n(%)	13 (33%)	11 (25%)	12 (33%)
• NEL[a] n(%)	2 (5%)	3 (7%)	3 (8%)
MCyR n(%) [95% CI]	28 (70%) (54-83)	23 (52%) (37-68)	21 (58%)
• CCyR n(%)	20 (50%)	17 (39%)	21 (58%)
• PCyR n(%)	8 (20%)	6 (14%)	0
Median PFS (months) (95% CI)	4 (2.9-5.6)	3 (2.0-4.2)	3.3
Hazard ratio (95% CI)		0.92 (0.58-1.47)	
Median OS (months) (95% CI)	6.5 (4.5-9.8)	9.1 (4.8-13.2)	NR
Hazard ratio (95% CI)		1.26 (0.78-2.04)	
Discontinuations due to Transplant	2	3	3

[a]Best haematologic response lasting for at least 28 consecutive days
key: OHR = objective haematologic response, CI = confidence interval, MaHR = major haematologic response, CHR = complete haematologic response, NEL = no evidence of leukaemia, MCyR = major cytogenic response, CCyR = complete cytogenic response, PCyR = partial cytogenic response, PFS = progression free survival, OS = overall survival.

Patient reported outcomes

No patient reported outcome data were reported across the included studies.

Safety evidence

This is an on-label use which has been considered by a regulator to have an acceptable safety profile.

There is no data comparing the safety profile of dasatinib with other cancer medicines or best supportive care.

Lilly et al[16] reported Grade 3/4 events were similar with once and twice daily dosing: leukocytopenia (53% and 70%), neutropenia (67% and 72%), thrombocytopenia (72% and 60%) and pleural effusions (3% versus 13%). There was one treatment related death reported in the twice daily group.

The START-L study[17] reported that the safety profile was in line with the stage of disease. The most significant grade 3/4 haematologic AE (in over 5%) was febrile neutropenia (11%) and non-haematological AEs (in over 5%) included diarrhoea (8%) and asthenia (8%) all of which were managed with dose reductions and/or interruptions. Two patients discontinued treatment due to toxicity.

Quality assessment of clinical evidence

The Lilly et al study was a phase III randomised study and START-L was a single arm phase II study, both were multicentre open label studies. Overall, the included studies were assessed to have low risk of bias (RoB). In the Lilly et al[16] study, randomisation was completed using a block randomisation procedure, thus limiting the risk of selection bias. As both trials used an open label design, they are at risk of outcome detection bias for subjective outcomes.

Clinical effectiveness considerations

Dasatinib can induce complete remission in Ph+ ALL patients.

START-L and Lilly et al studies demonstrated that dasatinib can induce complete remission in patients with imatinib resistant or intolerant disease[16, 17]. The complete cytogenetic response ranged from 39% to 58%, and the complete haematologic response ranged from 25% to 33%. A lower complete haematologic response compared to the cytogenetic response is expected due to incomplete bone marrow recovery, despite the absence of Ph+ leukaemia cells[16, 17].

Across the dasatinib arms of the Lilly et al and START-L studies median PFS ranged from 3 to 4 months[17]. There is some uncertainty regarding the START-L study's PFS estimate, as confidence intervals were not reported, and the median follow-up was 8 months, with 58% of patients having progressed or died[17]. The Lilly et al study reported median overall survival ranging from 6.5 months (95% CI 4.6-9.8) in the once-daily arm to 9.1 months (95% CI 4.8-13.2) in the twice-daily arm[16]. Despite 34 out of 40 patients dying in the once-daily arm and 33 out of 44 in the twice-daily arm, the confidence intervals are wide, likely due to the small numbers in each arm and the considerable variation in patient outcomes[16].

The NHS Scotland Cancer Medicines Outcomes Programme – Public Health Scotland (CMOP-PHS) provided a management report on the use of TKIs in patients with Philadelphia positive ALL in Scotland from 2015-2023. This report was used to assess the generalisability of findings reported in the literature to patients in Scotland. The CMOP-PHS report is available on request from PHS.

There is uncertainty on the comparative efficacy of dasatinib to other treatments.

