National Institute for Health and Care Excellence

Single Technology Appraisal (STA)

Idelalisib for treating chronic lymphocytic leukaemia [ID764]

Response to consultee and commentator comments on the draft remit and draft scope (pre-referral)

Comment 1: the draft remit

Section	Consultee/ Commentator	Comments	Action
Appropriateness	CLL Support Association	Yes	Comments noted.
	Gilead Sciences	It is appropriate to refer this topic to NICE for appraisal.	Comments noted.
	GSK	Yes	Comments noted.
	Lymphoma Association	Yes, it is very appropriate for NICE to assess these new agents in CLL/SLL (see comment immediately below).	Comments noted.
	Napp Pharmaceuticals	Yes it is appropriate	Comments noted.
	Royal College of Pathologists	It is appropriate and timely to refer this topic to NICE for appraisal	Comments noted.
Wording	CLL Support Association	Yes	Comments noted.

Section	Consultee/ Commentator	Comments	Action
	Gilead Sciences	The wording of the remit reflects the issue.	Comments noted. The wording of the remit has been updated to reflect the patient population in the positive opinion received from the European Medicines Agency's Committee for Medicinal Products for Human Use in September 2014. The remit has therefore been updated to state: 'To appraise the clinical and cost effectiveness of idelalisib within its licensed indication for treating chronic lymphocytic leukaemia'.
	GSK	No comment	Comments noted.
	Lymphoma Association	In line with the ibrutinib scoping remit, this could include small lymphocytic lymphoma. The exact licensed indication is not yet known.	Comments noted, Idelalisib will be appraised in line with its marketing authorisation. The marketing authorisation for

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			idelalisib in the UK is in combination with rituximab for the treatment of adult patients with chronic lymphocytic leukaemia 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.
	Napp Pharmaceuticals	Yes.	Comments noted.
	Royal College of Pathologists	Yes	Comments noted.
Timing Issues	CLL Support Association	This appraisal should be given a high priority as eventually the majority of the CLL patient population will relapse from current therapies and could obtain substantial benefit from this new therapy.	Comments noted. NICE has scheduled this topic into its work programme. For further details see the NICE website: http://www.nice.org.uk/g

Section	Consultee/ Commentator	Comments	Action
			uidance/indevelopment/gid-tag488
	Gilead Sciences	Given the high unmet need and poor prognosis seen in some patients with relapsed CLL, e.g. patients with deleted 17p chromosomes or TP53 mutation, it is Gilead Sciences' view that this topic should be referred as promptly as practically possible	Comments noted. NICE has scheduled this topic into its work programme. For further details, see the NICE website: http://www.nice.org.uk/guidance/indevelopment/gid-tag488.
	GSK	No comment	Comments noted.
	Lymphoma Association	Patients are aware of these new drugs and would like to see them appraised at the earliest opportunity.	Comments noted. NICE has scheduled this topic into its work programme. For further details, see the NICE website: http://www.nice.org.uk/guidance/indevelopment/gid-tag488.
	Napp Pharmaceuticals	Given there are other drugs affecting the BCR signalling pathway about to be licensed, such as ibrutinib, should they be considered together in a Multiple	Comments noted. Attendees at the

Section	Consultee/ Commentator	Comments	Action
		Technology Appraisal?	scoping workshop agreed that the Single Technology Appraisal (STA) process is the most appropriate. This topic has been referred to NICE by the Secretary of State for Health as an STA that covers both of the populations in the marketing authorisation for idelalisib. The remit has therefore been updated to state: 'To appraise the clinical and cost effectiveness of idelalisib within its licensed indication for treating chronic lymphocytic leukaemia.'
	Royal College of Pathologists	This proposed appraisal should be considered urgent, because Ibrutinib seems to show marked efficacy in phase II and III trials	Comments noted. NICE has scheduled this topic into its work programme. For further details, see the NICE website:

