Seladelpar for treating primary biliary cholangitis [ID6429]

For public – confidential information redacted

- **Technology appraisal committee D [10 September 2025]**
- **Chair:** Megan John
- **External assessment group:** Peninsula Technology Assessment Group (PenTAG)
- **Technical team:** Madiha Adam, Emily Leckenby, Lizzie Bell
- **Company:** Gilead

Seladelpar for treating primary biliary cholangitis [ID6429]

- ✓ **Background and ACM1 summary**
- ❑ Consultation responses
- ❑ Key issues
- ❑ Cost effectiveness results

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Draft guidance recommendation

RECAP

Seladelpar should not be used within its marketing authorisation to treat primary biliary cholangitis, including pruritus, in adults:

- with ursodeoxycholic acid (UDCA), if the primary biliary cholangitis has not responded well enough to UDCA, or
- alone, if UDCA cannot be tolerated

Reasons committee made this decision:

- Uncertainty in the treatment pathway (DG section 3.2, 3.3)
- Important uncertainties in the methodology and results of the indirect comparisons (DG 3.7, 3.8)
- Unclear if the model reflected the effect of itching and other aspects of PBC on quality of life (DG 3.12)
- More evidence needed to generate robust cost-effectiveness estimates

Consultation responses received from:

- Gilead (company) – provided new evidence and base case
- Patient and clinical organisations:
  - British Association for the Study of the Liver (BASL)
  - British Hepatology Pharmacist Group
  - Ipsen
  - PBC Foundation

Equality considerations (DG 3.15):

- Noted differences in prevalence and outcomes by sex and age, noting poorer outcomes in men and younger patients, and fertility concerns in younger women.
- Will consider potential difference in prevalence and outcomes within groups with protected characteristics.

Abbreviations: DG, draft guidance; ICER, incremental cost-effectiveness ratio; PBC, primary biliary cholangitis; UDCA, ursodeoxycholic acid

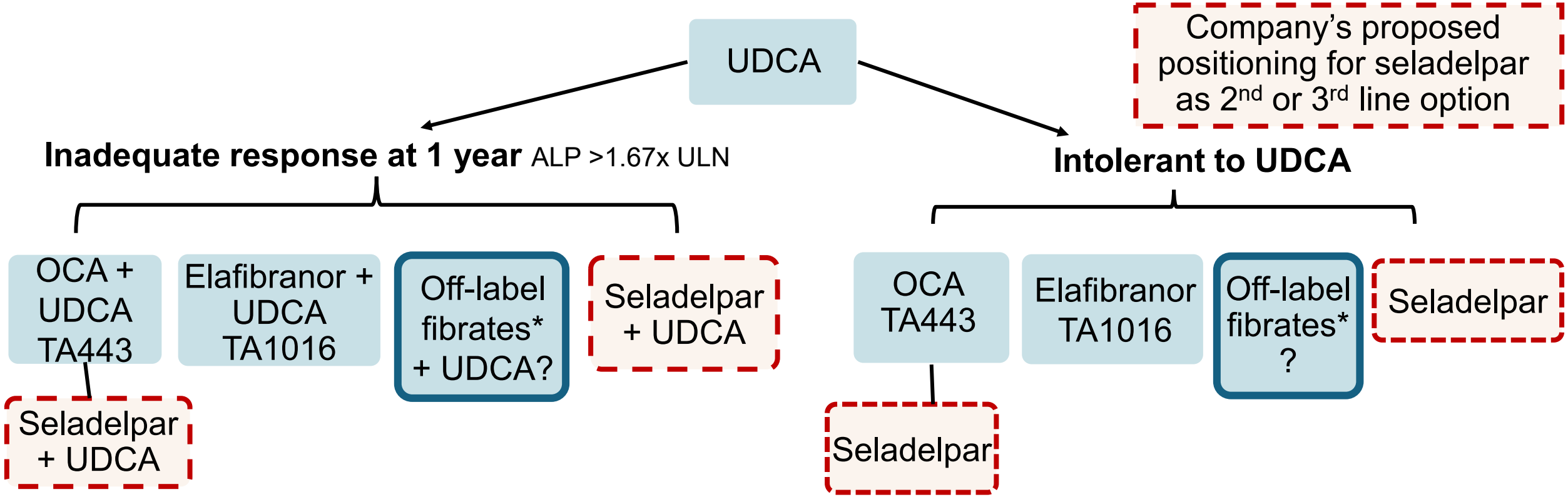
Technology (seladelpar, Livdelzi®, Gilead)

