National Institute for Health and Care Excellence

Single Technology Appraisal (STA/MTA)

Idelalisib for treating refractory follicular lymphoma

Response to consultee and commentator comments on the draft remit and draft scope

Please note: Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees.

Comment 1: the draft remit

Section	Consultee/ Commentator	Comments [sic]	Action
Appropriateness	Gilead Science	No comments	Noted.
	Royal College of Pathology and British Society of Haematology	It is appropriate that the data evaluating the effectiveness of idelalisib monotherapy in assessed by NICE. Although this is a subgroup arm of a phase II trial, there is no clear standard of care in the setting of relapsed, refractory FL that is both rituximab and alkylator refractory.	Comments on appropriateness and standard of care noted.
Wording	Gilead Science	No comments	Noted.
	Royal College of Pathology and British Society of Haematology	Yes	Comment noted.
Timing Issues	Gilead Sciences	No comments	Noted.

Section	Consultee/ Commentator	Comments [sic]	Action
	Royal College of Pathology and British Society of Haematology	Standard level of urgency	Comment noted.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Gilead Sciences	No comments	Noted.
	Royal College of Pathology and British Society of Haematology	Accurate and complete	Comment noted.
The technology/ intervention	Gilead Sciences	No comments	Noted.
	Royal College of Pathology and British Society of Haematology	Accurate	Comment noted.
Population	Gilead Sciences	No comments	Noted.
	Royal College of Pathology and British Society of Haematology	The population is defined in the appendix, although it would be helpful to absolutely specify the definition of 'refractory' within the document. I.e. does refractory refer to those patients that don't response but also those that relapse within a certain time frame post rituximab / alkylator therapy. This should be clarified. There are no absolute need to consider subgroups	Comment noted. The background section of the scope defines rituximab refractory as cancers that do not

Section	Consultee/ Commentator	Comments [sic]	Action
		separately, although in the course of time to clear group of patients with the highest level of unmet clinical need is those that relapse within 24 months of first line therapy (POD24) and this data is of particular interest to collect in the longer term.	respond to rituximab or relapse soon after finishing treatment. The marketing authorisation for idelalisib does not define refractory and therefore it is not possible to further define refractory in the scope. The comment on the unmet clinical need is noted. No changes are needed to the scope.
Comparators	Gilead Sciences	No comments	Noted
	Royal College of Pathology and British Society of Haematology	The standard treatments mentioned are currently used in the NHS and are reasonable comparators. As mentioned in the 'background' section, I would however add now that obinutuzumab-bendamustine could be used in the setting of 'double refractory' FL (i.e. those that are rituximab and alkylator refractory) and therefore should also be considered a possible comparator – although there will be little clinical data available outside of the initial licensing trial (GADOLIN). Clearly there is no direct comparator as the data are from a subgroup of a phase II trial.	Comment noted. Obinutuzumab-bendamustine is available through the Cancer drugs fund for people whose follicular lymphoma has been previously treated with a rituximab-containing therapy (rituximab induction therapy with or without rituximab mainentance). It is

Section	Consultee/ Commentator	Comments [sic]	Action
			therefore a second treatment after rituximab. It is anticipated that idelalisib would be taken after obinutuzumab-bendamustine because the marketing authorisation for idelalisib is for third-line use. Because obinutuzumab-bendamustine is used earlier in the treatment pathway than idelalisib it has not been included as a comparator in the scope.
Outcomes	Gilead Sciences	No comments	Noted
	Royal College of Pathology and British Society of Haematology	Yes	Noted
	Gilead Sciences	No comments	Noted

Section	Consultee/ Commentator	Comments [sic]	Action
Economic analysis	Royal College of Pathology and British Society of Haematology	Nil specific comments to add	Noted
Equality and Diversity	Gilead Sciences	No comments	Noted
	Royal College of Pathology and British Society of Haematology	No issues	Noted
Other considerations	Gilead Sciences	No comments	Noted
	Royal College of Pathology and British Society of Haematology	Key questions / points as above: 1. Definitions for 'double refractory' should be clarified 2. Consider the comparator of obinutuzumab-bendamustine Consider the subgroup of POD24 as a potential subgroup of patients with the clearest unmet need and a group that idelalisib seems as active in as those that don't progress within 24 months of first line treatment.	Comments noted. Please see responses above for 1 and 2. The unmet need of the POD24 group has been noted. Subgroups for whom the technology is likely to be more clinically or cost effective are listed in the scope. As the outcomes for the POD24 group are anticipated to be the same as the whole population for whom

