National Institute for Health and Care Excellence

Single Technology Appraisal (STA)

Idelalisib in combination with ofatumumab for chronic lymphocytic leukaemia [ID817]

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,	Comment noted. No action required.
	Gilead Sciences	It is not appropriate to refer this topic to NICE for appraisal. Guidance on the use of idelalisib in combination with idelalisib is not required. In clinical practice idelalisib in combination with ofatumumab for the treatment of CLL is unlikely to be prescribed based on current usage of ofatumumab. Furthermore ofatumumab was previously assessed by NICE in this indication and was not recommended and has been removed from the CDF list • Further details are provided below: • Use of ofatumumab in clinical practice is limited with only 6% of CLL patients and 8% of relapsed CLL patients prescribed the drug. • Ofatumumab has was delisted from the CDF in January 2015 on the basis that the CDF panel considered the clinical benefits of treatment with ofatumumab in patients with relapsed CLL to be insufficient to merit retention within current CDF funding (see http://www.england.nhs.uk/wp-content/uploads/2015/01/ncdf-summ-	Comment noted. The decision as to whether or not to refer this topic to NICE for appraisal will be made at the Ministers' discretion, taking into account the comments received during consultation on the draft scope and the discussion that took place at the scoping workshop. No action required.

Section	Consultee/ Commentator	Comments	Action
	Gilead Sciences (cont.)	ofatumb-relps-rfrct-cll.pdf). • NICE does not recommend ofatumumab for people with chronic lymphocytic leukaemia that is refractory to treatment with two other drugs called fludarabine and alemtuzumab (TA202, October 2010) In addition an appraisal of the clinical and cost effectiveness of idelalisib within its licensed indication for chronic lymphocytic leukaemia is currently on going with guidance anticipated October 2015. In clinical practice idelalisib in combination with ofatumumab will be used at the same point in the treatment pathway as idelalisib in combination with rituximab with the latter regimen preferred (i.e. shorter infusion times). An additional appraisal of a combination which will not be used in clinical practice will is not an inappropriate use of NICE resources and is not required. On the basis that we do not consider an appraisal is required we have not commented on the remit or the draft scope.	
	Janssen	Yes.	Comment noted. No action required.
	Roche Products	Yes	Comment noted. No action required.
Wording	CLL Support Association	yes	Comment noted. No action required.

Section	Consultee/ Commentator	Comments	Action
	Gilead Sciences	No – as stated above	Comment noted. The decision as to whether or not to refer this topic to NICE for appraisal will be made at the Ministers' discretion, taking into account the comments received during consultation on the draft scope and the discussion that took place at the scoping workshop. No action required.
	Janssen	Yes, the wording of the remit does reflect the issues.	Comment noted. No action required.
	Roche Products	-	No action required.
Timing Issues	CLL Support Association	Unknown. Dependent on the success of other novel therapy appraisals and the availability of comparative data.	Comment noted. No action required.

Section	Consultee/ Commentator	Comments	Action
	Gilead Sciences	Guidance on the use of idelalisib in combination with ofatumumab for previously treated CLL is not required for the reasons stated above.	Comment noted. The decision as to whether or not to refer this topic to NICE for appraisal will be made at the Ministers' discretion, taking into account the comments received during consultation on the draft scope and the discussion that took place at the scoping workshop. No action required.
	Roche Products	-	No action required.
Additional comments on the draft remit	CLL Support Association	It is difficult to provide comments in full as trial data is not currently available in the public arena. Trial data is planned for publication at ASCO at the end of the month; we should then be able to comment further during the scoping workshop on June 3rd.	Comment noted. No action required.
	Roche Products	-	No action required.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments	Action

Section	Consultee/ Commentator	Comments	Action
Background information	CLL Support Association	Accurate but incomplete. Patients with CLL may live with a considerable burden of symptoms impacting on their quality of life. This is true in both the 'watch and wait' and relapsed groups of patients.	Comment noted. The scope has been amended to reflect this comment.

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	Leukaemia CARE	We have a number of comments to make with regards to the background. Firstly with regards to the symptoms, we would like 'weight loss' to be changed to 'unexplained weight loss'. Secondly with regards to the symptoms, we would like some reference to the emotional impact a diagnosis of blood cancer can have on patients and their carers, family and friends. In particular this includes feelings of shock/disbelief, denial, anger, fear/uncertainty, resentment, blame/guilt, isolation and depression. As such there may be a profound impact on their physical and psychological wellbeing. Thirdly with regards to the incidence of CLL which is listed as 2300. Previous scoping of idelalisib (in combination with rituximab - ID 764) referred to incidence as 2700. Additionally CRUK refer to incidence as 3233 (2011). We would like some clarification of anticipated incidence of CLL.	Comment noted. The background section of the scope has been amended to read 'unexplained weight loss'. The background section of the scope aims to provide a short account of the disease area and clinical management. The emotional impact from diagnosis is not specific to blood cancer because it occurs with other types of cancer. Therefore, this does not need to be included in the scope. The yearly incidence of CLL in the scope has been updated to 2700 patients, in line with the latest incidence statistics for England published on Cancer Research UK.

Section	Consultee/ Commentator	Comments	Action
	Roche Products	-	No action required.
The technology/ intervention	CLL Support Association	yes	Comment noted. No action required.
	Roche Products	-	No action required.
Population	CLL Support Association	yes but also include 'people with refractory/relapsed CLL and first line treatment for people with poor prognosis cytogenetics'	Comment noted. Scoping workshop attendees agreed to update the population in the scope to include adults with untreated chronic lymphocytic leukaemia associated with 17p deletion or TP53 mutation.
	Roche Products	Patients with a presence or absence of 17p deletion may be appropriate for separate consideration	Comment noted. Subgroups by the presence or absence of 17p deletion, and by the presence or absence of TP53 mutation, have been included in the scope.