The available evidence is non-comparative with no placebo-controlled arms, active control arms using alternative TKIs or active control arms without a TKI. Accepted clinical practice is to use a second or third generation TKI after imatinib failure. This makes the relative efficacy of dasatinib alone or in combination with either chemotherapy or immunotherapy, or compared to alternative TKIs very uncertain. Relapsed ALL progresses rapidly without active treatment, with reported overall survival less than two months in patients who relapse after SCT and do not receive further treatment[9]. Dasatinib is anticipated to be used on its own or in combination with other treatments. It is not anticipated that dasatinib would displace other treatments. There are no routinely available TKIs in Scotland for use in second line setting but individual requests may be considered.

The patient populations in the studies may reflect those treated in clinical practice although there are some generalisability concerns

Both the Lilly et al study and the START-L study only included patients who were either intolerant to or resistant to imatinib, which aligns with the proposed use of dasatinib[16, 17]. Almost all patients in the studies had undergone prior chemotherapy, with 25 to 42% having had a prior stem cell transplant. The dosage of prior imatinib was also similar to what would be expected in routine clinical practice.

The median age in the Lilly et al study was 52 and 51 years in the once-daily and twice-daily arms, respectively and the median age in the START-L study was 46 years which may be younger than the patient population treated in Scotland. [16, 17]

Both studies prohibited the use of other anti-cancer therapies alongside dasatinib however in clinical practice, dasatinib is frequently used in combination with chemotherapy or immunotherapy. The Lilly and START-L studies do not provide efficacy or safety information for dasatinib in combination with other treatments.[16, 17].

Three of 65 patients in the Lilly et al study and 6 of the 31 patients in the START-L study with identifiable mutations had the T315l mutation, respectively. This mutation confers inherent resistance to dasatinib, which may have resulted in lower efficacy in these studies compared to the population treated in Scotland. Ponatinib is routinely available in Scotland for patients with the T315l mutation.

The safety profile of once daily dasatinib dosing in the relapsed setting is uncertain but there were no unexpected toxicities.

Dasatinib's safety profile is well described in the chronic myeloid leukaemia population, based on study data for nearly 1,000 patients but there is less robust safety data for Ph+ ALL population[18].

The proposal and the licensed dosing regimen are for once-daily dosing. The EMA updated the product licence based on evidence from the Lilly et al study, which demonstrated similar efficacy but a more favourable safety profile with the 140 mg once daily dosing[19]. The START-L study used a twice-daily dosing regimen, which may limit the generalisability of these results for safety[17]. The observed side effects were consistent with the known safety profile, with most grade 3 or 4 adverse events being haematological in nature. Diarrhoea, infection, bleeding, pleural effusions and fluid accumulation were the most serious non-haematological adverse effects.

4. Patient group summary

A joint Patient group partner statement was received from Blood Cancer UK and Leukaemia care, both organisations are registered charities. Blood Cancer UK has received 1.61% pharmaceutical company funding in the past two years. Leukaemia Care has received 18.82% pharmaceutical company funding in the past two years. Representatives from Leukaemia Care participated in the NCMAG Council meeting. A representative from Leukaemia Care participated in the NCMAG Council meeting. The key points from the joint submission are summarised below:

- ALL is a rare and rapidly progressing form of leukaemia. ALL symptoms appear quickly with many patients receiving a diagnosis following an emergency presentation, which the patient group partners noted can have a profound impact on the psychological health of the patient.
- Symptoms include fatigue, bone and joint pain, rapid weight loss and bruising and bleeding, which can impact on patients' ability to participate in normal activities like work, education and exercise.
- Introduction of dasatinib may lead to better outcomes in the resistant and intolerant population, it would improve treatment options where there is no routinely accessible TKI following imatinib. The absence of a routinely accessible TKI in this space has a substantial emotional burden on patients.

5. Benefit-risk balance

This is an on-label use which the UK medicines regulator has judged to have a favourable benefit-risk balance[18]. Dasatinib has been shown to induce complete remission in some patients who are resistant or intolerant to prior imatinib therapy.

