NHS England

**Engagement Report**

## Topic details

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| **Title of policy or policy statement:** | Crizotinib for patients with relapsed or refractory ALK-positive anaplastic large cell lymphoma (ALCL) or ALK-positive unresectable inflammatory myofibroblastic tumour (IMT) [2330] |
| **Programme of Care:** | Cancer |
| **Clinical Reference Group:** | Children and Young Adult Cancer Services |
| **URN:** | 2330 |

## 1. Summary

This report summarises the feedback NHS England received from engagement during the development of this policy proposition, and how this feedback has been considered.

## 2. Background

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 type of non-Hodgkin lymphoma (NHL). In ALK-positive ALCL, the abnormal T-cells mutate to produce a protein called anaplastic lymphoma kinase (ALK) on their surface. This ALK mutation drives abnormal growth of cancer cells. It most commonly affects children and young adults, with it being more common in males. ALK-positive ALCL represents approximately 9 paediatric cases and 100 adult cases per year in England. ALK-positive ALCL usually presents with painless swelling of lymph nodes in the neck. Other symptoms include tiredness, night sweats, fevers and unexplained weight loss.

ALCL is usually diagnosed with a biopsy of an enlarged lymph node. Genetic testing can be performed to determine if the type of ALCL present is ALK-positive. First-line treatment for adults with ALCL is chemotherapy (brentuximab vedotin in combination with cyclophosphamide, doxorubicin and prednisone). Some patients with early stage ALK-positive ALCL may also have radiotherapy. First-line treatment for paediatric patients is a combination of chemotherapy agents, which may include brentuximab vedotin. Following chemotherapy, some patients may be suitable for allogenic haemopoietic stem cell transplantation (allo-HSCT). For both adult and paediatric ALK-positive ALCL patients, there is no agreed consensus about treatment options following relapse or lack of response to chemotherapy.

Inflammatory myofibroblastic tumour (IMT) is a rare tumour and occurs in less than 1 in 1 million people. IMT forms on mucosal surfaces (e.g. eyes, mouth and lungs) and mesentery. IMTs are considered resistant to conventional chemotherapy and radiation, with surgical resection being the mainstay of treatment. However, surgical resection is not always possible due to tumours being in close proximity to vital structures or advanced disease at presentation. In patients with unresectable disease, chemotherapy, systemic corticosteroids and non-steroidal anti-inflammatory drugs are offered for symptom control.

Crizotinib is an ALK inhibitor, which targets the ALK mutation found in ALK-positive ALCL and ALK-positive IMT. Crizotinib is an oral, hard tablet that can be taken by patients at home.

The proposed use for crizotinib for ALK-positive ALCL is for:

- Paediatric patients (aged 3-18) with relapsed or refractory disease after first-line chemotherapy
- Adult patients (aged ≥ 18 years) with relapsed or refractory disease following first-line and/or second-line treatment with brentuximab vedotin

The proposed use for crizotinib for ALK-positive IMT is for:

- Adult patients (aged ≥ 18 years) or paediatric patients (aged 2-18) who are not suitable for complete surgical resection

This is proposed as a routinely commissioned treatment option. Crizotinib is currently licensed for the treatment of paediatric patients (aged ≥ 6 to < 18 years) with relapsed or refractory systemic ALK-positive ALCL, and paediatric patients with recurrent or refractory ALK-positive unresectable IMT. The use of crizotinib in paediatric patients < 6 years with relapsed or refractory systemic ALK-positive ALCL outlined, and in paediatric patients ≥ 2 years with unresectable IMT in this policy proposition is therefore off-label.

## 3. Engagement

NHS England has a duty under Section 13Q of the NHS Act 2006 (as amended) to 'make arrangements' to involve the public in commissioning. Full guidance is available in the Statement of Arrangements and Guidance on Patient and Public Participation in Commissioning. In addition, NHS England has a legal duty to promote equality under the Equality Act (2010) and reduce health inequalities under the Health and Social Care Act (2012).

The policy proposition underwent a four-week stakeholder testing between the 18th July 2024 and 15th August 2024 with registered stakeholders from the following Clinical Reference Groups:

- Chemotherapy
- Radiotherapy
- Children and Young People's Cancer

Respondents were asked the following consultation questions:

- Do you support the proposal for routine commissioning based on the evidence review and within the criteria set out in the proposal?
- Do you believe that there is any additional information that we should have considered in the evidence review?
- Do you believe that there are any potential positive and/or negative impacts on patient care as a result of making this treatment option available?
- Do you support the Equality and Health Inequalities Impact Assessment?
- Does the Patient Impact Summary present a true reflection of the patient and carers lived experience of this condition?
- Do you have any further comments on the proposal?
- Please declare any conflict of interests relating to this document or service area.

The comments have then been shared with the Policy Working Group to enable full consideration of feedback and to support a decision on whether any changes to the proposition might be recommended.

A 13Q assessment has been completed following stakeholder testing.

The Programme of Care has decided that the proposition offers a clear and positive impact on patient treatment, by potentially making a new treatment available which widens the range of treatment options without disrupting current care or limiting patient choice, and therefore further public consultation was not required. This decision has been assured by the Patient & Public Voice Advisory Group.