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			http://www.nice.org.uk/guidance/indevelopment/gid-tag488.
Additional comments on the draft remit	GSK	None	Comments noted.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments	Action
Background information	CLL Support Association	There is a need to clarify further the toxicity of current treatments, the chronic nature of CLL and the difficulty in treating relapsed disease.	Comments noted. The background section of a scope is intended to be a brief introduction to the clinical area and treatment pathway . The background section has been up-dated to include first-line treatments for people with chronic lymphocytic leukaemia associated with 17p deletion or TP53 mutation in order to reflect the patient population specified in the marketing authorisation for idelalisib in the UK.
	Gilead Sciences	The background information is accurate, but to be complete it should contain information about the CLL patients with high risk disease characterised by the presence of cytogenetic mutation or abnormalities (17p deletion or TP53 mutation). This group of patients has a clearly differentiated and worst OS prognosis to the other CLL patients and respond very poorly to most of the	Comments noted. The background section of a scope is intended to be a brief introduction to the clinical area and

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		available therapies.	treatment pathway. The back ground section has been up-dated to include first-line treatments for people with chronic lymphocytic leukaemia associated with 17p deletion or TP53 mutation in order to reflect the patient population specified in the marketing authorisation for idelalisib in the UK.
	GSK	The latest estimates from Cancer Research UK, suggests that approximately 3000 people are diagnosed with CLL each year.	Comment noted. The background section of a scope is intended to be a brief introduction to the clinical area and treatment pathway. The background statistics reflect those NICE identified as the most recently reported for England (rather than the UK as a whole).

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	Lymphoma Association	The survival rates vary hugely depending on stage, from living for 10+ years, possibly without even needing any treatment, to living for only a few years with all the available treatments.	Comments noted. The background section of a scope is intended to be a brief introduction to the disease area and treatment pathway. The background statistics reflect those NICE identified as the most recently reported for England.
	Napp Pharmaceuticals	We agree that bendamustine is commonly used off label and is available through the Cancer Drugs Fund in relapsed CLL. The CDF does not specifically mention that patients need to be unsuitable for FCR in their approved criteria. Furthermore IMS data (imshealth: CLL Enhanced Tumour Study, Q1 2014) shows that 41% of 2nd line CLL patients in the UK receive a bendamustine containing regimen (84% of these are in combination with rituximab).	Comments noted. The background section of the scope has been updated.
	Roche Products Limited	The final sentence on the technology section should be changed to reflect the phase III RCT: 'It has been studied in combination with rituximab compared with placebo in combination with rituximab in adults with previously treated CLL for whom intensive cytotoxic chemotherapy (for example, FCR) is not suitable, who are unable to receive cytotoxic due myleotoxicity or comorbidities and whose has progressed within 24 months of last treatment.'	Comments noted. The 'Technolgy section' has been up-dated to specify that idelalisib has a marketing authorisation in the UK in combination with

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			rituximab in adult patients with chronic lymphocytic leukaemia 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.
	Royal College of Pathologists	The information is accurate. for completeness i would recommend the following change: NICE does not recommend ofatumumab for treating CLL refractory to fludarabine and alemtuzumab (NICE technology appraisal guidance 202), but it is available through the Cancer Drugs Fund." to be changed to "NICE does not currently ……..Fund, and is considering new recommendations for the use of ofatumomab in prevously untreated patients [ID642]".	Comments noted. The background section of the scope has been updated.
The technology/ intervention	CLL Support Association	There is a need to specify the mechanism of action of this first-in-class PI3K inhibitor.	Comments noted. The scope is only intended to provide a brief description of the technology. A more detailed description of the technology and its mode of action will be

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			included in the company's submission to NICE.
	Gilead Sciences	Partially. Idelalisib is a highly selective oral inhibitor of the delta isoform of the PI3 kinase, a central signalling enzyme involved in the B-cells activation, proliferation and homing pathways.	Comments noted. The scope is only intended to provide a brief description of the technology. A more detailed description of the technology and its mode of action should be included in the company's submission to NICE.
	GSK	No comments	Comment noted. No action required.
	Lymphoma Association	It might be helpful to specify it is the PI3Kδ enzyme here.	Comments noted. The scope is only intended to provide a brief description of the technology. A more detailed description of the technology and its mode of action will be included in the