Marketing authorisation	Adults with PBC in combination with UDCA who have an inadequate response to UDCA alone, or as monotherapy in those unable to tolerate UDCA
Mechanism of action	• Selective PPARδ agonist • Reduces bile acid synthesis and accumulation • Anti-inflammatory
Administration	10 mg orally once daily
Price	• The list price: £3,155.00 per pack of 30 capsules of 10mg seladelpar • Confidential PAS discount in place

Abbreviations: PAS, patient access scheme; PBC, primary biliary cholangitis; PPAR, peroxisome proliferator-activated receptor; UDCA, Ursodeoxycholic acid;

Treatment pathway

RECAP



- UDCA is established 1st line treatment option (BSG/PBC guidelines).

*At ACM1 committee considered:

- fibrates could be a potential comparator for people with PBC and pruritus in NHS practice.
- a comparison of benefits and costs between seladelpar and fibrates would be informative.
- it would be useful for NICE to re-issue scope to include fibrates as comparator.

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Abbreviations: ALP, alkaline phosphatase; OCA: obeticholic acid; PBC: primary biliary cholangitis; TA, technology appraisal; UDCA, ursodeoxycholic acid; ULN, upper level of normal

Summary of clinical evidence

RECAP

Indirect comparisons → no head-to-head trials of seladelpar compared with OCA, or elafibranor

Trial data	RESPONSE	
	Seladelpar	Placebo
Composite outcome at 12 months	79/128 (61.7%)	13/65 (20.0%)
ALP baseline and response sub-outcomes		
Baseline ALP, U/L, mean (SD)	314.6 (123.0)	313.8 (117.7)
ALP <1.67× ULN, n/N (%)	84/128 (65.6)	17/65 (26.2)
≥ 15% decrease in ALP n/N (%)	107/128 (83.6)	21/65 (32.3)
Bilirubin baseline and response sub-outcome		
Baseline total bilirubin mg/dl, mean (SD)	0.769 (0.3)	0.737 (0.3)
Total bilirubin ≤ 1.0× ULN, n/N (%)	104/128 (81.3)	50/65 (76.9)

Company base case at ACM1:

- Seladelpar + UDCA vs. UDCA + placebo (RESPONSE)
- Bayesian NMA: OCA + UDCA vs. UDCA + placebo (POISE, COBALT, NCT03633227)
- Anchored MAIC: Elafibranor + UDCA vs. UDCA + placebo (ELATIVE)

EAG base case at ACM1:

- Noted uncertainty associated with using different methods for each comparison
- Preferred Bayesian NMA → fewer concerns with transitivity than the low ESS with MAIC

Committee conclusions at ACM1

- Seladelpar clinically effective in improving ALP levels and reducing pruritus vs. placebo (DG 3.5)
- Trial outcomes in RESPONSE trial were informative for decision making (DG 3.4)
- Bayesian NMA should be used for all ITCs (inappropriate to use separate method for each comparison) (DG 3.7)

Abbreviations: ESS, effective sample size; ITC, indirect treatment comparison; MAIC, Matching-Adjusted Indirect Comparison; NMA, Network Meta-analysis; OCA, obeticholic acid; PBC, primary biliary cholangitis; RCT; Randomised Controlled Trial; TA, technology appraisal; UDCA, ursodeoxycholic acid