### Engagement Results

The policy received 5 stakeholder responses:

- 1 NHS Foundation Trust
- 1 Charity
- 1 Professional Organisation
- 1 Clinician
- 1 Patient

Given the rarity of both ALK-positive ALCL and IMT, this was deemed a good number of responses and there was a range of stakeholders represented. All stakeholders agreed with the policy proposition and felt that this offered patients a positive change.

### How has feedback been considered?

Responses to engagement have been reviewed by the Policy Working Group. The following themes were raised during engagement.

| Keys themes in feedback | NHS England Response |
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| **Relevant Evidence** | |
| Most of the stakeholders agreed the relevant evidence had been identified. One stakeholder did not respond to this question. | No further action |
| One stakeholder noted that the CRISP trial (phase 1B trial of crizotinib either in combination or as a single agent in paediatric patients with ALK, ROS1 or MET positive malignancies) is ongoing. The ALCL arm is near complete for recruitment. | As the paper is not currently published it cannot be considered as part of the evidence base in line with the published NHS England Methods: National Clinical Policies. |
| One stakeholder commented that they were uncertain about the place of crizotinib in 1st relapse in CD3-ve, ALK +ve, ALCL 12 months after diagnosis. The EICNHL Relapse-ALCL trial showed that this group of patients achieved 5 year EFS of 81% with single-agent vinblastine. | The policy proposition is inclusive of CD3-ve ALK+ve ALCL patients. In the EICNHL Relapse-ALCL patients received vinblastine and were a low-risk group, and therefore this trial does match the PICO for the evidence review. The trial also had small numbers. |
| **Policy Proposition** | |
| All stakeholders supported the policy proposition. | Noted. |

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| One stakeholder raised that crizotinib should not be used for patients with CNS due to poor penetration, unless used with intrathecal therapy as a last resort.<br><br>One stakeholder noted that the Lansky score is usually applied to patients 16 years age. They also commented that most paediatricians are not used to the ECOG scoring and most would use the Karnofsky scale for patients 16 years +.<br><br>One stakeholder disagreed with age limit for crizotinib in the policy being set as > 3 for ALCL and > 2 for IMT. They commented that the safety profile of chemotherapy and BMT is less favourable and toxicity will not differ between the different ages set in the inclusion criteria for ALCL and IMT. | This is outside the scope of the policy proposition. No further action required.<br><br>The Centre of International Blood and Marrow Transplant Research applies the Lansky score to those above 16 years. The inclusion criteria have been changed so that the Lansky score is applied to those < 16 years, rather than ≤ 12 years. Patients above 16 years would be under adult care hence the ECOG scale is more appropriate.<br><br>This age limit for this policy proposition has been restricted in line with the independent evidence review and the SmPC for crizotinib which states that 'no safety or efficacy data are available for crizotinib treatment in ALK-positive ALCL paediatric patients below 3 years of age or ALK-positive IMT paediatric patients below 2 years of age. The policy proposition has followed the published methods and reflects the published evidence on safety. |
| **Impact Assessment** | |
| One stakeholder noted that the patient impact statement would benefit from more detail. | No specific changes to the Patient Impact Assessment (PIA) were suggested in this comment. The PPV member reviewed the PIA and added comments on the effect crizotinib could have on patients and expanded on some of the impacts on patients (e.g. chemotherapy side effects leading to non-adherence for ALCL). |
| **Current Patient Pathway** | |
| One stakeholder commented that it was not clear in the policy that crizotinib was available after the 1st relapse. They also commented that crizotinib should be available if patients have previously responded to crizotinib, ceased therapy and subsequently relapsed.<br><br>One stakeholder commented that presumably the aim of crizotinib is to get a child to resectability in IMT and this is not reflected in the patient pathway on page 8. | The flowchart already shows that crizotinib can be used after the 2nd relapse. There is no evidence to support the use of crizotinib when it has been used previously.<br><br>The patient pathway has been amended to make it clear that patients who have failed 2nd line and subsequent treatments are eligible for crizotinib. The exclusion criteria have been amended to make it clear that crizotinib use specifically is an exclusion to treatment.<br><br>The aim of crizotinib is not to get patients to resectability as this will not be possible for some patients. Surgery may be attempted after crizotinib, however this is not the case for all. The patient pathway on page 8 has been amended to highlight crizotinib should be continued alongside 'best supportive care.' |
| **Potential impact on equality and health inequalities** | |

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| All stakeholders agreed with the equalities and health inequalities impact assessment. | No further action required. |
| **Changes/addition to policy** | |
| See above | See above |

### 4. Has anything been changed in the policy proposition as a result of the stakeholder testing and consultation?

The following change(s) based on the engagement responses has (have) been made to the policy proposition:

- Policy proposition:
  - Inclusion Criteria: Lansky score has been changed to be used for patients ≤ 16 years rather than ≤ 12 years
  - Exclusion criteria: The exclusion criteria have been amended to make it clear that crizotinib use specifically is an exclusion to treatment.
  - Patient pathway page 7 (ALCL): The patient pathway has been amended to make it clear that patients who have failed 2nd line and subsequent treatments are eligible for crizotinib.
  - Patient pathway page 7 (IMT): The patient pathway on page 8 has been amended to highlight crizotinib should be continued alongside 'best supportive care.'
- PIA:
  - This was updated to mention that the side effects of chemotherapy can lead to non-adherence with treatment.

### 5. Are there any remaining concerns outstanding following the consultation that have not been resolved in the final policy proposition?

No