NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Tagraxofusp for treating blastic plasmacytoid dendritic cell neoplasm

Final scope

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. A report published in 2018 suggested there have been fewer than 100 cases identified[3]. The incidence of BPDCN in the United States has been estimated at 0.45 cases per 1 million people in 2016[4]. Applying this figure to the 2018 mid-year population of England, the number of people diagnosed with BPDCN 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 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 (CD123) 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. It is administered by intravenous infusion.

Tagraxofusp does not currently have a marketing authorisation in England. It has been studied in 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.

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Intervention(s)	Tagraxofusp
Population(s)	People with blastic plasmacytoid dendritic cell neoplasm (BPDCN)
Comparators	Established clinical practice without tagraxofusp including (but not limited to): • Intensive chemotherapy, such as FLAG-IDA • Non-intensive chemotherapy, such as azacitidine (does not currently have a Marketing Authorisation in the UK for this indication) • Radiotherapy • Best supportive care (including transfusion support, growth factor support, management of infections)
Outcomes	The outcome measures to be considered include: • response rate (including partial response rate, duration of response and skin 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	**Related Guidelines:** Haematological cancers: improving outcomes (2016) NICE

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and NICE Pathways	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 (2018/2019) 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

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

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

4 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

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