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			company's submission to NICE.
	Napp Pharmaceuticals	Yes	Comment noted. No action required.
	Roche Products Limited	The Intervention should be changed to reflect the phase III RCT and include only 'Idelalisib in combination with rituximab.'	Comment noted. The intervention specified in the scope has been updated to reflect the marketing authorisation of idelalisib in the UK.
	Royal College of Pathologists	Yes	Comment noted.
Population	CLL Support Association	The population will ultimately be all relapsed CLL patients. Specific subtypes many benefit more than others and these should be clarified.	Comment noted. The population specified in the scope has been updated to reflect the patient population specified in the marketing authorisation of idelalisib in the UK, that is: Adults with chronic lymphocytic leukaemia who have received at

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			least one therapy or adults with untreated chronic lymphocytic leukaemia associated with 17p deletion or TP53 mutation for whom chemo-immunotherapy is not suitable.
	Gilead Sciences	The population defined is likely to be appropriate; but depending on the final wording of the marketing authorisation it might need to be adjusted. As discussed above, high risk CLL patients can be seen as a distinct subgroup.	Comment noted. The population specified in the scope has been updated to reflect the patient population specified in the marketing authorisation of idelalisib in the UK, that is: Adults with chronic lymphocytic leukaemia who have received at least one therapy or adults with untreated chronic lymphocytic leukaemia associated with 17p deletion or TP53 mutation for

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			whom chemo-immunotherapy is not suitable.
	GSK	No comments	Comment noted. No action required.
	Lymphoma Association	Should the reasons why other cytotoxic therapy is not appropriate be clearly defined, as in the eligibility criteria for the Study 116 trial? Patients with deletion 17p appear to get the same benefit as other groups when treated with idelalisib and rituximab, whereas with most other treatments their outcome is much poorer. The difference in benefit may therefore be greater if the number in this subgroup is sufficient for analysis.	Comments noted. The population specified in the scope has been updated to reflect the patient population specified in the marketing authorisation of idelalisib in the UK, , that is: Adults with chronic lymphocytic leukaemia who have received at least one therapy or adults with untreated chronic lymphocytic leukaemia associated with 17p deletion or TP53 mutation for whom chemo-immunotherapy is not

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			suitable.
	Napp Pharmaceuticals	The population should be consistent with the regulatory trial. Patients should have progressed within 24 months after last treatment and not able to receive cytotoxic therapy. Previous treatment should include a CD20 based regimen or 2 cytotoxic regimens. We would also like to ask whether patients with 17p deletion should be considered separately.	Comment noted. The population specified in the scope has been updated to reflect the patient population specified in the marketing authorisation of idelalisib in the UK, that is: Adults with chronic lymphocytic leukaemia who have received at least one therapy or adults with untreated chronic lymphocytic leukaemia associated with 17p deletion or TP53 mutation for whom chemo-immunotherapy is not suitable.
	Roche Products Limited	The population should be changed to reflect the phase III RCT: 'People with relapsed chronic lymphocytic leukaemia, for whom cytotoxic therapies are not suitable due to reduced renal function, therapy-induced myelosuppression or major coexisting illnesses.'	Comments noted. The population specified in the scope has been updated to reflect the

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			patient population specified in the marketing authorisation of idelalisib in the UK, that is: Adults with chronic lymphocytic leukaemia who have received at least one therapy or adults with untreated chronic lymphocytic leukaemia associated with 17p deletion or TP53 mutation for whom chemo-immunotherapy is not suitable.
	Royal College of Pathologists	Should "People with relapsed or refractory chronic lymphocytic leukaemia or small lymphocytic leukaemia, for whom cytotoxic therapies are not suitable" be changed to People with relapsed or refractory chronic lymphocytic leukaemia or small lymphocytic leukaemia, for whom fludarabine-based therapies are not suitable?	Comments noted. The population specified in the scope has been updated to reflect the patient population specified in the marketing authorisation of idelalisib in the UK, that is:

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			Adults with chronic lymphocytic leukaemia who have received at least one therapy or adults with untreated chronic lymphocytic leukaemia associated with 17p deletion or TP53 mutation for whom chemo-immunotherapy is not suitable.
Comparators	CLL Support Association	These should also include Ofatumumab in England where it is available through the Cancer Drugs Fund.	Comments noted. The comparators in the scope have been updated. Attendees at the scoping workshop agreed that 'ofatumumab' and 'corticosteroids (with or without rituximab)' are used for treating people with relapsed or refractory CLL and should be included in the scope. The comparators in the

Section	Consultee/ Commentator	Comments	Action
			scope have been further updated to reflect established clinical practice for the 2 patient populations specified in the marketing authorisation for idelalisib in the UK, that is: Adults with chronic lymphocytic leukaemia who have received at least one therapy or adults with untreated chronic lymphocytic leukaemia associated with 17p deletion or TP53 mutation for whom chemo-immunotherapy is not suitable.
	Gilead Sciences	Given the patient populations proposed in the draft scope, comparators including a cytotoxic agent (e.g. bendamustine, chlorambucil, fludarabine) would not constitute relevant comparator. For such patients, there is paucity of options, and among the clinically relevant one, single agent anti-CD20, such as rituximab constitute a relevant comparator. Beyond those, best supportive care (BSC) would also constitute an appropriate comparator. BSC consists of appropriate measures to treat and reduce the risk of infection e.g.	Comments noted. The comparators in the scope have been updated. Attendees at the scoping workshop agreed that 'ofatumumab' and

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		antimicrobial prophylaxis, immunisation, GCSF and immunoglobulin infusions. Patients may also require red cell/blood transfusion and platelet transfusion to manage anaemia and thrombocytopenia (irradiated blood products are recommended for those who have received fludarabine or alemtuzumab as previous treatment). Fludarabine, bendamustine or chlorambucil in combination or not with rituximab could represent clinically relevant options for relapsed CLL patients with a suitable performance status (e.g. with less comorbidities).	'corticosteroids (with or without rituximab)' are used for treating people with relapsed or refractory CLL and should be included in the scope. The scope has been further up-dated to reflect clinical practice for the 2 patient populations specified in the marketing authorisation for idelalisib in the UK, that is: Adults with chronic lymphocytic leukaemia who have received at least one therapy or adults with untreated chronic lymphocytic leukaemia associated with 17p deletion or TP53 mutation for whom chemo-immunotherapy is not suitable.

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	GSK	The comparators in the draft scope are appropriate.	Comment noted. The comparators in the scope have been updated to reflect established clinical practice in England for the 2 patient populations specified in the marketing authorisation for idelalisib in the UK, that is: Adults with chronic lymphocytic leukaemia who have received at least one therapy or adults with untreated chronic lymphocytic leukaemia associated with 17p deletion or TP53 mutation for whom chemo-immunotherapy is not suitable.
	Lymphoma Association	As a drug licensed in this setting, it would seem appropriate to include ofatumumab as a comparator, even if it is not often used in the UK.	Comments noted. The comparators in the

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		For some patients included in the trial population, bendamustine might also be too toxic.	scope have been updated. Attendees at the scoping workshop agreed that 'ofatumumab' and 'corticosteroids (with or without rituximab)' are used for treating people with relapsed or refractory CLL and should be included in the scope.The comparators in the scope have been further updated to reflect established clinical practice in England for the 2 patient populations specified in the marketing authorisation for idelalisib in the UK, that is: Adults with chronic lymphocytic leukaemia who have received at least one therapy or adults with untreated