Committee preferred assumptions following ACM1 (1/2)

Company accepted committee assumptions for:

- Baseline ALP distribution (no patients start from ALP normalisation and mild state)
- Long term discontinuation rate (ratio of 0.12 based on RESPONSE and ASSURE)

No	Key issue and committee	Committee preference	Company response	Changes to company base case?
1	Exclusion of fibrates as comparators (DG 3.3)	• Considering fibrates as a potential comparator	Not included as a comparator	No
2	Uncertainty in the relative effectiveness of seladelpar in comparison with existing treatment options (DG 3.7)	• Full description of the ITC and explanation of its uncertainty (scenario analyses to explore impact of uncertainty) • Bayesian NMA to be done for ITC for all comparators	• Provided updated ITC report • Provided scenario analysis including 3 comparators in a single network	No – suggested alternative approach

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Abbreviations: ITC, indirect treatment comparison; NMA, network meta-analysis; OCA, obeticholic acid;

Committee preferred assumptions following ACM1 (2/2)

No	Key issue	Committee preference	Company response	Changes to company base case?
3	Treatment discontinuation rate (0 to 12 months) (DG 3.11)	• Use of ITC-derived rates	• Scenario using real world evidence for OCA, ITC for seladelpar and elafibranor	No – suggested alternative approach
4	Source for health state utility data (DG 3.12)	• Same data source (RESPONSE) to be used for utility values for ALP health states and pruritus • Commentary on how well the model captures quality of life in PBC, supported by relevant literature where available	• Identified alternative source of pruritic disutilities (Hussain et al, 2023) • Proposed alternative application of current disutility values for pruritus	No – suggested alternative approach

Abbreviations: ITC, indirect treatment comparison; OCA, obeticholic acid;

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Summary of consultation responses received

Patient and professional groups highlight fibrates should not be a comparator

Concerns about fibrates as comparators	**PBC Foundation (patient):**	• Lack of PBC-specific expertise in fibrate discussions. • Fibrates used more in general hospitals → specialist centres favour OCA. • Safety concerns (liver/kidney toxicity) and discontinued repurposing programme. • Fibrates not genuinely compared with OCA and elafibranor.
	BHPG (professional):	• Fibrates not licensed, access is variable, and no new real-world evidence. • Including fibrates may reduce access to seladelpar (licenced treatment). • Elafibranor faced similar pathway uncertainties; seladelpar should not be held to a different standard.
	BASL (professional):	• Comparisons with fibrates focus on effectiveness, not safety. • >10% of UK fibrate users develop liver enzyme elevations, not seen with seladelpar.
Support for Seladelpar **BASL:**		• Seladelpar normalises ALP in 1 in 4 patients → not achieved by other licensed therapy. • Strong ALP reduction in cirrhotic patients; better than OCA, no data yet for elafibranor. • Long-term efficacy and safety data (ASSURE) underrepresented → shows durable response and anti-pruritic effects.

Ipsen (comparator company):		• Incorrect claims made during ACM1:
		  • Elafibranor does have positive pruritus data (5-D Itch, PBC-40 Itch).
		  • PBC-40 is validated and widely used for HRQoL in PBC.

Abbreviations: ACM, appraisal committee meeting; ALP, alkaline phosphatase; BASL, The British association for the study of the liver; BHPG, British hepatology pharmacy group; HRQoL, health-related quality of life; OCA, obeticholic acid; PBC, primary biliary cholangitis; 5-D, 5-dimension

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Key issue 1: Exclusion of fibrates as comparator (1/2)

Large ICER impact

Recap from ACM1

- Company: fibrates not a comparator.
- EAG: uncertainty that fibrates used solely to manage itching and are not an active 2nd line treatment.
- Clinical expert at ACM1: fibrates are used as a second-line treatment.
- Committee preference: requested more evidence about fibrates as a comparator.