Section	Consultee/ Commentator	Comments	Action
Comparators	CLL Support Association	It is unlikely that FCR would be used for many patients with relapsed CLL due to comorbidities	Comment noted. Scoping workshop attendees considered that some patients may still be fit enough to receive this combination in the relapsed setting. In addition, the dose of the treatment may be reduced if appropriate to lessen the adverse reactions and improve tolerability. No action required.
	Janssen	See 'questions for consultation' below.	Comment noted. No action required.
	Roche Products	Rituximab monotherapy should be included as a comparator	Comment noted. Scoping workshop attendees understood that rituximab monotherapy is sometimes used in the US in people with previously treated CLL, but not in the UK. No action required.

Section	Consultee/ Commentator	Comments	Action
Outcomes	CLL Support Association	yes	Comment noted. No action required.
	Roche Products	-	No action required.
Economic analysis	CLL Support Association	Unknown, see above.	Comment noted. No action required.
	Janssen	The economic analysis section states that for drugs funded by the CDF, the economic modelling should use the cost incurred by the Cancer Drug Fund. These negotiated discounts are confidential and this information is not available to other manufacturers for use in economic modelling. Janssen does not support the use of confidential discount prices in HTA submissions, and believes that modelling using UK list price is appropriate.	Comment noted. Modelling should use the CDF prices in accordance with the Methods Guide 2013, which states that nationally available price reductions should be used in the reference case analysis.
	Roche Products	-	No action required.
Equality and Diversity	CLL Support Association	no change needed	Comment noted. No action required.
	Roche Products	-	No action required.

Section	Consultee/ Commentator	Comments	Action
Innovation	CLL Support Association	yes – first in class non chemotherapy small molecule therapy – a step change in the management of the condition. Should have significant and substantial positive impact on the health of patients with CLL . Significant anxiety is a frequently reported emotional issue in patients with CLL. This non chemo treatment will offer benefits that will alleviate this. Preservation of the immune system will have significant health benefits (approx. 50% of CLL patients die of infections).	Comment noted. The company is encouraged to describe the innovative nature of idelalisib in combination with ofatumumab in their evidence submission. The Committee would normally consider this information during the course of the appraisal. No action required.
	Roche Products	No - idealisib in combination with ofatumumab provides an additional treatment option in addition to those listed as comparators.	Comment noted. The company is encouraged to describe the innovative nature of idelalisib in combination with ofatumumab in their evidence submission. The Committee would normally consider this information during the course of the appraisal. No action required.

Section	Consultee/ Commentator	Comments	Action
Other considerations	Roche Products	-	No action required.
NICE Pathways [Delete section if not relevant]	Roche Products	The ofatumumab licensed indication in refractory CLL, is for the treatment of CLL in patients who are refractory to fludarabine and alemtuzumab. It would therefore seem appropriate for idelalisib in combination with ofatumumab to fit into the same position in the NICE blood and bone marrow cancer pathway as per ofatumumab licence.	Comment noted.
Questions for consultation	Janssen	Ofatumumab monotherapy should be added to the list of comparators because, although it is not currently funded, it was used previously through the CDF and delisted as a result of newer products coming to market; furthermore, it is the only other drug therapy with a license in this indication aside from ibrutinib and idelalisib in combination with rituximab. Bendamustine with or without rituximab, chlorambucil, ibrutinib, idelalisib with rituximab, and BSC can be considered as established clinical practice in the NHS for previously treated CLL. High-does corticosteroids with or without rituximab would be considered suitable for high-risk CLL patients. It should be included as a comparator for this proposed appraisal; however, Janssen recognise there is a lack of clinical data for this regimen in this setting. We do not consider that the use of idelalisib in combination with ofatumumab can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation. Janssen feel that the STA process is the appropriate method for appraising this topic.	Comment noted. Scoping workshop attendees understood that the use of ofatumumab monotherapy in clinical practice is negligible. The clinical expert stated that high-dose corticosteroids with or without rituximab is not routinely used for previously treated CLL. No action required.

Section	Consultee/ Commentator	Comments	Action
Additional comments on the draft scope	CLL Support Association	It is difficult to provide comments in full as trial data is not currently available in the public arena. Trial data is planned for publication at ASCO at the end of the month; we should then be able to comment further during the scoping workshop on June 3rd.	Comment noted. No action required.
	Janssen	Within the "Related NICE recommendations and NICE Pathways" section, reference is made to ID749, Technology Appraisal in Preparation, 'Ibrutinib for treating chronic lymphocytic leukaemia'. It states that the earliest anticipated date of publication is December 2015 but this has been updated on the NICE website to be June 2016.	Comment noted. The earliest anticipated date of publication has been updated in the scope.
	Roche Products	-	No action required.

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

Department of Health
Pfizer
Royal College of Nursing
Royal College of Pathologists

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:
1.	African Caribbean Leukaemia Trust (ACLT)	NICE Secretariat		Removed	This organisation's interests are closely not related to the appraisal topic and as per our inclusion criteria and equalities commitments. Therefore the African Caribbean Leukaemia Trust (ACLT) have been removed from the matrix under 'patient/carer' groups.
2.	Anthony Nolan	NICE Secretariat		Removed	This organisation's interests are closely not related to the appraisal topic and as per our inclusion criteria and equalities commitments. Therefore Anthony Nolan have been removed from the matrix under 'patient/carer' groups.

3.	Delete Blood Cancer	NICE Secretariat		Removed	This organisation's interests are closely not related to the appraisal topic and as per our inclusion criteria and equalities commitments. Therefore Delete Blood Cancer have been removed from the matrix under 'patient/carer' groups.