Tafasitamab with lenalidomide for treating relapsed or refractory diffuse large B-cell lymphoma

For public and projector – CIC information redacted [redacted]

Third appraisal committee meeting (post appeal)

Technology appraisal committee C [14 February 2023]

Chair: Stephen O'Brien

Evidence assessment group: Kleijnen Systematic Reviews

Technical team: Owen Swales, Ross Dent

Company: Incyte

TAFA + LEN for R/R DLBCL

→ **Appraisal recap**

- Appeal outcome:
  - Appeal summary
  - Upheld appeal point
  - FAD rewording
- ICERs
- Summary

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Abbreviations: FAD, final appraisal determination; ICERs, incremental cost-effectiveness ratios; R/R DLBCL, relapsed or refractory diffuse large B-cell lymphoma

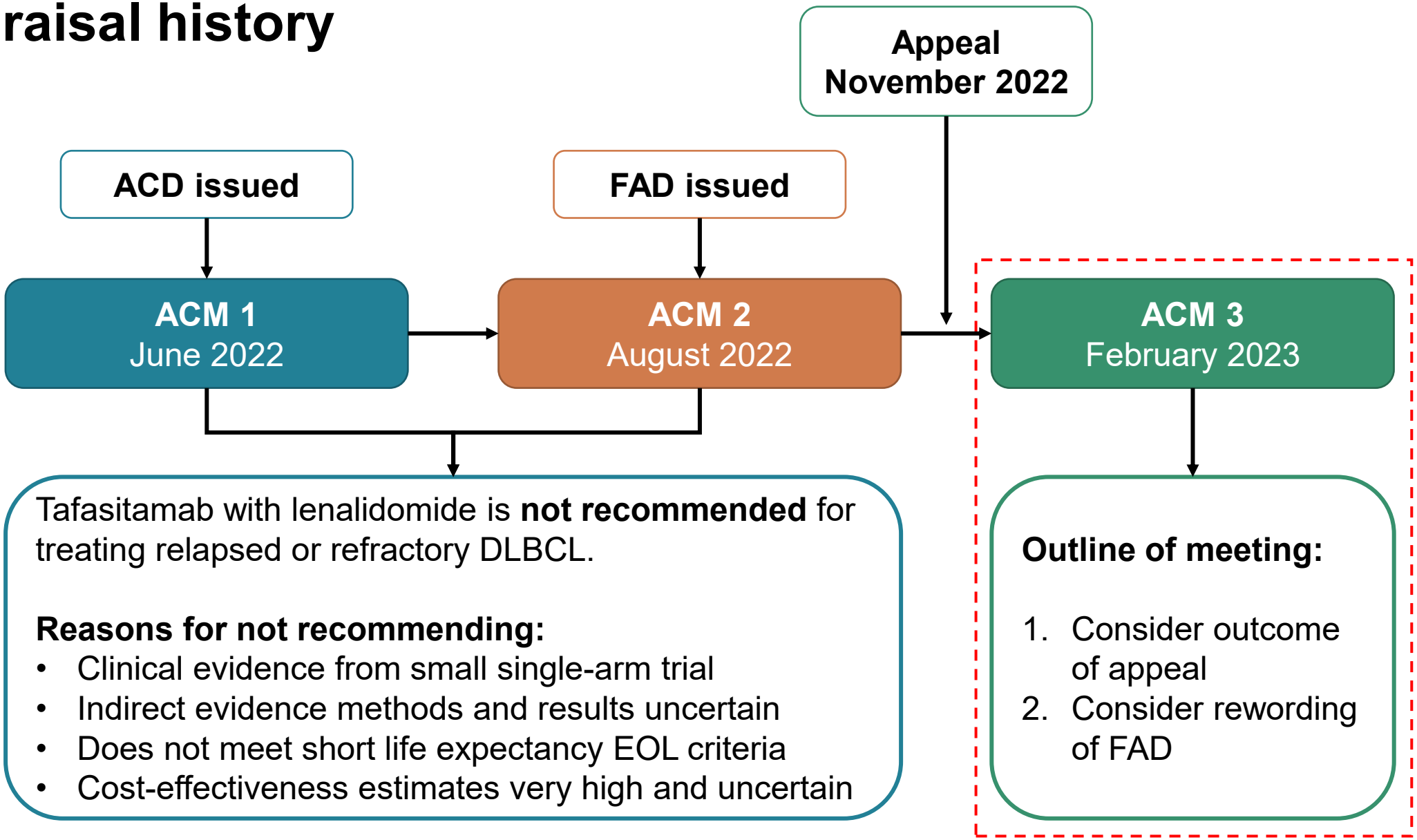
Tafasitamab (Minjuvi, Incyte)

