

National Institute for Health and Clinical Excellence

Single Technology Appraisal (STA)

Pralatrexate for the treatment of relapsed or refractory peripheral T-cell lymphoma

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

Comment 1: the draft remit

Section	Consultees	Comments	Action
Appropriateness	Royal College of Pathologists & British Society for Haematology	Yes, this is an appropriate topic for NICE appraisal	Comment noted.
	Allos Therapeutics	The prevalence of PTCL in the UK is very low and the prevalence of relapsed or refractory PTCL, while difficult to quantify, is even lower. Therefore the impact of pralatrexate on NHS resources is likely to be minimal. There are no currently approved therapies and no standard of care for the treatment of this condition in the UK and there is little available data on the management of PTCL with which to compare the cost effectiveness of pralatrexate. Therefore, whilst there is a significant unmet medical need for patients with PTCL, the appropriateness of undertaking this Single Technology Appraisal may be questioned.	Comments noted. If this topic is formally referred to NICE as a technology appraisal, the reliability of the available evidence will be considered by the Committee when formulating its recommendations.

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Wording	Royal College of Pathologists & British Society for Haematology	Yes	Comment noted.
	Allos Therapeutics	The wording is appropriate.	Comment noted.
Timing Issues	Royal College of Pathologists & British Society for Haematology	Not urgent	Comment noted.
	Allos Therapeutics	The suggested timing is appropriate.	Comment noted.

Comment 2: the draft scope

Section	Consultees	Comments	Action
Background information	Royal College of Pathologists & British Society for Haematology	Nodal PTCL is not just found in the neck but other nodal sites, eg. axillae and groin	The scope has been amended accordingly.
	Allos Therapeutics	The background information states that people with relapsed or refractory PTCL are treated with best supportive care. Whilst all patients should receive best supportive care, patients also receive a wide range of active treatments for the condition that fall outside of the definition of supportive care as described in the NICE guidance on cancer services published in March 2004. These treatments include platinum and non-platinum	The scope has been amended to reflect this information.

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		containing multi-agent chemotherapy as well as various single agents.	
The technology/ intervention	Royal College of Pathologists & British Society for Haematology	Yes	Comment noted
	Allos Therapeutics	Yes	Comment noted.
Population	Royal College of Pathologists & British Society for Haematology	Yes	Comment noted
	Allos Therapeutics	This section refers to “people with relapsed or refractory PTCL”. For clarity, it should refer to “adults with relapsed or refractory PTCL”.	The scope has been amended accordingly.
		<p>There are no data to suggest that separate analysis of groups or subgroups would be useful. Peripheral T-cell lymphomas are a heterogeneous group of aggressive non-Hodgkin’s lymphomas. Data for pralatrexate covers most of the recognised subtypes and includes:</p> <ul style="list-style-type: none"> • PTCL (unspecified) • Anaplastic large cell lymphoma (primary systemic type) • Angioimmunoblastic T-cell lymphoma • Transformed mycosis fungoides • Blastic NK lymphoma (with skin, lymph node, or visceral involvement) 	Comments noted. Following discussion at the scoping workshop, it was agreed that it would not be necessary to specify particular subtypes of PTCL within the population definition.

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		<ul style="list-style-type: none"> • T/NK-cell lymphoma-nasal • Extranodal peripheral T/NK-cell lymphoma (unspecified) • Adult T-cell leukemia/lymphoma (HTLV 1+) 	
Comparators	Royal College of Pathologists & British Society for Haematology	There are a large number of "salvage" chemotherapy regimens used to treat relapsed refractory lymphoma (eg. platinum based regimens) which would not be considered "supportive care". However, to date second and subsequent line therapies have not significantly changed survival outcomes in PTCL	<p>During the scoping workshop, the clinical experts suggested that pralatrexate would most likely be used in the UK for patients who currently receive active treatment. Noting that platinum-based chemotherapy regimens are the most commonly used treatments for patients who have relapsed or refractory disease, they suggested that this would be a more appropriate comparator than best supportive care.</p> <p>Accordingly, the scope has been amended to remove best supportive care from the comparators and insert platinum-based chemotherapy.</p>
	Allos Therapeutics	<p>The comparator in the draft scope is given as best supportive care. We do not consider that this is an appropriate comparator.</p> <p>All patients with PTCL should receive best supportive care according to the definition within the NICE guidance on cancer services (published March 2004). This would include those receiving pralatrexate or other active treatment such as multi-agent</p>	Best supportive care has been removed as a comparator from the scope and has been replaced with platinum-based chemotherapy, in line with advice from the clinical specialists at the scoping workshop