Section	Consultee/ Commentator	Comments [sic]	Action
			idelalisib is indicated, POD24 has not been added as a subgroup in the scope.
Innovation	Gilead Sciences	No treatments are currently recommended for patients refractory to two previous lines of therapy. Idelalisib is associated with an ORR of 54.2% with 11.1% in CR at 24 months.	Comment noted.
	Royal College of Pathology and British Society of Haematology	Yes this is innovative and meets a potential unmet clinical need. I believe the QALY calculation will satisfy the health-related benefits here. The data available are: PI3Kδ inhibition by idelalisib in patients with relapsed indolent lymphoma. Gopal AK, Kahl BS, de Vos S, Wagner-Johnston ND, Schuster SJ, Jurczak WJ, Flinn IW, Flowers CR, Martin P, Viardot A, Blum KA, Goy AH, Davies AJ, Zinzani PL, Dreyling M, Johnson D, Miller LL, Holes L, Li D, Dansey RD, Godfrey WR, Salles GA. N Engl J Med. 2014 Mar 13;370(11):1008-18. doi: 10.1056/NEJMoa1314583 Idelalisib is effective in patients with high-risk follicular lymphoma and early relapse after initial chemoimmunotherapy. Gopal AK, Kahl BS, Flowers CR, Martin P, Ansell SM, Abella-Dominicis E, Koh B, Ye W, Barr PM, Salles GA, Friedberg JW. Blood. 2017 Jun 1;129(22):3037-3039. doi: 10.1182/blood-2016-12-757740.	Comments and references noted.

Section	Consultee/ Commentator	Comments [sic]	Action
		Efficacy and safety of idelalisib in patients with relapsed, rituximab- and alkylating agent-refractory follicular lymphoma: a subgroup analysis of a phase 2 study. Salles G, Schuster SJ, de Vos S, Wagner-Johnston ND, Viardot A, Blum KA, Flowers CR, Jurczak WJ, Flinn IW, Kahl BS, Martin P, Kim Y, Shreay S, Will M, Sorensen B, Breuleux M, Zinzani PL, Gopal AK. Haematologica. 2017 Apr;102(4):e156-e159. doi: 10.3324/haematol.2016.151738. Results of a multicentre UK-wide compassionate use programme evaluating the efficacy of idelalisib monotherapy in relapsed, refractory follicular lymphoma. Eyre TA, Osborne WL, Gallop-Evans E, Ardeshna KM, Kassam S, Sadullah S, Sidra G, Culligan D, Arumainathan A, Shankara P, Bowles KM, Eyre DW, Peng YY, Pettengell R, Bloor A, Vandenberghe E, Collins GP. Br J Haematol. 2017 Mar 24. doi: 10.1111/bjh.14665.	
Questions for consultation	Gilead Sciences	• BSC can be defined as palliative care • NICE guidelines do not cover patients refractory to two previous line of therapy specifically. Therefore, the current NICE pathway would need to be extended • One of the benefits not captured in the QALY calculation would be the reduction in lymph nodes size • No barriers in the adoption pf this technology have been identified	Comments noted. No changes needed to the scope.
	Royal College of Pathology and British Society of Haematology	*Should rituximab containing regimens be included or are people refractory to treatment with rituximab?* This would depend on clinician preference, and their individual definition of 'rituximab refractory' – hence the importance of clarifying that definition.	Comment noted. The definition of ritixumab refractory is given in the background section to the scope. That is,

Section	Consultee/ Commentator	Comments [sic]	Action
			Cancers that do not respond to rituximab or relapse soon after finishing treatment
		If applicable, 'How should best supportive care be defined?' Typically: antibiotics, palliative measures, transfusion support, holistic support. Not to include active agents targeting the disease biology.	Comment noted.
		Where do you consider idelalisib will fit into the existing NICE pathway, Blood and bone marrow cancers overview: lymphoma. Pathway created December 2013? This can be added under the section of 'relapsed / refractory FL' in the same therapeutic area where it was previously assessed by NICE: 'Idelalisib for treating follicular lymphoma that is refractory to 2 prior treatments (terminated appraisal)'	Comment noted.
		To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly. No	Comment noted.
Additional comments on the draft scope	Royal College of Pathology and British Society of Haematology	As above. All other comments/ questions addressed within the document	Comment noted.

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

Anthony Nolan