NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Pirtobrutinib for treating chronic lymphocytic leukaemia or small lymphocytic lymphoma after 1 or more BTK inhibitors

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of pirtobrutinib within its marketing authorisation for treating chronic lymphocytic leukaemia or small lymphocytic lymphoma after 1 or more BTK inhibitors.

Background

Chronic lymphocytic leukaemia (CLL) is the most common form of chronic leukaemia and is a type of cancer that affects the white blood cells. It tends to progress slowly over many years. The risk of developing CLL increases with age and is more common in men. CLL mostly affects older people and is rare in people 40 years of age and younger.[1-3] Around 3,900 people are diagnosed with CLL in the UK each year.[2]

In CLL, the material found inside some bones (bone marrow) produces too many white blood cells, called lymphocytes, that aren't fully developed and don't work properly. CLL usually progresses slowly, but over time people can develop anaemia, swollen lymph nodes, spleen enlargement and unexplained weight loss. People with CLL may live with a considerable burden of symptoms and an increased susceptibility to infection impacting on their quality of life, whether or not they have had treatment.[1] Small lymphocytic lymphoma (SLL) is considered the same condition as CLL, as most people with CLL or SLL have abnormal white blood cells in locations that overlap, including lymph nodes, spleen, blood and bone marrow.[4]

Treatment of CLL is complex and depends on several factors such as stage of disease, previous treatment, patient's age, symptoms, and general state of health. Many people with CLL will not have symptoms when they are first diagnosed and will have a period of active surveillance. When treatment is needed, most people will have a targeted treatment such as acalabrutinib, zanubrutinib, ibrutinib, or venetoclax. Some people may have chemoimmunotherapy. If the disease relapses, or is refractory to initial treatment, there are a number of further treatment options.[3] Table 1 below summarises the treatment options which are currently available as routine practice in the NHS in England for relapsed or refractory CLL.

Table 1. Treatment options for relapsed or refractory CLL in NHS practice

NICE technology appraisal	Date	Treatment option for relapsed or refractory CLL	Population
TA931	November 2023	Zanubrutinib	relapsed or refractory CLL in adults

TA796	June 2022	Venetoclax	• people with a 17p deletion or TP53 mutation whose disease has progressed after a B-cell receptor pathway inhibitor or • people without a 17p deletion or TP53 mutation whose disease has progressed after both chemo-immunotherapy and a B-cell receptor pathway inhibitor
TA689	April 2021	Acalabrutinib	previously treated CLL in adults
TA561	February 2019	Venetoclax with rituximab	people who have had at least 1 previous therapy
TA429	January 2017	Ibrutinib	people who have had at least 1 previous therapy
TA359	October 2015	Idelalisib with rituximab	people whose disease has been treated but has relapsed within 24 months
TA193	July 2010	Rituximab in combination with fludarabine and cyclophosphamide	people with relapsed or refractory CLL except when the condition: • is refractory to fludarabine (that is, it has not responded to fludarabine or has relapsed within 6 months of treatment) or • has previously been treated with rituximab, unless: - in the context of a clinical trial, at a dose lower than the dose currently licensed for chronic lymphocytic leukaemia or - in the context of a clinical trial, in combination with chemotherapy other than fludarabine and cyclophosphamide
TA29	September 2001	Fludarabine	people who have had to stop their first chemotherapy treatment

The technology

Pirtobrutinib (Jaypirca, Lilly) does not currently have a marketing authorisation in the UK for chronic lymphocytic leukaemia. It has been studied in a clinical trial, compared with idelalisib plus rituximab or bendamustine plus rituximab, in adults with CLL or SLL who have previously had treatment with at least 1 BTK inhibitor.

Intervention(s)	Pirtobrutinib
Population(s)	Adults with CLL or SLL who have previously had at least 1 BTK inhibitor
Subgroups	Adults with CLL or SLL who have previously had both a BTK inhibitor and venetoclax
Comparators	• Zanubrutinib • Acalabrutinib • Ibrutinib • Venetoclax (if disease has progressed after a B-cell receptor pathway inhibitor) • Venetoclax with rituximab • Idelalisib with rituximab
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rate • adverse effects of treatment • health-related quality of life.
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. The availability of biosimilar and generic products should be taken into account.

Other considerations	Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations	**Related technology appraisals:** Zanubrutinib for treating chronic lymphocytic leukaemia (2023) NICE technology appraisal guidance 931 Venetoclax for treating chronic lymphocytic leukaemia (2022) NICE technology appraisal guidance 796 Acalabrutinib for treating chronic lymphocytic leukaemia (2021) NICE technology appraisal guidance 689 Venetoclax with rituximab for previously treated chronic lymphocytic leukaemia (2019) NICE technology appraisal guidance 561 Ibrutinib for previously treated chronic lymphocytic leukaemia and untreated chronic lymphocytic leukaemia with 17p deletion or TP53 mutation (2017) NICE technology appraisal guidance 429 Idelalisib for treating chronic lymphocytic leukaemia (2015) NICE technology appraisal guidance 359 Rituximab for the treatment of relapsed or refractory chronic lymphocytic leukaemia (2010) NICE technology appraisal guidance 193 Guidance on the use of fludarabine for B-cell chronic lymphocytic leukaemia (2001) NICE technology appraisal guidance 29 **Related Guidelines:** Haematological cancers: improving outcomes (2016). NICE guideline 47 Review date to be confirmed. **Related Quality Standards:** Haematological cancers (2017). NICE quality standard 150.
Related National Policy	The NHS Long Term Plan (2019) NHS Long Term Plan NHS England (2023) NHS manual for prescribed specialist services (2023/24)

Questions for consultation

Where do you consider pirtobrutinib will fit into the existing care pathway for CLL/SLL?

Would pirtobrutinib be a candidate for managed access?

Do you consider that the use of pirtobrutinib 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.

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 proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which pirtobrutinib will be licensed;
- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. 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 tell us what evidence should be obtained to enable the committee to identify and consider such impacts.

NICE intends to evaluate this technology through its Single Technology Appraisal process. (Information on NICE's health technology evaluation processes is available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation).

References

1. Chronic lymphocytic leukaemia (2023) NHS. Accessed February 2025
2. Chronic lymphocytic leukaemia (CLL) incidence statistics (2024) Cancer Research UK. Accessed February 2025
3. Chronic lymphocytic leukaemia (CLL) (2024). Cancer Research UK. Accessed February 2025
4. Small lymphocytic lymphoma (SLL) (2021). Macmillan Cancer Support. Accessed February 2025.