Single Technology Appraisal

Pirtobrutinib for treating relapsed or refractory chronic lymphocytic leukaemia after a BTK inhibitor [ID6269]

Committee Papers

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

SINGLE TECHNOLOGY APPRAISAL

Pirtobrutinib for treating relapsed or refractory chronic lymphocytic leukaemia after a BTK inhibitor [ID6269]

Contents

The following documents are made available to stakeholders:

1. **Comments on the Draft Guidance from Eli Lilly and Company Ltd**

2. **Consultee and commentator comments on the Draft Guidance** from:
   a. AstraZeneca UK
   b. UK CLL Forum

3. **Comments on the Draft Guidance from expert** Dr Renata Walewska, Consultant Haematologist, Clinical Expert nominated by Eli Lilly and Company Ltd

4. **Comments on the Draft Guidance received through the NICE website**

Any information supplied to NICE which has been marked as confidential, has been redacted. All personal information has also been redacted.

NICE National Institute for Health and Care Excellence

Pirtobrutinib for treating relapsed or refractory chronic lymphocytic leukaemia after a BTK inhibitor [ID6269]

Draft guidance comments form

Consultation on the draft guidance document – deadline for comments: 5pm on **Monday 11 May 2026**. Please submit via NICE Docs.

	Please read the checklist for submitting comments at the end of this form. We cannot accept forms that are not filled in correctly. The Appraisal Committee is interested in receiving comments on the following: • has all of the relevant evidence been taken into account? • are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence? • are the provisional recommendations sound and a suitable basis for guidance to the NHS? NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the preliminary recommendations may need changing in order to meet these aims. In particular, please tell us if the preliminary recommendations: • could have a different impact on people protected by the equality legislation than on the wider population, for example by making it more difficult in practice for a specific group to access the technology; • could have any adverse impact on people with a particular disability or disabilities. Please provide any relevant information or data you have regarding such impacts and how they could be avoided or reduced**.**
Organisation name – Stakeholder or respondent (if you are responding as an individual rather than a registered stakeholder please leave blank):	Eli Lilly and Company Limited

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Please disclose any past or current, direct or indirect links to, or funding from, the tobacco industry.	Nil
Name of commentator person completing form:	[redacted]

Comment number	Comments Insert each comment in a new row. Do not paste other tables into this table, because your comments could get lost – type directly into this table.
1	**Has all of the relevant evidence been taken into account?** Lilly agree that all relevant evidence has been taken into account and have no further comments on this question from the Committee.

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2	**Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?** Lilly agree that the summaries of clinical and cost effectiveness are reasonable interpretations of the evidence and have no further comments on this question.
3	**Are the provisional recommendations sound and a suitable basis for guidance to the NHS?** Lilly agree that the provisional recommendations are sound and a suitable basis for guidance to the NHS and have no further comments on this question.
4	**Please let us know if you think that the preliminary recommendations may need changing in order to meet these aims. In particular, please tell us if the preliminary recommendations:** • **could have a different impact on people protected by the equality legislation than on the wider population, for example by making it more difficult in practice for a specific group to access the technology;** • **could have any adverse impact on people with a particular disability or disabilities.** **Please provide any relevant information or data you have regarding such impacts and how they could be avoided or reduced.** Lilly have no comments to raise regarding the above points on equality in access.

Insert extra rows as needed

Checklist for submitting comments

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Organisation name – Stakeholder or respondent (if you are responding as an individual rather than a registered stakeholder please leave blank):	AstraZeneca UK

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Please disclose any past or current, direct or indirect links to, or funding from, the tobacco industry.	N/A
Name of commentator person completing form:	[redacted]

Comment number	Comments Insert each comment in a new row. Do not paste other tables into this table, because your comments could get lost – type directly into this table.
1	We are concerned that section 3.19 of the draft guidance claims that "*the available evidence suggests that cBTKis are at least as effective as BCL2is for first-line CLL*". This statement is unclear and may be misleading depending on how it is interpreted. We agree that both covalent BTK inhibitors (cBTKis) and BCL2 inhibitors (BCL2is) have demonstrated improvements in overall survival (OS) and progression-free survival (PFS)