Table 1 Technology details

Marketing authorisation	• Tafasitamab in combination with lenalidomide followed by tafasitamab monotherapy for treating adult patients with relapsed or refractory DLBCL who are not eligible for ASCT
Mechanism of action	• Monoclonal antibody that targets the CD19 antigen expressed on the surface of pre-B and mature B lymphocytes • Potential synergy with lenalidomide, an immunomodulatory agent that enhances the activity and recruitment of natural killer (NK) cells. NK cells are engaged by tafasitamab
Administration	• 12 mg per kg body weight administered as an intravenous infusion. • Taken until disease progression or unacceptable toxicity • Lenalidomide oral capsules for up to 12 cycles of 28 days
Price	• List price of £705 per vial of tafasitamab; lenalidomide list price of £4,368 for 21 pack • Year 1 list price of [redacted] for 12 months treatment (£120,639 for tafasitamab) • Year 2 onwards list price of £95,049 for 12 months treatment (tafasitamab monotherapy) • A patient access scheme is available for tafasitamab and a confidential CMU price for lenalidomide

Abbreviations: ASCT, autologous stem cell transplant; CMU, commercial medicines unit; DLBCL, diffuse large B-cell lymphoma; EMA, European Medicines Agency; MHRA, Medicines and Healthcare products Regulatory Agency; NK, natural killer

Appraisal history



Abbreviations: ACD, appraisal consultation document; ACM, appraisal committee meeting; DLBCL, diffuse large B-cell lymphoma; EOL, end of life; FAD, final appraisal document

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Appeal summary

Appeals submitted by company, Lymphoma Action and professional groups

- 4 points submitted
- 1 point upheld
- 1 suggestion for clarification

Committee asked to:	• Appraise the technology on the basis that the NICE end of life criteria apply • Consider the extent, if any, to which this influences the eligibility of tafasitamab for use through the Cancer Drugs Fund
Committee to consider rewording FAD to:	• Clarify the efforts that were made to acquire the most relevant estimates of the cost of lenalidomide to the NHS at the time of publication of the FAD, as well as the sensitivity analyses that were undertaken around these costs, which were presented to the committee for their consideration

