NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Tagraxofusp for treating blastic plasmacytoid dendritic cell neoplasm

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of tagraxofusp within its marketing authorisation for treating patients with blastic plasmacytoid dendritic cell neoplasm.

Background

Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is an aggressive type of blood cancer which affects blastic, or immature white blood cells (plasmacytoid dendritic cells) and causes large numbers of these cells to build up taking the place of normal blood cells. It typically affects the skin, where cancerous plasmacytoid dendritic cells penetrate the skin causing non-itchy lesions which look like bruises, but in advanced stages these cells may also affect the liver, spleen, blood and lymph nodes. One of the main characteristics of BPDCN is over-expression of the interleukin-3 receptor alfa in cells. BPDCN has been categorised by the World Health Organization as a myeloid neoplasm.

BPDCN can occur in people of any age but the median age at diagnosis is between 60 and 70 years.[1] Around 75% to 90% of cases occur in men.[2] The exact prevalence of BPDCN is unknown due to the difficulty of accurately diagnosing the disease and there are wide-ranging differences in reported prevalence and incidence rates. The prevalence of BPDCN was estimated at 1.2 in 10,000 people in the EU in 2015,[3] whereas a report published in 2018 suggested there have been less than 100 cases identified.[4] The incidence of BPDCN has been estimated at 0.45 cases per 1 million people in 2016.[5] Applying these figures to the 2018 mid-year population of England, the estimated number of people living with BPDCN in England would be around 6,700 and the number of people diagnosed with that condition is estimated at around 25 new cases per year.

There is currently no formal standard of care for people with BPDCN. Patients may initially receive radiotherapy or medicines prescribed for people with other types of blood cancers, such as AML or lymphoma. People may initially respond well to chemotherapy regimens however, relapses may be frequent, leading to poor overall survival. If response to chemotherapy is not achieved, patients may be offered stem cell transplantation, (where stem cells from a matched donor are provided to help restore the bone marrow).

The technology

Tagraxofusp (Elzonris; Stemline Therapeutics) is a fusion protein targeting the cells that express the interleukin-3 receptor on their cell surface. It is formed by fusing interleukin-3 with the diphtheria toxin. Tagraxofusp binds to the interleukin-3 receptors on the cell surface and delivers the toxin which inhibits protein synthesis and causes these cells to die. Tagraxofusp does not currently have a marketing authorisation in England. It has been studied in phase I/II clinical trials in adults with BPDCN as a first-line therapy or therapy to treat people who have relapsed from their

standard treatment or had recurrent episodes of BPDCN and is administered by intravenous infusion.

Intervention(s)	Tagraxofusp
Population(s)	People with blastic plasmacytoid dendritic cell neoplasm (BPDCN)
Comparators	• Established clinical practice without tagraxofusp • Stem-cell transplant • Best supportive care
Outcomes	The outcome measures to be considered include: • response rate (including partial response rate and duration of response) • overall survival • progression free survival • 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.
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 and NICE Pathways	**Related Guidelines:** Haematological cancers: improving outcomes (2016) NICE guideline NG47 Review date not provided **Related Quality Standards:** Haematological cancers (2017) NICE quality standard QS150

	Review date not provided **Related NICE Pathways:** Blood and bone marrow cancers (2018) NICE Pathway
Related National Policy	**NHS England:** The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) NHS England (2018) NHS England » NHS England Funding and Resource 2018/19: Supporting 'Next Steps for the NHS Five Year Forward View' NHS England (2013/14) NHS Standard Contract for Cancer: Radiotherapy (All Ages). B01/S/a NHS England (2013/14) NHS Standard Contract for Haematopoietic Stem Cell Transplantation (Adult) B04/S/a NHS England (2013/14) NHS Standard Contract for Cancer: Chemotherapy (Adult). B15/S/a NHS England (2013, revised 2015) Clinical Commissioning Policy: Haematopoietic Stem Cell Transplantation (HSCT) (All Ages): Revised. NHS England B04/P/a **Department of Health and Social Care:** Department of Health (2016) NHS Outcomes Framework 2016-2017: Domains 2-5 Department of Health (2014) The national cancer strategy: 4th annual report Department of Health (2011) Improving outcomes: a strategy for cancer Department of Health (2009) Cancer commissioning guidance **Other policies:** Independent Cancer Taskforce (2015) Achieving world-class cancer outcomes: a strategy for England 2015-2020

Questions for consultation

Have all relevant comparators for tagraxofusp been included in the scope? Which treatments are considered to be established clinical practice in the NHS for blastic plasmacytoid dendritic cell neoplasm (BPDCN)?

Is there a current standard of care for people with BPDCN? If so, please confirm what this is?

Where in the pathway would tagraxofusp be used? Is it expected that tagraxofusp will be used to help people move onto haematopoietic stem cell therapy or would tagraxofusp be used as an alternative to haematopoietic stem cell therapy?

Have all the relevant outcomes been considered? Are all outcomes listed appropriate?

Are there any subgroups of people in whom tagraxofusp is expected to be more clinically effective and cost effective or other groups that should be examined separately? Should people who proceed to haematopoietic stem cell transplant and those who do not be considered separately?

Are there any other subgroups of people in whom tagraxofusp is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Epidemiological sources report conflicting incidence and prevalence rates. What is the incidence and prevalence of BPDCN in the UK? Please provide the sources for the most relevant UK epidemiological data.

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 tagraxofusp 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.

Do you consider tagraxofusp to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a ‘step-change’ in the management of the condition)?

Do you consider that the use of tagraxofusp can result in any potential significant and 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 Appraisal Committee to take account of these benefits.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute’s Technology Appraisal

processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).

NICE has published an addendum to its guide to the methods of technology appraisal (available at https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisals/methods-guide-addendum-cost-comparison.pdf), which states the methods to be used where a cost comparison case is made.

- Would it be appropriate to use the cost comparison methodology for this topic?
- Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators?
- Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant?
- Is there any substantial new evidence for the comparator technology/ies that has not been considered? Are there any important ongoing trials reporting in the next year?

References

1 Pagano L, Valentini CJ, Grammatico S and Pulsoni A (2016) Blastic plasmacytoid dendritic cell neoplasm: diagnostic criteria and therapeutical approaches. British Journal of Haematology, 174: 188–202

2 Pemmaraju N (2016) Blastic plasmacytoid dendritic cell neoplasm. Clinical Advances in Hematology & Oncology. 14: 220-222

3 European Medicines Agency (2015) European Medicines Agency. Recombinant human interleukin-3 truncated diphtheria toxin fusion protein for treatment of blastic plasmacytoid dendritic cell neoplasm. Accessed July 2019

4 Meloni-Ehrig A (2018) Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN) Atlas of Genetics and Cytogenics in Oncology and Haematology. 22: 246-251

5 Alsidawi S, Figueiredo G, Westin M et al (2016) Blastic Plasmacytoid Dendritic Cell Neoplasm. a Population-Based Analysis from the SEER and NCDB Databases. Blood. 128: 4789

