reference no: 2330
Publication date: 16 July 2026

Clinical Commissioning Policy:

Crizotinib for patients with relapsed or refractory ALK-positive anaplastic large cell lymphoma (ALCL) or ALK-positive unresectable inflammatory myofibroblastic tumour (IMT) [2330]

Summary

Crizotinib is not recommended to be available as a routinely commissioned treatment option for patients with relapsed or refractory ALK-positive ALCL or ALK-positive unresectable IMT.

Committee discussion

Clinical Panel considered the evidence base and the recommendation was made to progress this policy. Please see Clinical Panel reports for full details of Clinical Panel's discussion.

The Clinical Priorities Advisory Group committee papers can be accessed here: Clinical Commissioning Policy: Crizotinib for patients with relapsed or refractory ALK-positive ALCL or ALK-positive unresectable IMT

What we have decided

NHS England has carefully reviewed the evidence to treat relapsed or refractory ALK-positive ALCL and ALK-positive unresectable IMT with crizotinib. NHS England recognises that the published evidence identifies that, at present, there is sufficient evidence to commission this treatment. However, following the relative prioritisation process undertaken in May 2026, NHS England has concluded that, balanced against other relative priorities that were also considered during this process, Crizotinib for patients with relapsed or refractory ALK-positive anaplastic large cell lymphoma (ALCL) or ALK-positive unresectable inflammatory myofibroblastic tumour will not be funded at this time within the resources available.

The evidence review can be accessed here: Clinical Commissioning Policy: Crizotinib for patients with relapsed or refractory ALK-positive ALCL or ALK-positive unresectable IMT

Links and updates to other policies

Not applicable

Plain language summary

About relapsed or refractory ALK-positive ALCL and ALK-positive unresectable IMT

Anaplastic large cell lymphoma (ALCL) is a rare type of blood cancer that occurs when white blood cells, known as T-cells, become abnormal. ALCL is a type of non-Hodgkin lymphoma (NHL). ALCL most commonly affects children and young adults and is more common in males. In ALK-positive ALCL, the abnormal T cells have a genetic change (mutation) that means they make a protein called anaplastic lymphoma kinase (ALK) on their surface. The ALK mutation drives the abnormal growth of the cancer cells and can be detected using tests. The most common sign of ALCL is painless swelling of lymph nodes in the neck. Some patients may also present with tiredness, night sweats, fevers and unexplained weight loss. These symptoms are called B symptoms. ALCL commonly spreads to areas outside of the lymph nodes, and most patients have advanced disease at presentation. The most common test for diagnosing ALCL is a biopsy, which is usually performed on an enlarged lymph node. The results of the biopsy can then be tested to determine if the type of ALCL present is ALK-positive.

Inflammatory myofibroblastic tumour (IMT) is a very rare type of tumour that can form on mucosal surfaces (such as in the eyes, mouth and lungs) and mesentery (which connects the organs in the abdomen). IMT usually originates in the lungs but can spread to other areas. The symptoms associated with IMT can vary depending on the size and location of the tumour. Some patients do not develop any specific symptoms and their disease is picked up by chance on imaging performed for other reasons. However, some patients may experience symptoms such as pain at the tumour site, tiredness, unexplained weight loss and fevers. In these instances, imaging is usually carried out which detects the tumour. This is generally followed by a biopsy, whereby a sample of tissue is taken from the tumour to confirm a diagnosis of IMT. These tumour cells can then be tested to determine if the IMT is ALK-positive.

About current treatment

ALCL is a chemotherapy-sensitive malignancy. First-line treatment for adults for previously untreated systemic ALCL is brentuximab vedotin in combination with cyclophosphamide, doxorubicin and prednisone (CHP). Some patients with early stage ALK-positive ALCL may also have radiotherapy. First-line treatment for paediatric patients is commonly with a combination of chemotherapy agents. There is no standard definition of refractory disease in the context of ALCL.

However, one possible definition of refractory disease is disease that returns within 3 months of treatment, or disease which is non-responsive to treatment; relapsed disease is suggested as disease that recurs 3 months or longer following treatment (Cheson et al, 2014, RECIL, 2017). For relapsed or refractory systemic ALCL in adults, second line treatment is with brentuximab vedotin, with the exception of adult patients with disease that is refractory (did not respond) to first line treatment with brentuximab vedotin. Following chemotherapy, some patients may be suitable for a donor (allogenic) stem cell transplant, to increase their chances of staying in remission.