Abbreviations: FAD, final appraisal document; NHS, national health service

Recap of end of life evidence considered by committee

Committee considered whether life expectancy would be less than 24 months

Figure 1 Modelled and published OS for pola-BR

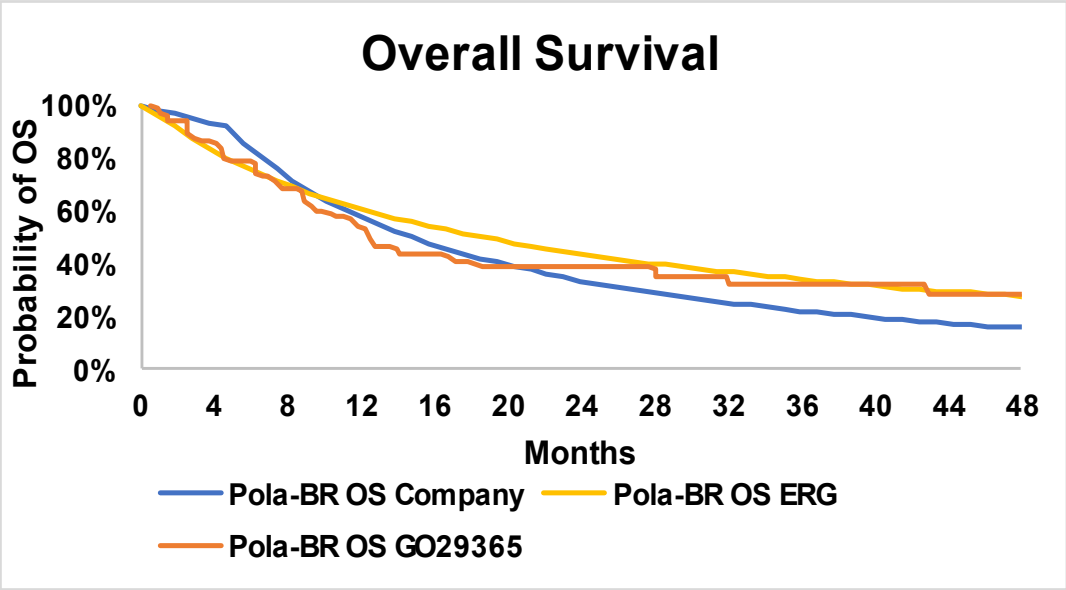


Table 2 Evidence on end-of-life criterion 1

Data source	Average OS	% alive at 24 months
Literature	**Median OS:** 8.2 to 12.5 months	-
Sehn 2022	**Median OS:** 12.4 months	38%
Northend 2022	**Median OS:** 10.2 months (stand-alone)	-
TA649	**Mean OS:** 37 months (discounted)	-
Company model	**Mean OS:** 29 months (undiscounted)	34%
ERG model	**Mean OS:** 48 months (undiscounted)	44%

GO29365 data digitised from Sehn 2022 Kaplan-Meier curves; company extrapolations based on Sehn 2020 (latest available at submission)

Abbreviations: ERG, evidence review group; OS, overall survival; pola-BR, polatuzumab vedotin plus bendamustine and rituximab

Upheld appeal point – end of life criterion 1 (1)

Appeal panel conclusions (1)

- *"noted that there was agreement between the appellants and the appraisal committee that the evidence considered in this appraisal showed a median survival for people with refractory or relapsed DLBCL of significantly less than 24 months but that the modelled mean survival was greater than 24 months"*
- *"the NICE Methods guide and the NICE Decision Support Unit … do not specify how the word "normally" should be interpreted … in previous NICE appraisals both the mean and median survival have been considered"*
- *"The appeal panel were aware that the NICE EOL criteria were founded on the principles in NICE's "guide to the use of Social Value Judgements" … the paramount consideration should be what the key stakeholders of NICE … would reasonably expect the word "normally" to mean … agreed with the conclusion of the previous avelumab appeal panel that where a significant majority of patients had died prior to 24 months, NICE stakeholders would consider it unreasonable to find that life-expectancy was not "normally less than 24 months", even if the mean life expectancy was greater than 24 months"*

Abbreviations: DLBCL, diffuse large B-cell lymphoma; EOL, end of life

Upheld appeal point – end of life criterion 1 (2)

Appeal panel conclusions (2)

- *"recently published 'real-world' data suggests that the significant majority of patients [with refractory or relapsed DLBCL] will have died within 10-13 months if they received conventional comparator treatment"*
- *"The appeal panel considered that the figure no more than "35% alive after 2 years" cited by the appeal panel in the avelumab appeal was intended by that panel to illustrate the panel's view that it was unreasonable of the NICE recommendations on avelumab to conclude that life expectancy was in excess of 24 months when a significant majority of patients had died at 24 months"*
- *"The panel agreed that the intention of the appeal panel in avelumab had not been to set a precedent or define a new numerical threshold that should be used in future NICE technology appraisals applying the EOL criteria"*
- *"Therefore, they considered the relevant test remained that set out in NICE's Methods guide, i.e., "the treatment is indicated for patients with a short life expectancy, normally less than 24 months."*