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			chronic lymphocytic leukaemia associated with 17p deletion or TP53 mutation for whom chemo-immunotherapy is not suitable.
	Napp Pharmaceuticals	The comparators listed are appropriate. We would like to comment that UK clinicians most commonly use Bendamustine in combination with rituximab in relapsed CLL. IMS data suggests that in 2nd line CLL patients in the UK, bendamustine is now the standard of care. 41% of CLL 2nd line patients receive a bendamustine containing regimen (84% of these are in combination with rituximab). The next most commonly prescribed treatment is FCR, which is declining in use and is now down to only 19% of patients. We would also like to suggest ofatumumab as a comparator. Ofatumumab is licensed in patients who are refractory to fludarabine and alemtuzumab and also available second line on the Cancer Drugs Fund if either fludarabine or alemtuzumab are inappropriate.	Comments noted. The comparators in the scope have been updated. Attendees at the scoping workshop agreed that 'ofatumumab' and 'corticosteroids (with or without rituximab)' are used for treating people with relapsed or refractory CLL and should be included in the scope.The comparators in the scope have been further updated to reflect established clinical practice in England for the 2

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			patient populations specified in the marketing authorisation for idelalisib in the UK, that is: Adults with chronic lymphocytic leukaemia who have received at least one therapy or adults with untreated chronic lymphocytic leukaemia associated with 17p deletion or TP53 mutation for whom chemo-immunotherapy is not suitable.
	Royal College of Pathologists	It depends on the decision of the population defined. Bendamustine and Chlorambucil are appropriate comparators if fludarabine-based therapies are not suitable. Otherwise Fludarabine-based therapies should also be considered.	Comments noted. The comparators in the scope have been updated.Attendees at the scoping workshop agreed that 'ofatumumab' and 'corticosteroids (with or without rituximab)' are used for treating people

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			with relapsed or refractory CLL and should be included in the scope.The comparators in the scope have been further updated to reflect established clinical practice in England for the 2 patient populations specified in the marketing authorisation for idelalisib in the UK, that is: Adults with chronic lymphocytic leukaemia who have received at least one therapy or adults with untreated chronic lymphocytic leukaemia associated with 17p deletion or TP53 mutation for whom chemo-immunotherapy is not suitable.

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Outcomes	CLL Support Association	Yes	Comment noted. No action required.
	Gilead Sciences	Yes	Comment noted. No action required.
	GSK	No comments	Comment noted. No action required.
	Lymphoma Association	Those with CLL/SLL who need active treatment but have exhausted the existing cytotoxic therapies or are unable to have these because of coexisting illness or previous side effects of therapy have a very short life-expectancy and often a poor quality of life due to recurrent infections, anaemia and other symptoms of advanced-stage disease, therefore accurate assessment of any benefits in terms of quality of life will be very important.	Comments noted. A more detailed description of the methods and results of how the quality of life was assessed in patients enrolled into the clinical trials will be included in the company's submission to NICE.
	Napp Pharmaceuticals	Yes	Comment noted. No action required.
	Royal College of Pathologists	Only exception will be response rates, which cannot take IWCLL criteria into account for the persistent lymphocytosis	Comments noted. Attendees at the scoping workshop agreed that response

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			rates are an important outcome measure in people with CLL and should remain in the scope.
Economic analysis	CLL Support Association	No issues.	Comment noted. No action required.
	Gilead Sciences	No comment	Comment noted. No action required.
	GSK	No comments	Comment noted. No action required.
	Lymphoma Association	It is questionable whether it is appropriate to use the cost to the Cancer Drugs Fund for comparator technologies. This is because this is unlikely to be the true cost in the future, given the uncertainty over whether the appropriate drugs will be available via the CDF in the future?	Comments noted. Where comparator technologies are available through the Cancer Drugs Fund, the cost incurred by the Cancer Drug Fund should be used in any economic analyses, rather than the list price. NICE's 'Guide to methods of technology appraisal' (2013) states

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			that "in the reference case, costs should relate to resources that are under the control of the NHS and personal and social services. These resources should be valued using the prices relevant to the NHS and personal and social services. The public list prices for technologies (for example, pharmaceuticals or medical devices) should be used in the reference-case analysis. When there are nationally available price reductions, then the reduced price should be used in the reference-case analysis to best reflect the price relevant to the NHS."
	Royal College of	Yes	Comment noted. No