NICE technical team

- The manual (section 6.2.4): *"can consider comparators that do not have regulatory approval …. When they are considered to be part of established clinical practice for the population in the NHS."*

NHSE

- Fibrates are used in different ways across the country with variable utilisation owing to the license status.
- They are not standard clinical practice.
- Including them will negatively impact patient access to the licensed treatment options.

Element	Company
Consistency with previous appraisals	• TA1016 FG 3.4: '[Abbas audit usage of] fibrates may have been used as add on for itching, rather than to treat' • TA443 FAD 4.3 'fibrates not disease modifying drugs, not appropriate comparator'.

Abbreviations: FAD, final appraisal document; FG, final guidance; ITC, indirect treatment comparison; MAIC, matching-adjusted indirect comparison; OCA, obeticholic acid; PBC, primary biliary cholangitis; SLR, systematic literature review; TA, technology appraisal; UDCA, ursodeoxycholic acid; ULN, upper limit of normal

Key issue 1: Exclusion of fibrates as comparator (2/2)

Large ICER impact

Element	Company	EAG
Clinical experts	• Consulted 5 clinical experts. • Fibrates only used in specific cases e.g., failure to approved therapies or combination for itch management.	• Consulted 3 clinical experts. • Fibrates used in some NHS centres, and supported by Abbas 2024 audit (may offer more representative view). • Fibrates are used to treat PBC – they are a PPAR agonist.
Safety concerns	• TA1016 'fibrates not widely used as a second-line treatment due to toxicity and limited efficacy'.	• Company should present safety data for fibrates from SLR to allow assessment.

ITC and MAIC	• Conducted SLR – 1 study Li, et al 2022
	  • ITC not feasible: differences in inclusion criteria, baseline characteristics, and response definitions.
	  • MAIC not feasible: extreme heterogeneity between RESPONSE & Li, et al populations.
		• SLR limited to studies reporting 12-month follow-up.
		• ITC comparing fibrates with seladelpar may not be feasible: a narrative synthesis of primary fibrate trials could have identified key evidence, trends, and comparisons with UDCA.

Committee member

- ITC with fibrates could consider AEs if data available for an NMA.
- Support company assessment that an NMA may not be appropriate. They are not standard clinical practice.

Cost-effectiveness impacts

- EAG expected seladelpar wouldn't be cost-effective vs fibrates but couldn't test this due to model constraints.

Should fibrates be considered as a comparator to seladelpar?

Abbreviations: ITC, indirect treatment comparison; MAIC, matching-adjusted indirect comparison; PBC, primary biliary cholangitis; SLR, systematic literature review; TA, technology appraisal;

Key issue 2: Uncertainty in indirect comparisons (1/3)

Large ICER impact

Recap from ACM1

- No head-to-head trials directly comparing seladelpar with comparators.
  - Company did an ITC using split Bayesian NMA (comparison with OCA) and MAIC (comparison with elafibranor) approach.
  - Estimates using each approach had uncertainty (wide credible intervals).
- Committee concluded consistent approach should be used for all ITCs; Bayesian NMA appropriate.

ACM2 considerations

Different definitions of outcomes across RESPONSE, ELATIVE and POISE

→ 2 different recalculations of the RESPONSE outcomes are required

→ Outcome recalculation leads to reversal of direction of absolute and relative effects

→ In agreement that separate comparisons appropriate, but MAIC or NMA?