6. Council Review |Clinical benefit-risk balance evaluation

After consideration of all the available evidence regarding the clinical benefits and risks, the Council were satisfied that the case had been made for the clinical effectiveness of dasatinib. Under the decision-making framework for value judgements, Council considered the clinical case to be compelling.

7. Economic Evidence Review Summary

Economic Overview

Type of economic evaluation

No relevant published cost-utility analysis was identified in the literature search. Therefore, a de-novo cost-comparison was performed.

Population, intervention, comparator and outcomes

The patient population consists of adults with Ph+ ALL, resistant or intolerant to prior therapy, and eligible for treatment with dasatinib. As discussed in Section 1, in the absence of routinely accessible TKI for this patient population, the comparator is management with no TKI. The economic analysis, being a cost-comparison, did not take into account clinical outcomes or health-related quality of life.

Costs

Dasatinib was costed at 140mg once daily until discontinuation. In the patient population under consideration, the approval of dasatinib for treatment is not anticipated to displace any existing TKI.

To calculate the average cost per patient, treatment duration was estimated based on the proxy of median PFS of 4 months. This value was derived from the group receiving a daily dose of 140mg in Lilly et al. (2010)[16] (Table 1).

Results

These exclude value added tax (VAT).

Using the BNF NHS indicative price for the cheapest generic alternative (accessed May 2024), the medicine acquisition cost of 140 mg of dasatinib, taken once daily for a treatment duration of 4 months, was £4,870 per patient.

The Council considered results using confidential NHSScotland medicine pricing agreements in decision making. NCMAG is unable to publish the results using confidential pricing due to commercial in confidence issues.

Cost-effectiveness considerations

Generalisability of the cost comparison

NHSScotland national framework prices for dasatinib were considered in confidence to increase the generalisability of the net costs. As of May 2024, the branded dasatinib is available as a single 140mg tablet with confidential Patient Access Schemes (PAS). The confidential national framework price of lower cost generic versions, in strengths of 100mg and 20mg as film-coated tablets, was used to calculate combined dose medicine acquisition cost.

Limitations of the cost comparison

As there is no routinely accessible TKI for this patient population, and medicines which are known to be frequently accessed through individual requests are not uniform throughout Scotland, no TKI comparator was considered. Therefore, the results of the cost-comparison show that dasatinib is a cost-increasing intervention compared to management with no TKI. Given the evidence supporting the clinical benefit of this intervention, it may offer clinical benefit compared to its comparator. However, given the absence of a quality-adjusted life year (QALY) estimate, an incremental cost-effectiveness ratio (ICER) is not available, and the cost-effectiveness remains unknown.

The analysis uses median PFS duration as a proxy for the average duration of treatment. However, this may be subject to uncertainty as the duration of treatment can vary widely due to patient-specific factors other than relapse, such as intolerance, resistance, transplantation, or death. Some patients may require dose reductions and/or interruptions in treatment, which is not accounted for. Due to data paucity, it is difficult to estimate the effect of these parameters on total costs.

There is uncertainty around subsequent treatments following dasatinib. The cost comparison analysis does not include the potential costs, or cost avoidance, of these treatments.

Given the estimated low patient numbers the costs associated with adverse events are not anticipated to significantly impact the total costs and were therefore excluded from the cost comparison.

Summary

In absence of a routinely accessible TKI, dasatinib is a cost-increasing intervention compared to management with no TKI. Given the clinical evidence supporting the benefit of this intervention, it may offer clinical benefit compared to management with no TKI. However, in the absence of an analysis to quantify treatment benefits in relation to costs, an ICER was not available, and the cost-effectiveness remains unknown.

8. Council review | Cost-effectiveness evaluation

After consideration of the available evidence, the Council accepted that the proposed intervention was cost-increasing, and that in the absence of a cost-effectiveness analysis, the cost-effectiveness remained unknown. In this situation Council was able to consider other relevant information including service impact and estimated net medicines budget impact under the decision-making framework for value judgements.

9. Service Impact

Dasatinib is an oral treatment that is currently frequently accessed in the resistant or intolerant setting via individual patient applications. Dasatinib may cause pleural effusions which may require outpatient monitoring or inpatient treatment. It is estimated that less than 5 patients per year may start treatment with dasatinib due to relapse or intolerance in Scotland. Overall, dasatinib is not expected to have a significant service impact.