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	Pathologists		action required.
Equality and Diversity	CLL Support Association	No issues.	Comment noted. No action required.
	Gilead Sciences	In addressing this appraisal NICE should be aware that CLL is a cancer of the elderly with a median age at diagnostic close to 70. Thus it is Gilead Sciences' view that any methodological aged-bias in assessing the cost-effectiveness of idelalisib for CLL should be avoided. Notably when considering the proposed methodologies to calculate Burden of Illness and Wider Societal Benefit aimed at informing Value-Based-Assessment of new interventions later this year.	Comments noted. Following the value based assessment consultation, NICE will undertake further work before making changes to the way it appraises new medicines and other technologies for use by the NHS. Any changes to NICE's methods need to be made as part of a wider review of the innovation, evaluation and adoption of new treatments (including those for cancers) involving patients, people working in or with the NHS, the life sciences industries and health researchers.

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	GSK	No comments	Comment noted. No action required.
	Royal College of Pathologists	I do not think that the proposed remit and scope need changing and equality criteria are met.	Comments noted. The remit and scope had been updated to relect the marketing authorisation of idelalisib in the UK, that is in combination with rituximab for the treatment of adult patients with chronic lymphocytic leukaemia 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.
Innovation	CLL Support Association	It is important to note that this new agent has a novel mechanism of action. It has the potential to provide a step change improvement in patient experience during therapy and to result in excellent QOL and prolonged remissions. The lower toxicity could mean that the number of further therapeutic options are	Comments noted. The company and other consultees will be able to fully describe why it considers ramucirumab

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		increased. QALY needs to recognise that this agent is not just extending life but provides significant and normal QOL for patients.	to be innovative in their evidence submissions, which will then be considered by the Appraisal Committee. Comment noted. Please note that the QALY reflects both mortality and health-related quality of life effects.
	Gilead Sciences	Idelalisib is the first in class targeted oral agent for the treatment of CLL and meets the 5 criteria for step-change innovation as laid out by the Kennedy Report, such that: Idelalisib significantly and substantially improves the way that a current need is met (superior clinical efficacy vs. an active agent coupled with a very manageable side effect profile and a treatment option for a significant proportion of patients who are unsuitable for cytotoxic therapies) Idelalisib meets a need which the NHS has identified as being important, as evidenced by the recent NHS Outcomes Framework that reflects the government commitment to improve cancer survival rates in the under-75s. Idelalisib has a robust evidence set providing research on a 'real' CLL patient population in which the product is effective (clinical trial including frail relapsed CLL patients unsuitable for chemotherapy or for whom chemotherapy is not effective, high-risk patients) Idelalisib has demonstrated an appropriate level of effectiveness with 92% of	Comments noted. The company and other consultees will be able to fully describe why it considers ramucirumab to be innovative in their evidence submissions, which will then be considered by the Appraisal Committee.

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		the patients showing a response to therapy.	
	GSK	No comments	Comment noted. No action required.
	Lymphoma Association	Yes. Idelalisib has an entirely new mechanism of action. It is oral therapy and has relatively few side effects. Its impact for this group of patients appears to be remarkable, as evidenced by the trial being stopped early by the data monitoring committee – a true 'step-change' in the management of CLL.	Comments noted. The company and other consultees will be able to fully describe why it considers idelalisib to be innovative in their evidence submissions, which will then be considered by the Appraisal Committee.
	Napp Pharmaceuticals	Yes, we do consider the technology to be innovative.	Comments noted. The company and other consultees will be able to fully describe why it considers idelalisib to be innovative in their evidence submissions, which will then be considered by the Appraisal Committee.
	Royal College of	This is a step-change in the management of CLL, which may result in	Comments noted. The