1 **Committee member comment:**
- MAIC vs NMA, depends on effect modifiers and whether results are suitable for decision making

2 **Committee member comment**
- Different definitions

EAG:
- Separate comparisons → impacts to fully-incremental analyses (seladelpar needs to be cost-effective compared to OCA **and** elafibranor)

Abbreviations: ALP, alkaline phosphatase; ANA, antinuclear antibodies; ITC, indirect treatment comparison; MAIC, Matching-Adjusted Indirect Comparison; NMA, Network Meta-analysis; OCA, obeticholic acid; ULN, upper limit of normal

Key issue 2: Uncertainty in indirect comparisons (2/3)

Considerable uncertainty due to low sample sizes and event numbers

Large ICER impact

Element	Company	EAG
1. MAIC for Ela vs NMA for Ela	• Statisticians = the presence of unbalanced effect modifiers → MAIC. • See appendix for distribution of effect modifiers.	• No clear evidence of effect modification for age or baseline ALP in the forest plot. • No evidence differences for bilirubin and cirrhosis (potentially an effect modifier) are clinically meaningful. • Evidence the matching process struggled to account for baseline differences and potentially introduced bias. • MAIC unlikely to meet TSD18 criteria of "less biased estimates" than the NMA and concerns about ESS.
2. Outcome definition	**Committee comment:** • Alternative outcome recalculation has an impact on relative effects. • If using the definition in RESPONSE (e.g., proportion with normalisation of ALP [≤ 1.0xULN]) then basing decisions on results base on other definitions may not be appropriate.	
Base case	• Elafibranor = MAIC • OCA = NMA	Two NMAs and ORs applied to calibrate hazards. • Elafibranor NMA: ELATIVE-matched ULN. • OCA NMA: POISE-matched ULN.

Committee member comments

- Particularly wide credible intervals for "ALP normalisation at 12 months" is trial design (linking by zero event study) and only head-to-head trial can resolve → results of this outcome are unavoidably uncertain.

Abbreviations: ALP, alkaline phosphatase; EAG, Evidence Assessment Group; ESS, effective sample size; MAIC, Matching-Adjusted Indirect Comparison; NMA, Network Meta-Analysis; OCA, Obeticholic Acid; ORs, odds ratios; TSD, technical support document; ULN, upper limit of normal

Key issue 2: Uncertainty in indirect comparisons (3/3)

Large ICER impact

- Example of NMA vs MAIC: ALP normalisation; ALP response (Toronto 1) analyses in appendix
- Other adjustments change the point estimate and credible intervals

ALP normalisation	Type	Approach	OR (95% CrI)
Versus elafibranor	NMA	• Bayesian with +1 continuity correction • Result +0.5 continuity correction	• [redacted] • [redacted]
	MAIC	-	• [redacted]
Versus OCA 5-10mg	NMA	• Bayesian with +1 continuity correction • Result +0.5 continuity correction	• [redacted] • [redacted]

EAG:

- EAG NMA broadly consistent with company NMA; particularly for elafibranor.
  - Difference in packages used to run code and different continuity error.
- Credible intervals highly dependent on the adjustments made to the placebo arms of the trials and the results of the NMA were highly uncertain.
- Note: 0.5 continuity results taken from ITC report as DG response had flipped odds ratios and relative risks.

- Do committee prefer a MAIC for seladelpar vs elafibranor or an NMA?
- How to overcome the uncertainty around the results?

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Abbreviations: ALP, alkaline phosphatase; DG, draft guidance; EAG: evidence assessment group; MAIC, Matching-Adjusted Indirect Comparison; NMA: network meta-analysis; OCA: obeticholic acid; OR: odds ratio; ULN: upper limit of normal

Key issue 3: Treatment discontinuation (1/2)

Large ICER impact

Recap from ACM1

- Committee preferred EAG approach: rates should be derived from the ITC and assumptions on the rate of discontinuation after 12 months should be derived from data from seladelpar trials, not elafibranor.