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	compared with traditional chemotherapy in first-line chronic lymphocytic leukaemia (1L CLL). However, it is important to distinguish between BCL2i monotherapies and BCL2i -based combination therapies in this setting. The current wording suggests equivalent efficacy between BTKis and BCL2is as monotherapies, which is not accurate. BCL2is as monotherapy, specifically Venetoclax monotherapy, are recommended in 1L CLL primarily for patients who are not suitable candidates for BTKis, according to the British Society of Haematology CLL guidelines (1). Consequently, the patient populations receiving these treatments are not directly comparable in terms of disease profile. In addition, there is currently insufficient evidence to suggest that BTKis are as effective as BCL2is monotherapies in first-line CLL. Therefore we propose removing this statement as it is not supported by any evidence base. If, on the other hand, the intention of the above statement in section 3.19 is to suggest comparable efficacy between BTKis and BCL2i-based combination therapies, this distinction should be made explicit to avoid misinterpretation. Based on the clinical evidence, we propose amending the statement as follows: *The available evidence suggests that cBTKis are at least as effective as BCL2i-based combinations for first-line CLL, namely venetoclax with obinutuzumab and venetoclax with ibrutinib.* This wording is more consistent with the available evidence and helps avoid potential confusion. References 1. Walewska R, Eyre TA, Bloor A, Follows G, Iyengar S, Johnston R, et al. 2025 British Society for Haematology Guideline for the treatment of chronic lymphocytic leukaemia. Br J Haematol. 2025;207(6):2296–2313. **https://doi.org/10.1111/bjh.70100**.
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Insert extra rows as needed

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Organisation name – Stakeholder or respondent (if you are responding as an individual rather than a registered stakeholder please leave blank):	UK CLL Forum [redacted]

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Please disclose any past or current, direct or indirect links to, or funding from, the tobacco industry.	Nil
Name of commentator person completing form:	[redacted]

Comment number	**Comments** Insert each comment in a new row. Do not paste other tables into this table, because your comments could get lost – type directly into this table.
Example 1	We are concerned that this recommendation may imply that ……..
1	The CLL Forum welcomes the positive recommendation of Pirtobrutinib in population previously exposed to both cBTKi and BCL2i, matching the criteria from the BRUIN trial and likely representing a significant benefit to patients who would otherwise be eligible for

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	Idelalisib/Rituximab. This population, commonly referred as double exposed, represent a group with a high clinical unmet need.
2	With regards to the population with prior exposure to cBTKi or BCL2i, but for whom cBTKi are not suitable and hence VenR or Venetoclax are options, the CLL Forum acknowledges the uncertainties of the evidence presented and the lack of direct randomised trials comparing these options with Pirtobrutinib. Despite of these uncertainties, we welcome the positive recommendation for this group of patients, providing the CLL community with an additional treatment alternative that may be preferred to a venetoclax-based regimen in certain clinical scenarios.
3	We also agree with the lack of evidence for cost-comparisons, to recommend Pirtobrutinib ahead of cBTKi at this point in time, but would welcome a re-evaluation of this comparison in light of future evidence that may allow an appropriate health-economic analysis.
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Insert extra rows as needed

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Organisation name – Stakeholder or respondent (if you are responding as an individual rather than a registered stakeholder please leave blank):	Renata Walewska, company nominated expert

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Please disclose any past or current, direct or indirect links to, or funding from, the tobacco industry.	N/A
Name of commentator person completing form:	Renata Walewska

Comment number	**Comments** Insert each comment in a new row. Do not paste other tables into this table, because your comments could get lost – type directly into this table.
Example 1	We are concerned that this recommendation may imply that ……..
1	As an expert, I am pleased to read the NICE recommendation for the CLL population, which aligns with the BRUIN 321 study population. These patients would only be able to

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	have Idelalisib rituximab, which is very toxic and difficult to deliver. I welcome having another treatment option to offer my patients.
2	The population with prior exposure to cBTKi or BCL2i, for whom cBTKi is not suitable, and Venetoclax or VenR are options, is a difficult group to investigate; therefore, there is a lack of robust data. Thank you to NICE for recommending pirtobrutinib to this group of patients
3	There is no evidence to recommend Pirtobrutinib before cBTKi; however, I look forward to the maturation of clinical trials and real-world evidence.
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Insert extra rows as needed

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Comments on the draft guidance received through the NICE website

Name	[redacted]
Organisation	N/A
Conflict	N/A
Comments on the DG:	

1 Recommendations (section 1.1)

I have read through the committee discussion and it isn't clear to me what we mean by 'not clinically appropriate'. I am assuming it's when a person has progressed on a cBTK or is intolerant to cBTK. Could we outline either in the recommendation or the in the committee discussion when retreatment would not be appropriate? I have also looked at the CDF and it isn't outlined.

What this means in practice (section 1.2):

- **BTK inhibitor**

Could this say covalent BTK inhibitor?

- **There is limited evidence comparing pirtobrutinib with covalent BTK inhibitors in people with CLL that has been previously treated.**

Could this say- There is limited evidence comparing pirtobrutinib, a non-covalent BTK inhibitor, with covalent BTK inhibitors (acalabrutinib, ibrutinib, zanubrutinib) in people with CLL that has been previously treated.- just so it is clearer on the first page to user.

Marketing authorisation indication - is indicated for (section 2.1)
'is indicated as monotherapy for'

Price - from company submission (section 2.3)
Will this be updated to dm+d pricing for final publishing?

Are the recommendations sound and a suitable basis for guidance to the NHS?
I don't think 'not clinically appropriate' is clear enough and could potentially lead to interpretation