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	Pathologists	substantial health-related benefits	company and other consultees will be able to fully describe why it considers idelalisib to be innovative in their evidence submissions, which will then be considered by the Appraisal Committee.
Other considerations	CLL Support Association	No issues.	Comment noted. No action required.
	GSK	None	Comment noted. No action required.
	Royal College of Pathologists	n/a	Comment noted. No action required.
Questions for consultation	CLL Support Association	The questions are appropriate. Best supportive care should include: • Regular monitoring • Blood product support where necessary • Infection, viral and fungal control together with referral to experts in these fields where necessary • Immune system monitoring and support and referral to immunologists	Comment noted. Attendees at the scoping scoping workshop agreed that f best supportive care t was an appropriate comparator and constituted of regular monitoring, blood

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		for their expertise • Referral for psychological support where necessary Co-ordination of all these support activities by the patient's consultant.	transfusions, infection control and psychological support. The scope has been updated accordingly..
	Gilead Sciences	*Will idelalisib always be used in combination with rituximab or could it be used as a monotherapy in UK clinical practice?* - The following information is confidential: [redacted] *Have all relevant comparators for idelalisib been included in the scope?* - It is Gilead Sciences' view that not all relevant comparators have been included in the scope. Indeed as discussed above for a number of relapsed CLL patients cytotoxic based therapies are not appropriate because of either their physical status or their cytogenetic profile. For those patients single agent rituximab is an option and is used in clinical practice (as documented in the SACT report on the 10 most used regimens for the treatment of CLL patients in the UK with rituximab being the fourth most commonly prescribed treatment).	Comment noted. The intervention specified in the scope has been updated to reflect the marketing authorisation of idelalisib in the UK., that is in combination with rituximab. The comparators in the scope have been updated. Attendees at the scoping workshop agreed that 'ofatumumab' and 'corticosteroids (with or without rituximab)' are used for treating people with relapsed or refractory CLL and should be included in

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		Should ofatumumab be considered as a comparator - Given that it is licensed and available via the cancer drug fund, ofatumumab similarly to single agent rituximab can be considered as a comparator *Are there any subgroups of people in whom idelalisib is expected to be more clinically effective and cost effective or other groups that should be examined*	the scope.The comparators in the scope have been up-dated further to reflect established clinical practice in England for the 2 patient populations specified in the marketing authorisation for idelalisib in the UK, that is: Adults with chronic lymphocytic leukaemia who have received at least one therapy or adults with untreated chronic lymphocytic leukaemia associated with 17p deletion or TP53 mutation for whom chemo-immunotherapy is not suitable. Comment noted. Attendees at the

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		separately? - Current evidence suggests that idelalisib is equally effective in all the relevant CLL patient subgroups.	scoping workshop agreed the scope should be updated to include the following subgroup (if the evidence allows), 'people with 17p deletion'. Please see the 'Other considerations' section of the scope for the inclusion of this subgroup.
		Where do you consider idelalisib will fit into the existing NICE pathway, 'blood and bone marrow cancers' - Person with leukemia -> CLL -> Treatment of relapsed or refractory disease	Comment noted. No action required.
	GSK	Should ofatumumab be considered as a comparator? Ofatumumab is licensed for the treatment of CLL in patients who are refractory to fludarabine and alemtuzumab. GSK acknowledges that ofatumumab is available via the Cancer Drugs fund and that there might be some use of this intervention in the population under	Comments noted. The comparators in the scope have been updated. Attendees at the scoping workshop agreed that 'ofatumumab' and

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		consideration. However we believe that the comparators in the draft scope are more likely to be used in the relapsed setting than ofatumumab.	'corticosteroids (with or without rituximab)' are used for treating people with relapsed or refractory CLL and should be included in the scope. The comparators in the scope have been up-dated further to reflect established clinical practice in England for the 2 patient populations specified in the marketing authorisation for idelalisib in the UK, that is: Adults with chronic lymphocytic leukaemia who have received at least one therapy or adults with untreated chronic lymphocytic leukaemia associated with 17p deletion or