Company response to DG (0 to 12 months)

- Company base case 0 to 12 months maintains cumulative discontinuation from ACM1
- Proposed scenario deriving rates from the ITC anchored to real world data for OCA (Abbas et al., 2023)
  - Refer to scenario as 'most realistic' but have not incorporated into base case

	Company base case		Alternative scenario		
Treatment	Rate	Source	Rate	Source	Justification
OCA	9.59%	Naively sourced from studies (ELATIVE, POISE)	22.1%	Abbas et al., 2023 as an anchor	
Elafibranor	6.73%		8.4%	ITC using OCA discontinuation (22.1%) as the anchor Average of elafibranor (10.4%) and seladelpar (6.4%)	No clinical rationale for differing rates between seladelpar and elafibranor
Seladelpar	9.59%	RESPONSE	8.4%		

Abbreviations: ITC, indirect treatment comparison; NMA, network meta-analysis; OCA, obeticholic acid; OLE, open-label extension

Key issue 3: Treatment discontinuation (2/2)

Large ICER impact

EAG comments on company alternative scenario (kept same base case)

- Anchoring discontinuation to a different external source (e.g., Abbas 2023) would break internal consistently.
- Prefers ITC anchored to seladelpar trial; consistent with how transition probabilities were generated.
- Disagree with identical discontinuation for seladelpar and elafibranor:
  - EAG: Consider it reasonable that patients and clinicians would continue longer on a treatment with fewer severe pruritus incidents, as shown in the ITC.

Committee member comments on company alternative scenario : simple averaging is inappropriate as it ignores differences in precision of 2 estimates. Unclear how uncertainty around the average is handled in the PSA, if varied at all.

Cumulative discontinuation at 12 months (UDCA tolerant and intolerant)	Seladelpar	Elafibranor	OCA
Company base case	6.73%	9.59%	9.59%
ITC (EAG and committee at ACM1 preference)	6.73%	11.02%	26.95%

Which approach for treatment discontinuation is most appropriate?

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Abbreviations: ITC, indirect treatment comparison; NMA, network meta-analysis; OCA, obeticholic acid; OLE, open-label extension

Key issue 4: Source for health state utility data (1/2)

Medium ICER impact

Recap from ACM1

- Committee preferred EAG's utility approach (MMRM-derived disutilities) but noted uncertainty around potential underestimation of pruritus disutility and whether the model accurately reflected QoL across ALP health states.
- Requested further explanation and supporting evidence from the literature.

Company response to DG

1. Base case: remains Smith et al.
   - Company proposes alternative application of the Smith et al. disutilities → original (0.87) exceeded general population norm (0.804); company derives baseline utility (0.81) directly from GLIMMER cohort using matched general population value (0.83) and RESPONSE multiplier (0.97), states this is more realistic but not used in base case.
2. Alternative literature source for pruritus disutility → Hussain et al. (2023) for pruritus disutilities for PSC which reported mean EQ-5D utilities.

Alternative scenarios presented by the company

Utility, PBC, no itch	Utility of PBC (GLIMMER trial)		Updated disutility by health state
0.81	Mild pruritus	0.75	-0.055
	Moderate pruritus	0.76	-0.055
	Severe pruritus	0.49	-0.320

Utility, PSC, no itch	Utility of PSC, by itch severity (on NRS scale)		Disutility by itch severity
0.81	Mild pruritus	0.77	-0.040
	Moderate pruritus	0.70	-0.110
	Severe pruritus	0.68	-0.130

Abbreviations: ALP, alkaline phosphatase; EQ-5D-3L, EuroQol-5 dimensions-3 levels; EQ-5D-5L, EuroQol-5 dimensions-5 levels; NRS, numerical rating scale; PSC, primary sclerosing cholangitis

Key issue 4: Source for health state utility data (2/2)

Medium ICER impact

EAG comments

1. Re-anchored values for Smith et al:
   - Severe pruritus disutility (-0.32) lacks face validity → same as heart failure hospitalization (TA679).
   - EAG expert disagreed with Smith et al. claims: NRS 7 patients may still work, unlike severe Parkinson's.
2. Hussain et al 2023:
   - Estimates more plausible than Smith et al. but based on PSC not PBC.
   - Results only available as a conference abstract, limited detailed appraisal of the study methods.
3. EAG base case:
   - Using values from MMRM2 mapping model using EQ-5D-3L data from RESPONSE:
     - Internally consistent and aligns with Rice et al. (UK PBC study, n=2,240) → small, non-significant disutility for itch (-0.018) associated with HRQoL impairment.
     - Model includes anti-pruritic drug costs; using high disutilities from less credible sources risks overestimating impact.

