National Institute for Health and Care Excellence
Final scope for the appraisal of inotuzumab ozogamicin for treating relapsed or refractory B-cell acute lymphoblastic leukaemia [ID893]
Issue Date: December 2016
repeat of the induction therapy. During the maintenance phase low dose chemotherapy is used, which typically consists of weekly methotrexate and daily mercaptopurine for an extended period of time to prevent relapse. For people with Philadelphia-chromosome-positive ALL, tyrosine kinase inhibitor therapy is added to these chemotherapy regimens. In adults with high risk acute ALL, stem cell transplantation and chemotherapy are considered equal first line treatment options.

Relapse or becoming refractory to initial treatment occurs in approximately 45% of people with newly diagnosed B-cell ALL. Although there is currently no standard of care for people with relapsed or refractory ALL, possible treatment options may include a combination chemotherapy based regimen of fludarabine, cytarabine and granulocyte colony-stimulating factor (FLAG), followed by stem cell transplantation where a suitable donor can be found, or best supportive care (including palliative care). Clofarabine is used outside its marketing authorisation in clinical practice in England through the Cancer Drugs Fund (CDF) for people with relapsed or refractory ALL 'with intent to use the treatment to bridge to bone marrow transplant' (at the time the scope was written; CDF transition funding remains in place until a commissioning decision from NHS England). Treatment of relapsed Philadelphia-chromosome-positive ALL includes re-induction therapy with tyrosine kinase inhibitors, such as imatinib or dasatinib, in addition to FLAG- or clofarabine-based chemotherapy.

The technology

Inotuzumab ozogamicin (Besponsa, Pfizer) is an antibody-drug conjugate of a monoclonal antibody. When inotuzumab ozogamicin binds to a CD22 antigen on a B-cell, it is absorbed into a malignant cell and leads to cell death.

Inotuzumab ozogamicin does not currently have marketing authorisation in the UK for ALL. It has been studied in clinical trials in adults with relapsed or refractory B-cell ALL with a CD22 expression.

<table>
<thead>
<tr>
<th>Intervention(s)</th>
<th>Inotuzumab ozogamicin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population(s)</td>
<td>Adults with relapsed or refractory B-cell acute lymphoblastic leukaemia (ALL)</td>
</tr>
</tbody>
</table>
### Comparators
For people who are able to take chemotherapy and have
- Philadelphia-chromosome-negative ALL:
  - fludarabine, cytarabine and granulocyte colony-stimulating factor (FLAG)-based combination chemotherapy
  - clofarabine-based combination chemotherapy (not appraised by NICE but funded via the CDF).
- Philadelphia-chromosome-positive ALL:
  - tyrosine kinase inhibitors alone or in combination with FLAG- or clofarabine-based chemotherapy.
For people who are unable to take chemotherapy:
- best supportive care (including palliative care).

### Outcomes
The outcome measures to be considered include:
- overall survival
- progression-free survival
- treatment response rates (including haematologic responses)
- time to and duration of response
- 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.
### Other considerations

If the evidence allows, the economic analysis will include stem cell transplant as a subsequent treatment after inotuzumab ozogamicin or its comparators. This should reflect the proportion of people who proceed to allogeneic stem cell transplant after each treatment, as well as the costs and quality-adjusted life year benefits of the procedure.

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:

- **Pegaspargase for treating acute lymphoblastic leukaemia** (2016). NICE technology appraisal TA408. Review date TBC.

#### Terminated appraisals:


#### Appraisals in development:

- Ponatinib for treating chronic myeloid leukaemia and acute lymphoblastic leukaemia NICE technology appraisals guidance [ID671]. Publication expected June 2017.

- Erythrocyte encapsulated asparaginase for treating acute lymphoblastic leukaemia asparaginase (suspended appraisal) NICE technology appraisals guidance [ID864].

- Blinatumomab for previously treated B-precursor acute lymphoblastic leukaemia NICE technology appraisals guidance [ID804]. Publication date to be confirmed.

#### Related Guidelines:

- **Haematological cancers: improving outcomes** (May 2016) NICE Guideline NG47. Review proposal date: September 2019.

- **Suspected cancer: recognition and referral** (June 2015). NICE guideline NG12.

## Related Quality Standards:

**Cancer services for children and young people**  
(February 2014) NICE quality standard 55. Review date TBC.

**Related NICE Pathways:**

**Blood and bone marrow cancers** (2014) NICE Pathway  
(note that this pathway does not include acute lymphoblastic leukaemia).

## Related National Policy


---

### References