Abbreviations: DLBCL, diffuse large B-cell lymphoma; EOL, end of life

Upheld appeal point – end of life criterion 1 (3)

Appeal panel conclusions (3)

- *"the panel understood the rationale for the preference of the committee, in this appraisal, to use the mean survival as the dominant consideration to inform the decision that the EOL criteria were not met, in view of the health economic implications of doing so"*
- *"the evidence showed that the median survival for patients with refractory or relapsed DLBCL is consistently less than 2 years and the significant majority of patients with this condition have died before 2 years, the committee's conclusion that the treatment does not meet the EOL requirement … does not adequately reflect how NICE's stakeholders would reasonably interpret and apply this criterion"*
- *"NICE's stakeholders would reasonably expect that the dominant evidence in determining qualification for the EOL criterion should reflect metrics of survival that are the most meaningful to [stakeholders] … it noted the consistent evidence … survival in the 'real world' that is considerably less than the modelled mean survival and more in keeping with the median survival reported in the literature"*
- ***"the committee decision that the first EOL criterion was not met in this appraisal was unreasonable in light of the evidence submitted to NICE"***

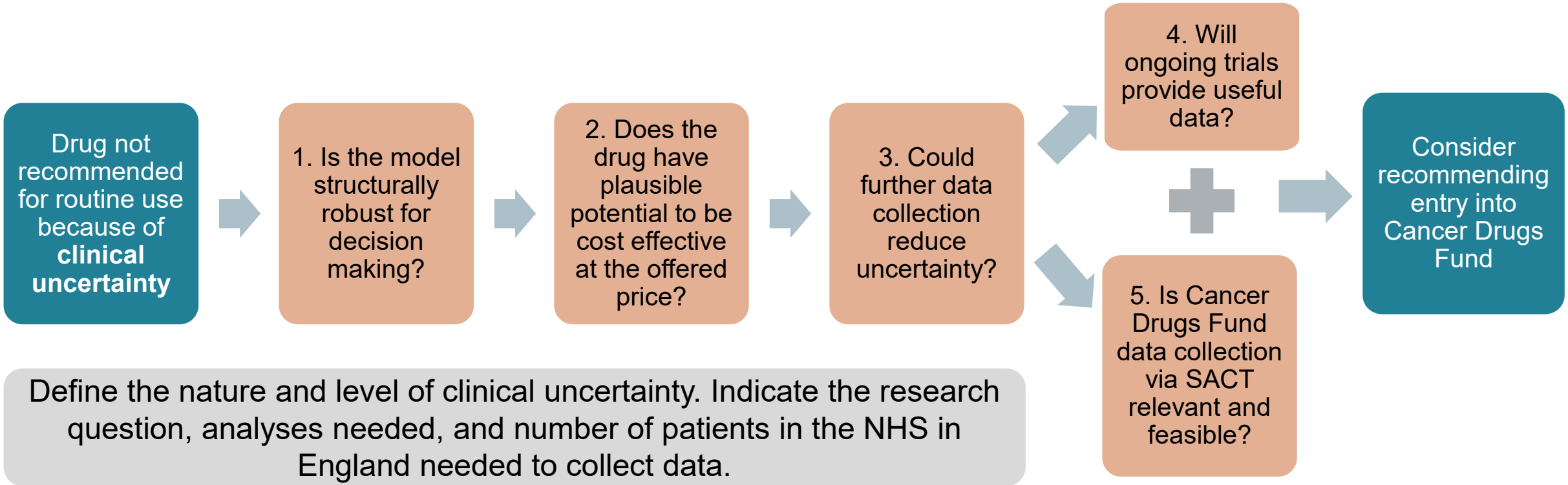
Abbreviations: DLBCL, diffuse large B-cell lymphoma; EOL, end of life

