**NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE**

**Health Technology Appraisal**

# Duvelisib for treating relapsed or refractory chronic lymphocytic leukaemia after at least 2 prior treatments

**Final scope**

## Remit/appraisal objective

To appraise the clinical and cost effectiveness of duvelisib within its marketing authorisation for treating relapsed or refractory chronic lymphocytic leukaemia after at least 2 prior treatments.

## Background

Chronic lymphocytic leukaemia (CLL) is the most common type of chronic leukaemia and is a type of cancer that affects lymphocytes, a type of white blood cell, and tends to progress slowly over many years. It mostly affects people 60 years of age and over and is rare in people 40 years of age and younger. In England there were 3,157 new cases of CLL in 2017. The risk of developing CLL increases with age and is more common in men.[1]

In CLL, the material found inside some bones (bone marrow) produces too many lymphocytes that aren't fully developed and don't work properly. Over time this can cause a range of problems, such as an increased risk of picking up infections, persistent tiredness, swollen glands and unusual bleeding or bruising.[2] People with CLL may live with a considerable burden of symptoms impacting on their quality of life, whether or not they have received treatment. Approximately 5% to 10% of people diagnosed with CLL are considered to have 'high-risk' disease, characterised by the presence of cytogenetic mutations or abnormalities (that is, 17p deletion or TP53 mutation)[3]. The presence of 17p deletion or TP53 mutation can increase both the rate of cell growth and the resistance of the disease to treatment. The presence of an immunoglobulin heavy chain gene (IgHV) mutation may also affect clinical outcomes.

Treatment for relapsed or refractory CLL is complex and depends on several factors, including the extent of the disease, mutation status, previous treatments, and the patient's age, symptoms and general state of health. The table below summarise 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 treated CLL in NHS practice**

| NICE technology appraisal | Treatment option | Population |
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| TA689 | acalabrutinib | for people who have had at least 1 previous therapy |
| TA561 | venetoclax with rituximab | for people who have had at least 1 previous therapy |
| TA193 | rituximab with fludarabine and cyclophosphamide | for people not refractory to fludarabine and who have not been previously treated with rituximab* |
| TA359 | idelalisib with rituximab | for people whose disease has been treated but has relapsed within 24 months |
| TA429 | ibrutinib monotherapy | for people who have had at least 1 previous therapy |
| Not applicable | bendamustine with or without rituximab | No marketing authorisation for this indication |
| *unless treated within the context of a clinical trial either at a lower dose than licensed or in combination with chemotherapy other than fludarabine and cyclosphosphamide. | | |

**The technology**

Duvelisib (Copiktra, Secura Bio) is a dual inhibitor of phosphatidylinositol 3 kinase (PI3K) δ and γ isoforms. The PI3K pathway promotes cell proliferation, growth, motility metabolism and survival. PI3K inhibitors have been shown to block growth and induce cell death. It is administered as oral capsules.

Duvelisib has a marketing authorisation in the UK for treating chronic lymphocytic leukaemia after at least 2 prior treatments.

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| **Intervention(s)** | Duvelisib |
| **Population(s)** | People with relapsed or refractory chronic lymphocytic leukaemia (CLL) after at least 2 prior therapies |
| **Comparators** | Established clinical management without duvelisib including but not limited to:<br>• venetoclax with rituximab<br>• ibrutinib<br>• chemoimmunotherapy such as bendamustine with rituximab or chlorambucil with rituximab<br>• acalabrutinib<br>• idelalisib with rituximab |

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| **Outcomes** | The outcome measures to be considered include:<br>• progression-free survival<br>• overall survival<br>• time to next treatment<br>• adverse effects of treatment<br>• 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.<br>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.<br>Costs will be considered from an NHS and Personal Social Services perspective.<br>The availability and cost of biosimilar products should be taken into account.<br>The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. |
| **Other considerations** | If the evidence allows the following subgroups will be considered:<br>• people with or without a 17p deletion or TP 53 mutation<br>• people with IgHV unmutated disease<br>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 and NICE Pathways** | **Related Technology Appraisals**:<br>Acalabrutinib for treating chronic lymphocytic leukaemia (2021) NICE technology appraisal guidance 689<br>Venetoclax in combination with rituximab for treating relapsed or refractory chronic lymphocytic leukaemia (2019) NICE technology appraisal guidance 561 |

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| | Venetoclax for treating chronic lymphocytic leukaemia (2017) NICE technology appraisal guidance 487<br><br>Ibrutinib for previously treated chronic lymphocytic leukaemia and untreated chronic lymphocytic leukaemia with 17p deletion or TP53 mutation (2017) NICE technology appraisal guidance 429<br><br>Idelalisib for treating chronic lymphocytic leukaemia (2015) NICE technology appraisal guidance 359<br><br>Rituximab for the treatment of relapsed or refractory chronic lymphocytic leukaemia (2010) NICE technology appraisal guidance 193<br><br>**Terminated appraisals**<br><br>Ofatumumab with chemotherapy for treating chronic lymphocytic leukaemia (terminated appraisal) NICE technology appraisal guidance 470<br><br>Idelalisib with ofatumumab for treating chronic lymphocytic leukaemia (terminated appraisal) NICE technology appraisal guidance 469.<br><br>Ibrutinib with bendamustine and rituximab for treating relapsed or refractory chronic lymphocytic leukaemia after systemic therapy (terminated appraisal) (2017) NICE technology appraisal guidance 437<br><br>**Appraisals in development (including suspended appraisals)**<br><br>Leukaemia (chronic lymphocytic, relapsed) - ofatumumab (maintenance) NICE technology appraisal guidance ID732. Publication date to be confirmed. Suspended February 2017<br><br>Idelalisib with bendamustine and rituximab for previously treated chronic lymphocytic leukaemia NICE technology appraisal guidance. Publication date to be confirmed. Suspended May 2018<br><br>**Related Guidelines:**<br><br>Haematological cancers: improving outcomes (2016) NICE guideline NG47.<br><br>**Related Quality Standards:**<br><br>Haematological cancers (2017) NICE quality standard 150 |

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| | **Related NICE Pathways:**<br>Blood and bone marrow cancers (2021) NICE pathway<br>http://pathways.nice.org.uk/ |
| **Related National Policy** | The NHS Long Term Plan, 2019. NHS Long Term Plan<br><br>NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) Chapter 105<br><br>Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domain 1 https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017 |

**References**

1. Cancer registration statistics, England: 2017 (2019). Office for National Statistics. Accessed July 2020

2. Chronic lymphocytic leukaemia. NHS Choices, accessed July 2020

3. Guidelines on the diagnosis, investigation and management of chronic lymphocytic leukaemia (2012). British Committee for Standards in Haematology. Accessed July 2020.