National Institute for Health and Care Excellence

Health Technology Evaluation

Seladelpar for previously treated primary biliary cholangitis [ID6429]

Response to stakeholder organisation 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 and proposed process

Section	Stakeholder	Comments [sic]	Action
Appropriateness of an evaluation and proposed evaluation route	Gilead Sciences (company)	We agree that it is appropriate to evaluate Seladelpar via the single technology appraisal route.	Thank you for your comment.
	The British Association for the Study of the Liver (BASL)	Appropriate for single technology appraisal: Seladelpar (product to be evaluated) amongst individuals with the chronic liver disease primary biliary cholangitis (PBC) who are either intolerant to, and/or incomplete- / non-responders to, first-line therapy in ursodeoxycholic acid.	Thank you for your comment.
	British Society of Gastroenterology	The evaluation is appropriate.	Thank you for your comment.
Wording	Gilead Sciences (company)	We agree the wording of the remit is appropriate.	Thank you for your comment.
	The British Association for	Broadly, yes. But some of the outcomes under assessment fall out of scope, based on the publicly available information about the product (for instance fatigue and abdominal pain).	Thank you for your comment. Please see

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	the Study of the Liver (BASL)		response under Outcomes, below.
	British Society of Gastroenterology	Yes [wording reflects the remit].	Thank you for your comment.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Gilead Sciences (company)	We agree with the background information.	Thank you for your comment.
	The British Association for the Study of the Liver (BASL)	Accurate.	Thank you for your comment.
	British Society of Gastroenterology	PBC is no longer known as Primary Biliary Cirrhosis, so it would be better to say here “previously known as Primary Biliary Cirrhosis”, rather than “also known…”	Thank you for your comment. We have made this change to the final scope.
Population	Gilead Sciences (company)	We agree with the defined population.	Thank you for your comment.
	The British Association for the Study of the Liver (BASL)	Yes [the population is appropriate].	Thank you for your comment.

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	British Society of Gastroenterology	Yes [the population is appropriate].	Thank you for your comment.
Subgroups	Gilead Sciences (company)	No, there are no subgroups of the population in whom Seladelpar alone or in combination with UDCA is more clinically effective.	Thank you for your comment.
	The British Association for the Study of the Liver (BASL)	Sub-groups in whom the technology may be more clinically and cost effective: 1) Early-moderate stage PBC (minimal / moderate fibrosis) with isolated elevated ALP values above the upper limit of normal 2) Individuals with pruritus 3) Those who have inadequately responded to ursodeoxycholic acid and/or obeticholic acid. Higher-risk groups, in whom the benefit / safety profile is less clear: 1) Those with advanced liver disease, defined as individuals who have cirrhosis, and either (a) clinically significant portal hypertension, (b) elevated serum bilirubin values (e.g. >2x the upper limit of normal), or (c) hypoalbuminaemia (<35 g/L)	Thank you for your comments. The subgroups identified for whom the technology may be more clinically and cost effective have been added to the final scope.
	British Society of Gastroenterology	No [there are no subgroups that should be considered separately].	Thank you for your comment.
Comparators	Gilead Sciences (company)	We do not agree that Fibrates or Elafibranor are suitable comparators for Seladelpar for this appraisal. Fibrates are used off-label and have documented toxicity and efficacy issues that are yet to be addressed. Discussions with clinical experts within the field of PBC suggests that fibrates are used as an adjunctive option to UDCA in patients that do not meet the current clinical criteria for Second line therapy.	Thank you for your comments. NICE agrees that fibrates should be removed, so the scope has been updated to reflect this. Elafibranor remains included as a potentially

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		The fibrate patient cohort discussed above would have an ALP between 1 and 1.67 ULN and would not be considered the same as the cohort for Seladelpar. Fibrates were not included in the OCA or ELA appraisal and therefore including these within the appraisal for Seladelpar would create inequity. Elafibranor is currently being appraised and therefore is not a standard treatment option in NHS clinical practice. Elafibranor is unlikely to be reimbursed until after the Seladelpar appraisal submission date and therefore not in clinical use within the UK.	relevant comparator (subject to NICE approval).
	Ipsen	We believe elafibranor should be a comparator for seladelpar.	Thank you for your comment. In order for Elafibranor to be considered as a relevant comparator it must be a standard option available within the NHS at the time of this evaluation. It has therefore been included in the scope as “subject to NICE evaluation”.
	The British Association for the Study of the Liver (BASL)	Yes [all relevant comparators have been included].	Thank you for your comment.
	British Society of Gastroenterology	Yes [all relevant comparators have been included].	Thank you for your comment.

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Outcomes	Gilead Sciences (company)	We agree with the outcome measures.	Thank you for your comment.
	The British Association for the Study of the Liver (BASL)	Yes, with the exception of fatigue and abdominal pain (these have not been assessed rigorously from an efficacy perspective).	Thank you for your comment. Fatigue and abdominal pain are symptoms of PBC and so the company may choose to present evidence on these outcomes in its submission to NICE.
	British Society of Gastroenterology	Yes [the outcomes listed are appropriate].	Thank you for your comment.
Equality	Gilead Sciences (company)	N/A	Thank you for your comment.
	The British Association for the Study of the Liver (BASL)	No major concerns.	Thank you for your comment.
	British Society of Gastroenterology	None identified.	Thank you for your comment.
Other considerations	Gilead Sciences (company)	We would like the committee to consider the time at which patients are trialled on UDCA before considering an alternative treatment option. We believe this	Thank you for your comment. No change to scope required.