Parameter	EAG base case	Company base case
Mild pruritus	-0.0041	-0.1150
Moderate pruritus	-0.0041	-0.1150
Severe pruritus	-0.0345	-0.3800

- Which source provides the most appropriate health state utility values for pruritus?
- Does the model accurately reflected QoL across ALP health states?

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Abbreviations: EQ-5D-3L, EuroQol-5 dimensions-3 levels; HRQoL, health-related quality of life; NRS, numerical rating scale; PBC, primary biliary cholangitis; PD, Parkinson's disease; PSC, primary sclerosing cholangitis; QoL; quality-of-life

Cost-effectiveness results

All ICERs are reported in PART 2 slides because they include confidential comparator PAS discounts

Committee decision making slide (1/2)

Issue	Committee preference at ACM1	Company base case at ACM2	EAG base case at ACM2
Exclusion of fibrates as comparators	• Consider fibrates as a potential comparator	Fibrates are not a relevant comparator	Fibrates are a relevant comparator to seladelpar
Uncertainty in the relative effectiveness of seladelpar in comparison with existing treatment options	• Full description of the ITC and explanation of its uncertainty (scenario analyses to explore impact of uncertainty) • Bayesian NMA to be done for ITC for all comparators	• Vs. elafibranor (MAIC) • Vs OCA (Bayesian NMA excluding elafibranor trial) • Scenario presented: including 3 comparators in a single network	Two NMAs: ELATIVE-matched ULN for elafibranor and POISE-matched ULN for OCA; ORs applied to calibrate hazards

Committee decision making slide (2/2)

Issue	Committee preference at ACM1	Company base case at ACM2	EAG base case at ACM2
Treatment discontinuation rate (0-12 months)	Use of ITC-derived rates	• Individual trial data from RESPONSE, ELATIVE, and POISE • Suggested alternative: average discontinuation rate from ITC for seladelpar and elafibranor, real-world evidence of discontinuation for OCA	Committee preference at ACM1: • ITC anchored to RESPONSE (seladelpar as anchor; comparators relative to seladelpar)
Source for health state utility data	• Same data source (RESPONSE) to be used for utility values for ALP health states and pruritus • Commentary on how well the model captures quality of life in PBC, supported by relevant literature where available	• Pruritus disutilities sourced from Smith et al. • Suggested alternatives: Adjusted Smith et al., disutilities and Hussain et al.	Committee preference at ACM1: • MMRM2 mapping model from EQ-5D-3L (pivotal seladelpar trial)

Cost-effectiveness results

Confidential discounts for comparators – ICERs in Part 2 slides

ICER ranges presented below

Summary – in both the UDCA tolerant and intolerant cohorts:

- Company base case is higher than £30,000 per QALY gained
- EAG base case is higher than the company's
- Seladelpar +/- UDCA has highest total costs and QALYs
  - QALY difference between seladelpar and elafibranor is small

Scenario analysis

- No scenario gives cost-effectiveness estimates within £20,000 to £30,000
- Pruritus disutility based on Hussain et al. gives highest increase in ICER

Seladelpar for treating primary biliary cholangitis

- ❑ Background and key issues
- ❑ Clinical effectiveness
- ❑ Modelling and cost effectiveness
- ❑ Other considerations
- ✓ **Summary**

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Summary of company and EAG base case assumptions