10. Budget Impact

In the absence of a cost-effectiveness analysis, a detailed budget impact analysis was conducted.

Patient uptake

The patient uptake was calculated using epidemiological data presented in Section 1. Approximately 2 to 3 adult patients with Ph+ ALL would either be resistant or intolerant to initial therapy with TKI. The number of patients expected to be treated with dasatinib in this population was estimated to be 2 in the first year and this number is expected to remain consistent on a yearly basis. The base case assumed that 100% of eligible patients would receive dasatinib. There is a lack of data on discontinuation rates in this line of treatment. Therefore, it was not included in the analysis.

Per patient medicine cost and treatment duration

The intervention will be distributed from secondary care, and as a result, medication prices in the budget impact analysis include VAT.

Dasatinib was costed at 140mg once daily until discontinuation, using the NHSScotland confidential national framework prices for a lower cost generic version. The duration of treatment would be equal to the median PFS of 4 months from Lilly et al. (2010) (Table 1)[16].

Comparator displacement

As there is no routinely accessible TKI for this patient population, and medicines accessed through individual request are not uniform throughout Scotland, management with no TKI was considered as the comparator. Therefore, it is anticipated that dasatinib will not displace any existing treatments.

Results

These prices include VAT.

In Year 1 the net medicines budget impact was estimated to be £11,688 annually (BNF list price, accessed May 2024) based on an uptake of 2 patients. In subsequent years the net medicines budget impact was estimated to remain the same.

Table 2 | Budget impact analysis base case results (list prices; Including VAT)

	Year 1	Subsequent years
Dasatinib in resistant or intolerant setting [a]		
Acquisition cost	£5,844	£5,844
Number of patients		
Eligible for treatment	2	2
Budget Impact		
Net budget impact	£11,688	£11,688

[a] Based on 140 mg dasatinib taken once daily for 4 months.

Limitations

In addition to the limitations listed in Section 7, the estimated number of patients who will need dasatinib was subject to uncertainty. The uptake was based on newly diagnosed (i.e. incident) cases per year and excludes existing cases. Given that the overall survival rate for this patient group is less than a year, the number of patients progressing to subsequent years is anticipated to be minimal. However, the net budget impact may increase in year 1 when accounting for existing cases eligible for dasatinib after failure of prior TKI.

The proposal form and real-world data suggests that dasatinib is currently being accessed, which may be through individual patient requests. Therefore, the Year 1 budget impact of the proposal may be overestimated as some patients may already be receiving dasatinib and these costs have not been accounted for.

There is uncertainty surrounding the discontinuation rates in this patient population. Due to the extremely low number of patients eligible for annual treatment, it was not included in the analysis. Including these could potentially lower the total cost. As a result, the base case estimate may be an overestimate.

Summary

The use of dasatinib will increase the budget impact for this patient group, compared to existing standard of care. However, real world data suggests some patients have been obtaining this through individual requests. Using the NHS indicative price for the cheapest generic alternative for dasatinib 140mg (BNF list price, accessed May 2024), the medicine acquisition cost was expected to be £5,844 per patient for 4 months of therapy with dasatinib. Based on uptake of two patients annually, the estimated net medicines budget impact was £11,688 in the steady state. VAT is included in these figures.

The Council considered the net medicines budget impact using more favourable confidential NHSScotland medicine pricing agreements in decision making. NCMAG is unable to publish the budget impact using confidential pricing 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 relevant discount pricing.

Separate information will be supplied by the boards to facilitate budget impact assessment.

11. Council review | Overall proposal evaluation

After consideration of all relevant information under the Decision-making framework for value judgements the Council made a decision to support this use.

12. Acknowledgements

NCMAG would like to acknowledge the patient group partners Blood Cancer UK and Leukaemia Care, for their valuable contribution.

We would also like to acknowledge the data provided by the Cancer Medicines Outcomes Programme – Public Health Scotland, which provided an evidence source and very helpful context for this review.

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This advice represents the view of the NCMAG Council 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.

Minor document amendments

Date	Previous version	Amendment	Updated version	Approved by