NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

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

Consultee and commentator comment form

Please use this form for submitting your comments on the draft remit, draft scope and provisional stakeholder list of consultees and commentators. It is important that you complete and return this form even if you have no comments otherwise we may chase you for a response.

Enter the name of your organisation here: British Association of Dermatologists

Comments on the draft remit and draft scope

The draft remit is the brief for an appraisal. Appendix B contains the draft remit. The draft scope, developed from the draft remit outlines the question that the appraisal will answer.

Please submit your comments on the draft remit and draft scope using the table below. **Please take note of any questions that have been highlighted in the draft scope itself** (usually found at the end of the document).

If you have been asked to comment on documents for more than one appraisal, please use a separate comment form for each topic, even if the issues are similar.

Please complete this form and upload it to NICE Docs by Wednesday 4 September 2019. If using NICE Docs is not possible please return via email to scopingta@nice.org.uk If you have any questions please contact the Scoping Project Manager, Michelle Adhemar on 44 (0)20 7045 2239 or at the email address above.

If you do not have any comments to make on the draft remit and draft scope, please state this in the box below.

Comment 1: the draft remit

Section	*Notes*	Your comments
Wording	*Does the wording of the remit reflect the issue(s) of clinical and cost effectiveness about this technology or technologies that NICE should consider? If not, please suggest alternative wording.*	
Timing Issues	*What is the relative urgency of this appraisal to the NHS?*	

Section	*Notes*	Your comments
Any additional comments on the draft remit		

Comment 2: the draft scope

Section	*Notes*	Your comments
Background information	*Consider the accuracy and completeness of this information.*	See amendments below under "any additional comments"
The technology/ intervention	*Is the description of the technology or technologies accurate?*	
Population	*Is the population defined appropriately? Are there groups within this population that should be considered separately?*	Not as likely to be useful for early stage patients, this is a rare cancer
Comparators	*Is this (are these) the standard treatment(s) currently used in the NHS with which the technology should be compared? Can this (one of these) be described as 'best alternative care'?*	Yes topical steroids are not a suitable comparator – these should be tried before Ledaga Phototherapy or TSEBT are suitable comparators but phototherapy requires attendance to hospital 2-3 x week for 12-16 weeks and TSEBT up to 5 weeks in attendance increases the risk of other skin cancers such that the number of treatments are limited. Interferon alpha and bexarotene should also be considered as comparators as these are first line systemic options when SDTs are contraindicated or ineffective.
Outcomes	*Will these outcome measures capture the most important health related benefits (and harms) of the technology?*	Yes, add pruritus score
Economic analysis	*Comments on aspects such as the appropriate time horizon.*	
Equality	*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*	• could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which the treatment is licenced? No • 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

Section	*Notes*	Your comments
	within the patient population for which [the treatment(s)] is/are/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.*	the technology; No • could have any adverse impact on people with a particular disability or disabilities. No
Other considerations	*Suggestions for additional issues to be covered by the appraisal are welcome.*	
Innovation	*Do you consider the technology 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 the technology 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.*	• Yes this is a much needed addition to our anti CTCL treatments, it is practical to use without trips to hospital nor risks of systemic effects and doesn't require monitoring • Skindex is a better measure of HRQoL in CTCL, patients live with a high symptom burden not reflected by QALY • Lessin SR, et al. JAMA Dermatol. 2013;149:25-32.
Questions for consultation	*Please answer any of the questions for consultation if not covered in the above sections. If appropriate, please include comments on the proposed process this appraisal will follow (please note any changes made to the process are likely to result in changes to the planned time lines).*	Would chlormethine gel be used for people with advanced disease, including CD30-positive, mycosis fungoides-type stage IIB or over, cutaneous T-cell lymphoma? They may be used for early stage lesions in patients with advanced disease – most CD30 positive lesions are advanced lesions Where do you consider chlormethine gel will fit into the existing NICE pathway, Non-Hodgkin's lymphoma? After topical corticosteroids as a reasonable alternative to phototherapy or for patients

Section	*Notes*	Your comments
		resistant to other SDT 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. No

Any additional comments on the draft scope

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 are scaly and may be weepy. They may progress to larger skin tumours, or spread to extensively involve the skin termed erythroderma. The lesions are frequently itchy and sometimes painful. Some people with cutaneous T-cell lymphoma experience swelling of the lymph nodes. Systemic spread may occur with lymphomatous involvement of lymph nodes or internal organs.

Within the group of cutaneous T-cell lymphoma, there are distinct subtypes. 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 in UK 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 skin directed therapies (SDT) 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 (chlormethine), and topical corticosteroids. Systemic therapies are aimed at treating late stage disease or early stage when SDT is contraindicated or refractory or include immunotherapy (interferon alpha) or retinoids (bexarotene) before chemotherapy (such as

Section	*Notes*	Your comments

methotrexate, gemcitabine, liposomal doxorubicin or multi-agent chemotherapy–cyclophosphamide, doxorubicin, vincristine, and prednisolone). 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 gel is a topical chemotherapy. It 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.

Comparators:

Other skin directed therapies such as photo therapy (PUVA, UVB), total skin electron beam therapy, topical chemotherapy, and first line systemic choices for stage IA-IIA such as interferon alpha and bexarotene.

Comment 3: provisional stakeholder list of consultees and commentators

The provisional stakeholder list of consultees and commentators (Appendix C) is a list of organisations that we have identified as being appropriate to participate in this appraisal. If you have any comments on this list, please submit them in the box below.

As NICE is committed to promoting equality and eliminating unlawful discrimination Please let us know if we have missed any important organisations from the lists contained within the stakeholder list, and which organisations we should include that have a particular focus on relevant equality issues.

If you do not have any comments to make on the provisional stakeholder list of consultees and commentators, please cross this box: ☒

Comments on the provisional stakeholder list of consultees and commentators

Comment 4: regulatory issues (to be completed by the company that markets the technology)

Section	*Notes*	Your comments
Remit	*Does the wording of the remit reflect the current or proposed marketing authorisation? If not, please suggest alternative wording.*	
Current or proposed marketing authorisation	*What are the current indications for the technology?*	
	What are the planned indications for the technology?	
	FOR EACH PLANNED INDICATION:	
	Which regulatory process are you following?	
	What is the target date (mm/yyyy) for regulatory submission?	
	What is the anticipated date (mm/yyyy) of CHMP positive opinion (if applicable)	
	What is the anticipated date (mm/yyyy) of regulatory approval?	
	What is the anticipated date (mm/yyyy) of UK launch?	
	Please indicate whether the information you provide concerning the proposed marketing authorisation is in the public domain and if not when it can be released. All commercial in confidence information must be highlighted and underlined.	
Economic model software	*NICE accepts executable economic models using standard software, that is, Excel , DATA, R or WinBUGs. Please indicate which software will be used. If you plan to submit a model in a non-standard package, NICE, in association with the ERG, will investigate whether the requested software is acceptable, and establish if you need to provide NICE and the ERG with temporary licences for the non –standard software for the duration of the appraisal. NICE reserves the right to reject economic models in non-standard software*	

Section	*Notes*	Your comments
Cancer Drugs Fund	*Please indicate whether this technology is likely to be a Cancer Drugs Fund candidate?*	

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