Assumption	Company base case	EAG base case
Fibrates as comparator	Fibrates are not a relevant comparator	Fibrates are a relevant comparator to seladelpar
ITC informing treatment effect	• vs. elafibranor (MAIC) • Vs. OCA (Bayesian NMA excluding elafibranor trial) • Scenario presented: including 3 comparators in a single network	Two NMAs: ELATIVE-matched ULN for elafibranor and POISE-matched ULN for OCA; ORs applied to calibrate hazards
Treatment discontinuation rate (0-12 months)	• Individual trial data from RESPONSE, ELATIVE, and POISE • **Suggested alternative**: average discontinuation rate from ITC for seladelpar and elafibranor, real-world evidence of discontinuation for OCA	ITC anchored to RESPONSE (seladelpar as anchor; comparators relative to seladelpar)
Pruritus disutility	• Pruritus disutilities sourced from Smith et al. • **Suggested alternative**: Adjusted Smith et al., disutilities and Hussain et al.	MMRM2 mapping model from EQ-5D-3L (pivotal seladelpar trial)

Abbreviations: EQ-3D, EuroQol-5 dimensions-3 levels; ITC, indirect treatment comparison; MAIC, Matching-Adjusted Indirect Comparison; MMRM, Mixed model for repeated measures; NMA, network meta-analysis; PBC, primary biliary cholangitis; UDCA, ursodeoxycholic acid

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Supplementary appendix

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Equality considerations

Equality issues

Company:	People with PBC face long wait times (3 to 4 months) and have higher mortality whilst on liver transplant lists compared to people with other liver diseases
Stakeholders in TA1016:	**Prevalence in women:** estimated that 90% of people with PBC are women globally, with incidence rates 5 to 6 times higher for women than men **Outcomes by age:** people diagnosed with PBC under the age of 50 experience more severe and progressive disease and poor treatment response compared with patients over the age of 50 at diagnosis **Outcomes by sex:** men are at greater risk for more advanced disease at diagnosis and poor treatment response compared with women
BHPG/ British Liver Trust	**Geography:** recent UK-wide audit highlights geographical disparities in care, with access to specialist teams and second-line treatments varying due to differences in local availability of resources

- EAG did identify any further equality issues
- No equality issues raised at scoping stage

Link back to main slide

Abbreviations: BHPG, British Hepatology Pharmacy Group; PBC, primary biliary cholangitis; TA, technology appraisal

Key issue 2: Uncertainty in indirect comparisons

Large ICER impact

ALP response (Tornoto 1)	Type	Approach	OR (95% CrI)
Versus elafibranor	NMA	• Bayesian • Company	• [redacted] • [redacted]
	MAIC	-	• [redacted]
Versus OCA 5-10mg	NMA	• Bayesian • Company	• [redacted] • [redacted]

Note: company results taken from ITC report as DG response had flipped odds ratios and relative risks

Back to main slide

Abbreviations: ALP, alkaline phosphatase; CrI: credible interval; DG, draft guidance; EAG: evidence assessment group; NMA: network meta-analysis; OCA: obeticholic acid; OR: odds ratio; ULN: upper limit of normal

Key issue 2: Uncertainty in indirect comparisons

Large ICER impact

Population characteristics	ELATIVE	RESPONSE	POISE
Baseline ALP mean U/L (SD)	321.9 (150.9)	314.3 (121.9)	323 (112.5)
Mean total bilirubin level-µmol/liter (SD)	9.6 (5.1)	12.9 (5.1)	11.1 (6.5)
Cirrhosis (%)	9.9 (8.3 in ELA and 13.2 in UDCA)	14.0	16.0
Age at diagnosis (SD) [95% CI]	-	49.2 (10.3)	47.3 (10.8)
Age at screening (mean ± SD)	[redacted]	[redacted]	
Bilirubin >ULN at baseline (%)	3.7	13.0 (15.6 in SEL and 7.7 in UDCA)	8.3

Back to main slide

Abbreviations: ALP, alkaline phosphatase; CI, confidence interval; SD, standard deviation; UDCA, ursodeoxycholic acid; ULN, upper limit of normal; SEL, seladelpar