IMTs are considered resistant to conventional chemotherapy and radiation. Therefore, surgical resection is the mainstay of treatment. However, surgical resection is not always possible either due to the close proximity of the tumour to vital structures or advanced disease at presentation. There is no currently commissioned standard care treatment for

adult or paediatric patients with unresectable IMT. Patients with unresectable disease may be offered chemotherapy, systemic corticosteroid therapy or non-steroidal anti-inflammatory drugs.

About crizotinib

Crizotinib is an ALK inhibitor (blocker), which targets the ALK mutation found in ALK-positive ALCL and ALK-positive IMT. Crizotinib is a tablet that is taken orally, and patients can take this themselves at home. For patients with relapsed or refractory ALK-positive ALCL, crizotinib is proposed either as a bridge to allogeneic haematopoietic stem cell transplant (allo-HSCT), or as an alternative to treatment with other types of chemotherapy. For patients with unresectable IMT crizotinib is proposed as a first line treatment for patients whose disease cannot be removed by surgery. This includes unresectable advanced disease at presentation or metastatic disease.

Epidemiology and needs assessment

Around 95 children (aged 0 to 14 years) are diagnosed with non-Hodgkin lymphoma (NHL) in England every year (Cancer Registration Statistics, 2022). ALCL accounts for about 10-15% of paediatric NHL (Prokoph et al, 2018) and it is estimated that 90% of cases of paediatric ALCL show aberrant expression of ALK fusion proteins (Turner et al. 2016). This equates to approximately 9 new paediatric cases of ALK-positive ALCL diagnosed per year in England.

In England approximately 10,500 adult patients are diagnosed with NHL each year (NDRS, 2023). ALCL accounts for approximately 1-3% of adult NHL cases (Zhang et al. 2022) and approximately 50% of adult ALCL contain the ALK fusion gene (Turner et al. 2016). This equates to approximately 100 new cases of ALK-positive ALCL in adults per year in England.

In both adults and children with ALK-positive ALCL, clinical consensus suggests a relapse rate of approximately 30% (Tsuyama et al. 2017). This indicates a total of around 30 adults and 3 children with ALK-positive relapsed or refractory ALCL will be eligible for crizotinib per year in England. Clinical consensus suggests that approximately 25 adults and 3 children will end up choosing to take crizotinib.

IMT is very rare and occurs in less than one in 1 million people (NIH National Cancer Institute, 2019). The European paediatric registry currently registers < 6 cases per year per country for children. In adults, clinical consensus estimates that 1-2 adults per year in England would be eligible for treatment with crizotinib. In total, it is likely that fewer than 5 (2 adults, 3 children) patients per year with unresectable IMT would be eligible for this treatment.

- Patients with relapsed or refractory ALK-positive ALCL who are determined by the treating clinician to have been optimised for allo-HSCT[1]
- Disease progression whilst on treatment
- Patient decision to stop treatment
- Unacceptable toxicity

Policy review date

This document will be reviewed when information is received which indicates that the policy requires revision. If a review is needed due to a new evidence base then a new Preliminary Policy Proposal needs to be submitted by contacting england.CET@nhs.net.

Our policies provide access on the basis that the prices of therapies will be at or below the prices and commercial terms submitted for consideration at the time evaluated. NHS England reserves the right to review policies where the supplier of an intervention is no longer willing to supply the treatment to the NHS at or below this price and to review policies where the supplier is unable or unwilling to match price reductions in alternative therapies.

Equality statement

Promoting equality and addressing health inequalities are at the heart of NHS England's values. Throughout the development of the policies and processes cited in this document, we have:

- Given due regard to the need to eliminate discrimination, harassment and victimisation, to advance equality of opportunity, and to foster good relations between people who share a relevant protected characteristic (as cited under the Equality Act 2010) and those who do not share it; and
- Given regard to the need to reduce inequalities between patients in access to, and outcomes from healthcare services and to ensure services are provided in an integrated way where this might reduce health inequalities.

Definitions

Chemotherapy	A cancer treatment where medicine is used to kill cancer cells. The most common types of chemotherapy are either given into a vein (intravenous) or as chemotherapy tablets (oral chemotherapy)
Mutation	A change or alternation to genetic material. Mutations can result in altered function of the gene which can be harmful or beneficial. In cancer the mutations are usually harmful
Radiotherapy	A cancer treatment where radiation is used to kill cancer cells
Refractory	A type of cancer that does not respond to treatment or becomes resistant to treatment
Relapsed	When cancer returns following treatment after a period of remission
Unresectable	A situation where the tumour or cancer is not able to be removed using surgery

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