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		<p>chemotherapy.</p> <p>Furthermore, the components of the umbrella term “best supportive care” vary from publication to publication and centre to centre. Therefore there is no acceptable data with which to compare the clinical benefit or cost effectiveness of best supportive care with pralatrexate.</p>	
		<p>Relapsed or refractory PTCL is usually a fatal disease for which there is no approved standard of treatment. There are currently no medicinal products approved for the treatment of PTCL and a paucity of published data on the treatment of this disease. We suggest that the active therapies used in routine clinical practice are selected as comparators. Those therapies most commonly used previously in patients included in the pralatrexate pivotal study were a variety of multi-agent chemotherapy regimens (platinum and non-platinum containing) and single agents.</p> <p>No single treatment regimen currently used in the NHS could be described as “best alternative care” for relapsed or refractory PTCL.</p>	<p>The scope has been amended to include platinum-based chemotherapy as a comparator.</p> <p>Comment noted.</p>
Outcomes	Royal College of Pathologists & British Society for Haematology	Yes	Comment noted
	Allos Therapeutics	The clinical outcomes listed are appropriate. In addition, time to response and duration of treatment are appropriate outcome measures as these impact cost and healthcare utilisation as well as patient	Time to response and duration of treatment have been included as relevant outcomes in the scope.

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		<p>exposure to drug.</p> <p>Overall survival, while accepted as the best overall outcome for oncology studies, is difficult to measure in this rare disease and there is likely to be a paucity of useful data for the appraisal.</p>	Comment noted.
Economic analysis	Royal College of Pathologists & British Society for Haematology	Yes	Comment noted.
	Allos Therapeutics	No comment	Response noted.
Equality and Diversity	Royal College of Pathologists & British Society for Haematology	No specific equality issues here. Of note, one sub-type of PTCL (ATLL) occurs almost exclusively in the Afro-Caribbean population	<p>During the scoping workshop, the clinical experts advised that although it is well recognised that ATLL occurs almost exclusively in people of African–Caribbean origin in the UK, there is no evidence of systematically differing prognosis or access to treatment amongst different racial groups.</p> <p>No amendments to the scope are required, although the issue is noted.</p>
	Allos Therapeutics	We have no suggestions on this section.	Comment noted.
Other considerations	Allos Therapeutics	No comment	Response noted.

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<p>Questions for consultation: <i>What do you consider to be the relevant clinical outcomes and other potential health related benefits of pralatrexate for the treatment of relapsed or refractory peripheral T-cell lymphoma, particularly when compared with currently used treatment options?</i></p>	<p>Royal College of Pathologists & British Society for Haematology</p>	<p>Improved response rate, PFS and OS in relapsed/refractory PTCL, compared to previous "best response" to treatment. Life expectancy in this group is on average only 3-4 months, any improvement on this would be considered as clinically important</p>	<p>Comment noted.</p>
	<p>Allos Therapeutics</p>	<p>See previous comments to 'Outcomes' in draft scope.</p>	<p>Comment noted.</p>
<p>Questions for consultation: <i>Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.</i></p>	<p>Royal College of Pathologists & British Society for Haematology</p>	<p>Data from a large Phase II single arm trial</p>	<p>Comment noted</p>
	<p>Allos Therapeutics</p>	<p>A few published studies are available that investigated treatment options for patients with relapsed or refractory PTCL. Generally, the trials have been small and performed in single institutions; most have evaluated treatment of a mixed group of lymphomas and all have used investigator determination of response.</p>	<p>Comment noted. At the scoping workshop, there was acknowledgment that PROPEL is the largest prospectively defined trial conducted in PTCL.</p>
<p>Questions for consultation: <i>How is relapsed or refractory peripheral T-cell lymphoma currently managed in clinical practice?</i></p> <ul style="list-style-type: none"> <i>Have the most appropriate comparators for the treatment of relapsed or refractory peripheral T-cell</i> 	<p>Allos Therapeutics</p>	<p>See previous comments to 'Comparators' in draft scope.</p>	<p>Comment noted.</p>

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<p><i>lymphoma been included in the scope?</i></p> <ul style="list-style-type: none"> <i>What does best supportive care consist of?</i> 			
<p>Questions for consultation: <i>Are there any subgroups of patients in whom the technology is expected to be more clinically effective and cost effective or other groups that should be examined separately?</i></p>	Allos Therapeutics	Although peripheral T-cell lymphomas are a heterogeneous group of aggressive non-Hodgkin's lymphomas, there are no data to suggest that separate analysis of groups or subgroups would be useful.	In discussion at the scoping workshop, it was confirmed that it would not be necessary to specify particular subtypes of PTCL as subgroups.
<p>Questions for consultation: <i>Are there any issues that require special attention in light of the duty to have due regard to the need to eliminate unlawful discrimination and promote equality?</i></p>	Allos Therapeutics	No	Comment noted.

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

Department of Health

Marie Curie Cancer Care

NHS Quality Improvement Scotland

Public Health Wales NHS Trust

RICE - Research Institute for the Care of Older People

Royal College of Nursing

Welsh Assembly Government

National Institute for Health and Clinical Excellence