NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Chlormethine gel for treating mycosis fungoides-type cutaneous T-cell lymphoma ID1589

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of chlormethine gel within its marketing authorisation for treating mycosis fungoides-type cutaneous T-cell lymphoma.

Background

Lymphomas are cancers of the lymphatic system. They are broadly divided into Hodgkin's and non-Hodgkin's lymphomas. Cutaneous T-cell lymphoma is a rare type of non-Hodgkin's lymphoma that affects the skin. It is caused by the uncontrolled growth of T-lymphocytes within the skin. Many types of cutaneous T-cell lymphoma start as flat red patches or plaques on the skin, which progress to skin tumours, and may be itchy and sometimes painful. Some people with cutaneous T-cell lymphoma experience swelling of the lymph nodes.

Within the group of cutaneous T-cell lymphoma, distinct subtypes can be distinguished. Mycosis fungoides is the most common type of cutaneous T-cell lymphoma. Between 2009 and 2013, 1,659 people were newly diagnosed with cutaneous T-cell lymphomas of which around 55% were mycosis fungoides.[1] It is usually a very slow-growing type of lymphoma that often only affects the skin and can stay under control for many years.

In England in 2017, there were around 12,065 new cases of non-Hodgkin's lymphomas and 796 people had a primary diagnosis of peripheral or cutaneous T-cell lymphoma.[2] There were 107 men and 72 women diagnosed with mycosis fungoides cutaneous T-cell lymphoma, in England in 2017.[2] Median survival with early stage disease, stage IA, IB and IIA, is reported as 35.5, 21.5 and 15.8 years, respectively. The prognosis is worse when the condition is not limited to the skin at the time of initial diagnosis (stages IIB through IV). Median survival for late stage disease, stages IIB, IIIA and IIIB, is reported to be 4.7, 4.7 and 3.4 years, respectively, and decreases further for stage IV disease.[3]

Current management of cutaneous T-cell lymphoma consists of skin directed therapies and systemic therapies. Skin directed therapies are the main treatment for Stage IA, IB or IIA disease and include photo therapy (such as psoralen and ultraviolet A treatment [PUVA] and narrow band ultraviolet B treatment [UVB]), total skin electron beam therapy, topical chemotherapy agents, and topical corticosteroids. Systemic therapies are aimed at treating

late stage disease, and include chemotherapy (such as methotrexate, gemcitabine, liposomal doxorubicin or multi-agent chemotherapy–cyclophosphamide, doxorubicin, vincristine, and prednisolone), immunotherapy (interferon alpha) or retinoids (bexarotene). TA577 recommends brentuximab vedotin for treating CD30-positive, mycosis fungoides-type stage IIB or over, cutaneous T-cell lymphoma after at least one prior systemic therapy. Stem cell or bone marrow transplant (such as allogeneic-SCT) and extracorporeal photopheresis (ECP) may also be a treatment option for some people. Treatment options for cutaneous T-cell lymphoma can be used either alone or in combination. People may have multiple sequential treatments and remain on maintenance therapy with palliative intent although there is no established standard of care

The technology

Chlormethine is an alkylating agent with antineoplastic and immunosuppressive properties. The product under appraisal (Ledaga, Recordati Rare diseases/Helsinn Healthcare SA) is an anhydrous gel that is applied topically to the affected skin area and can be self-administered by patients.

Chlormethine gel has a marketing authorisation for the topical treatment of mycosis fungoides-type cutaneous T-cell lymphoma in adult patients.

Intervention(s)	Chlormethine gel
Population(s)	Adults with mycosis fungoides-type cutaneous T-cell lymphoma
Comparators	Other skin directed therapies such as photo therapy (PUVA, UVB), total skin electron beam therapy, topical chemotherapy, and topical corticosteroids.
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rates • time to relapse • 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	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: Brentuximab vedotin for treating CD30-positive cutaneous T-cell lymphoma (2019). NICE Technology Appraisal 577. Review date April 2022. Appraisals in development: Mogamulizumab for previously treated cutaneous T-cell lymphoma ID1405. NICE technology appraisal guidance. Expected publication date: 26 August 2020. Related Guidelines: Non-Hodgkin's lymphoma: diagnosis and management (2016) NICE guideline 52. Haematological cancers: improving outcomes (2016) NICE guideline 47. Related Quality Standards: Haematological cancers (2017) NICE quality standard 150 Related NICE Pathways: Non-Hodgkin's lymphoma (2019) NICE pathway
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1, 3, 4 and 5. https://www.gov.uk/government/publications/nhs-

	outcomes-framework-2016-to-2017 NHS England (2013/14) NHS Standard Contract for Cancer: Chemotherapy (Adult). B15/S/a.

Questions for consultation

Have all relevant comparators for chlormethine gel been included in the scope?

Which skin directed therapies are considered to be established clinical practice in the NHS for treating mycosis fungoides cutaneous T-cell lymphoma? How should established clinical management be defined?

Would chlormethine gel be used for people with advanced disease, including CD30-positive, mycosis fungoides-type stage IIB or over, cutaneous T-cell lymphoma?

Are the outcomes listed appropriate?

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

Where do you consider chlormethine gel will fit into the existing NICE pathway, Non-Hodgkin's lymphoma?

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 the treatment is licenced?

- 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 chlormethine gel 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 chlormethine gel 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).

References

1. Public Health England (2016) Registration of Cutaneous T-Cell Lymphoma (CTCL) in England. National Cancer Registration and Analysis Services Short Report 2016397

2. ONS (2019) Cancer registration statistics, England: 2017 dataset, accessed June 2019.

3. Committee for Medicinal Products for Human Use (2016) Ledaga: EPAR - Public assessment report, accessed July 2019.