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			TP53 mutation for whom chemo-immunotherapy is not suitable.
	Lymphoma Association	Trials have suggested synergism between idelalisib and rituximab, so it is likely to be best used in combination.	Comment noted. The intervention specified in the scope has been updated to reflect the marketing authorisation of idelalisib in the UK., that is in combination with rituximab.
		On the current NICE pathway, idelalisib would fit under Chronic Lymphocytic Leukaemia; Treatment for relapsed or refractory disease. However, as it has shown good responses in terms of lymph node reduction, it should also appear as SLL on the Lymphoma section, which we have recommended should be split into High-grade and Low-grade types, so SLL could be added as a heading under low-grade.	Comment noted. No action required.
		Best supportive care would involve regular follow-up with a CLL specialist, along with:	Comment noted. Attendees at the scoping scoping

Section	Consultee/ Commentator	Comments	Action
		• blood product support if required • antibiotics to treat infection if required • immunoglobulin therapy in those with recurrent infection and hypogammaglobulinaemia.	workshop agreed that best supportive care was an appropriate comparator and constituted of regular monitoring, blood transfusions, infection control and psychological support. The scope has been updated accordingly.
	Napp Pharmaceuticals	Idelalisib should be used as per the licensing regulatory trial. It is difficult to comment on the existing NICE pathway given the new treatment options. Given there are other drugs affecting the BCR signalling pathway about to be licensed, such as ibrutinib, should they be considered together in a Multiple Technology Appraisal?	idelalisib will be appraised in line with its marketing authorisation that is in combinstion with rituximab. Comment noted. Comment noted. Attendees at the scoping workshop agreed the Single Technology Appraisal (STA) process is the

Section	Consultee/ Commentator	Comments	Action
			most appropriate to consider for this topic. This topic has been referred to NICE by the Secretary of State for Health as an STA that covers both of the populations in the marketing authorisation for idelalisib. The remit has therefore been updated to state: 'To appraise the clinical and cost effectiveness of idelalisib within its licensed indication for treating chronic lymphocytic leukaemia'.
Additional comments on the draft scope	GSK	No further comments.	Comment noted. No action required.
	Napp Pharmaceuticals	We would like clarification on which chemotherapies are included in cytotoxic agents.	Comment noted.The comparators in the scope have been updated to reflect established clinical practice in England for

Section	Consultee/ Commentator	Comments	Action
			the 2 patient populations specified in the marketing authorisation for idelalisib in the UK, that is: Adults with chronic lymphocytic leukaemia who have received at least one therapy or adults with untreated chronic lymphocytic leukaemia associated with 17p deletion or TP53 mutation for whom chemo-immunotherapy is not suitable.

The following consultees/commentators indicated that they had no comments on the draft remit and/or the draft scope

- Healthcare Improvement Scotland

Single Technology Appraisal (STA)

Idelalisib for treating previously treated chronic lymphocytic leukaemia in people unable to receive intensive cytotoxic chemotherapy

Response to consultee and commentator comments on the provisional matrix of consultees and commentators (pre-referral)

Version of matrix of consultees and commentators reviewed: Provisional matrix of consultees and commentators sent for consultation					
Summary of comments, action taken, and justification of action:					
	Proposal:	*Proposal made by:*		*Action taken:* Removed/Added/Not included/Noted	*Justification:*
	Public Health Wales NHS Trust	NICE Secretariat		Moved	This organisation has been re-classified as 'Associated Public Health Group – commentator'
	Chronic Myeloid Leukaemia Support Group (CML Support)	PIP		Removed	PIP recommended removal at scoping matrix sign-off as not directly relevant on a CLL matrix.

	British Association for Services to the Elderly (BASE)	British Association for Services to the Elderly (BASE)		Removed	Organisation has disbanded
	Commissioning Support Appraisals Service	Commissioning Support Appraisals Service		Removed	Completed as per the specific organisations request.
	Health Research Authority	Health Research Authority		Removed	Completed as per the specific organisations request.
	Research Institute for the Care of Older People (RICE)	Research Institute for the Care of Older People (RICE)		Removed	Completed as per the specific organisations request.

	Delete Blood Cancer	PIP		Added	Delete Blood Cancer meets the inclusion criteria and has a close interest in this appraisal topic therefore this organisation has been added to the matrix as a patient group consultee.