Upheld appeal point – end of life criterion 1 summary

Appeal panel conclusions summary

- All parties agree median survival less than 24 months, mean survival more than 24 months
- Interpretation of the word “normally” should be what the key stakeholders of NICE would reasonably expect the word “normally” to mean
- Stakeholders would consider it unreasonable to find that life-expectancy was not “normally less than 24 months” where most patients had died prior to 24 months and mean survival was greater than 24 months
- “35% alive after 2 years” cited by the avelumab appeal panel was not setting a precedent/new threshold
- Relevant test is that in NICE’s Methods guide, i.e., “short life expectancy, normally less than 24 months”
- Dominant evidence used to determine the end of life criterion should reflect survival metrics that are the most meaningful to stakeholders
- Consistent real world evidence shows survival is less than mean survival and aligned with median survival
- **Unreasonable to conclude end of life criterion 1 is not met in light of the evidence**

Cancer Drugs Fund reconsideration



Define the nature and level of clinical uncertainty. Indicate the research question, analyses needed, and number of patients in the NHS in England needed to collect data.

- Ongoing data collection in L-MIND is currently being analysed and will provide approximately [redacted] longer follow up for OS, PFS and DoR to address uncertainty in survival extrapolations
- The firmMIND study is currently recruiting. This single arm Phase 3 study will provide data similar to the L-MIND study to fulfil conditions for regulatory approvals

NICE

Abbreviations: DoR, duration of response; NHS, national health service; OS, overall survival; PFS, progression-free survival; SACT, Systemic Anti-Cancer Therapy

Committee to consider rewording FAD

Current FAD, section 3.9:

- "It noted that the company's and ERG's base case probabilistic ICERs (including all the confidential discounts)…were higher than the range normally considered a cost-effective use of NHS resources"

NICE technical team suggested addition:

- "In considering the decision-making ICERs, the committee accounted for all the confidential discounts for comparator and subsequent treatments. This included the impact of the loss of price exclusivity on the price for lenalidomide. During the second committee meeting, it considered the live interim tender price for lenalidomide as provided by the Cancer Drugs Fund lead, as well as pricing scenarios including the estimated price discount for generic lenalidomide up to and including a 100% discount (i.e., no cost for lenalidomide). During the third committee meeting, the committee considered the nationally available tender price for generic lenalidomide as confirmed by the Commercial Medicines Unit. The prices agreed through the framework are commercial in confidence. The committe noted that the company's and ERG's base case probabilistic ICERs (including all the confidential discounts and lenalidomide pricing scenarios)…were higher than the range normally considered a cost-effective use of NHS resources"

Abbreviations: ERG, evidence review group; FAD, final appraisal document; ICER, incremental cost-effectiveness ratio; NHS, national health service

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Cost-effectiveness results

All ICERs are reported in PART 2 slides

because they include confidential

comparator PAS discounts

Summary

- Company's base case ICER against pola-BR is **higher than the range** that would usually be considered a cost-effective use of NHS resources for treatments given at the end of life
- EAG's base case ICER against pola-BR is **higher than the range** that would usually be considered a cost-effective use of NHS resources for treatments given at the end of life

Abbreviations: EAG, evidence assessment group; ICER, incremental cost-effectiveness ratio; NHS, national health service; PAS, patient access scheme; Pola-BR, polatuzumab vedotin plus bendamustine and rituximab

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Summary

Committee will now move to Part 2 of the meeting

In Part 2 of the meeting, committee will:

- View ICERs which include the most relevant and current confidential prices for all treatments
- Appraise tafasitamab with lenalidomide on the basis that the NICE end of life criteria apply
- Consider the extent, if any, to which this influences the eligibility of tafasitamab for use through the Cancer Drugs Fund
- Consider rewording the FAD to clarify the efforts that were made to acquire the most relevant estimates of the cost of lenalidomide during ACM2

Abbreviations: ACM, appraisal committee meeting; FAD, final appraisal document; ICER, incremental cost-effectiveness ratio

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Thank you.