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		should be based on clinician judgement and not a defined period of 12 months.	
Questions for consultation	Gilead Sciences (company)	**Gilead Sciences response to Questions for consultation:** 1: Where do you consider seladelpar will fit into the existing care pathway for primary biliary cholangitis? **Gilead Response:** SEL will be prescribed in secondary care with routine follow up in secondary care. In recognition of the increased workload prescribing of second line therapies by specialist centres as Hubs and the inequalities of access for patients this can create who have been extensively manged by spoke centres prior to SLT initiation. Gilead would like the consultation to consider allowing spoke centres to prescribe this treatment following MDT approval at the Hub site from the outset of any positive recommendations by NICE. 2: For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention. **Gilead Response:** UDCA is prescribed by Primary care in many areas of the country following initiation by a specialist in Secondary care. Comparator second line therapies such as Ocaliva are only prescribed and dispensed via secondary care usually via the Specialist Centre unless there is an agreed shared care protocol in place allowing spoke prescribing.	Thank you for your comments.

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		3:Would seladelpar be a candidate for managed access? **Gilead Response:** We do not believe that Seladelpar is a candidate for managed access. 4: Are fibrates (such as bezafibrate and fenofibrate) relevant comparators for seladelpar? **Gilead Response:** Fibrates are not licenced in the UK for use in treating patients with PBC. Fibrates have not been included in previous appraisals for Ocaliva and now Elafibranor and therefore we believe inclusion would also create inequity in the process if included in the Seladelpar appraisal. Discussions with Clinical experts within the field of PBC suggests that fibrates are used as an adjunctive option to UDCA in patients that do not meet the current clinical criteria for Second line therapy. The fibrate patient cohort discussed above would have an ALP between 1 and 1.67 ULN and would not be considered the same as the cohort for Seladelpar. 5: Do you consider that the use of seladelpar can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation? Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.	

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		Gilead Response: Seladelpar is a once daily, oral capsule, which does not require dose titration. This simple dosing regimen may benefit patients. 6: NICE is considering evaluating this technology through its cost comparison evaluation process. 6.1: Is seladelpar likely to be similar in its clinical effectiveness and resource use to any of the comparators? Or in what way is it different to the comparators? **Gilead Response:** Seladelpar is clinically more effective at ALP normalisation and reduction in itch, with a comparable side effect profile compared to Ocaliva and UDCA. 6.2: Will seladelpar be used in the same place in the treatment pathway as the comparator(s)? Have there been any major changes to the treatment pathway recently? If so, please describe. **Gilead Response:** Seladelpar will be used as a second line option following intolerance or inadequate response to UDCA or as a third line option in those patients who are intolerant or do not adequately respond to Ocaliva. Currently there are no additional options for those patients with PBC who cannot tolerate Ocaliva. 6.3: Will seladelpar be used to treat the same population as the comparator(s)?	

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		Gilead Response: Seladelpar will be used to treat a similar population to those patients currently receiving Ocaliva however can also be used to treat those who are intolerant or who have not improved on current Ocaliva treatment. 6.4: Overall is seladelpar likely to offer similar or improved health benefits compared with the comparators? **Gilead Response:** We believe Seladelpar will offer improved health benefits compared to OCA due to its significant benefit on PBC related itch and demonstrable clinical efficacy in normalisation of ALP. 6.5: Would it be appropriate to use the cost-comparison methodology for this topic? **Gilead Response:** No	
	British Society of Gastroenterology	Where do you consider seladelpar will fit into the existing care pathway for primary biliary cholangitis? - Prescribed in secondary care with routine follow-up in secondary care For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention - All PBC pharmacologic management and follow up should be in secondary care	Thank you for your comments.

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		Are fibrates (such as bezafibrate and fenofibrate) relevant comparators for seladelpar? Yes, fibrates are used by many teams as part of PBC care Do you consider that the use of seladelpar can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation? No • Is seladelpar likely to be similar in its clinical effectiveness and resource use to any of the comparators? Or in what way is it different to the comparators? - It may have broader population than obeticholic acid (i.e. more advanced liver disease), but other comparators would be similar population. It may have stronger effect on itch that many comparators (but not all) • Will seladelpar be used in the same place in the treatment pathway as the comparator(s)? Have there been any major changes to the treatment pathway recently? If so, please describe. seladelpar (and elafibranor) expected to occupy a position similar to obeticholic acid (i.e. add on for urso incomplete response, or single agent for urso intolerant). • Will seladelpar be used to treat the same population as the comparator(s)? Yes in general, although some comparators (i.e. obeticholic acid) are not suitable for use in more advanced liver disease. • Overall is seladelpar likely to offer similar or improved health benefits compared with the comparators? The published data for both seladelpar and elafibranor suggest they will be an improvement on many current comparators, both in terms of biochemical efficacy and itch control. Would it be appropriate to use the cost-comparison methodology for this topic? If the above issues can be addressed within it, yes.	NICE considers that fibrates are not a direct active comparator (see Comparators section above), but rather are part of the background treatments that people with PBC will be offered. So fibrates have been removed from the comparator section of the final scope.

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

- British Liver Trust
- Genetic Alliant UK