National Institute for Health and Care Excellence

Highly Specialised Technology Evaluation (HST)

Birch bark extract for treating skin wounds associated with dystrophic and junctional epidermolysis bullosa [ID1505]

Response to consultee and commentator comments on the draft remit and draft scope

Please note: Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees.

Comment 1: the draft remit

Section	Consultee/ Commentator	Comments [sic]	Action
Appropriateness	Amryt Pharma	Yes. However, we consider this to be a highly appropriate topic for HST. We believe that Oleogel-S10 meets all of the HST criteria (see further comments on this under questions for consideration).	Comment noted. The product now has a marketing authorisation in Great Britain and is referred to as birch bark extract with the brand name Filsuvez gel. This topic meets the criteria for consideration as a highly specialised treatment. The scope has been amended to reflect this.
	NHS England and NHS Improvement	It is the opinion of NHS England that it is appropriate that NICE appraise this technology	Comment noted. This topic has been scheduled as a Highly Specialised

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			Technology Appraisal (HST) into the technology appraisal program. The scope has been updated.
	DEBRA UK	Yes. I am surprised and somewhat concerned that this has not been routed via the highly specialised technology (HST route). I would have anticipated that this should take into account the existing commissioning of the National Epidermolysis Bullosa service with its defined service specification	Comment noted. This topic meets the criteria for consideration as a highly specialised treatment. The scope has been amended to reflect this
Wording	Amryt Pharma	Yes. The wording of the remit adequately reflects the issues of clinical and cost-effectiveness about Oleogel-S10	Comment noted. The product now has a marketing authorisation in Great Britain is referred to as birch bark extract with the brand name Filsuvez gel. It is indicated only for skin wounds associated with dystrophic and junctional epidermolysis bullosa. The title and remit have been updated to reflect this.

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	NHS England and NHS Improvement	Yes, the remit does address the clinical issues and the cost effectiveness	Comment noted. The remit and title have been amended to reflect the wording in the marketing authorisation.
	DEBRA UK	Yes	Comment noted. The remit and title have been amended to reflect the wording in the marketing authorisation.
Timing Issues	Amryt Pharma	Oleogel-S10 phase III registration study top line data will readout in Q3/Q4 2020. Regulatory timelines will be confirmed post data readout. As there is a significant unmet need in these rare, clinically distinct EB types. There is an urgency to ensure that eligible patients have access to Oleogel-S10 as soon as possible following regulatory approval.	Comment noted. The NICE process aims to publish guidance as soon as possible after a marketing authorisation is granted.
	NHS England and NHS Improvement	As a rare disease with no other treatments expected in the near future, phase 3 clinical trial completed and new patients potentially requiring treatment this evaluation should be considered as relatively urgent	Comment noted. The NICE process aims to publish guidance as soon as possible after a marketing authorisation is granted.
	DEBRA UK	Given the severity of EB and the unmet need patients and their families have, this should be deemed an urgent appraisal	Comment noted. The NICE process aims to publish guidance as soon as possible after a

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			marketing authorisation is granted
Additional comments on the draft remit	Amryt Pharma	No additional comments.	Comment noted.

Comment 2: the draft scope

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Background information	Amryt Pharma	Our view is that the background information is potentially confusing and should be simplified to focus on DEB, JEB and KS which are clinically distinct forms of EB. Historical estimates suggest that overall EB affects approximately 1 in 17,000 live births and approximately 5,000 adults and children in the UK. However, the vast majority of these patients have milder and clinically distinct forms of EB (predominantly EB simplex). For the avoidance of doubt, this larger group of clinically distinct patients are not indicated for treatment with Oleogel -S10 and are not reliant upon the highly specialist support and prescribing conditions from any of the four EB centres. According to September 2019 data, numbers of JEB, DEB and Kindler syndrome patients registered with the UK EB service were **72**, **675** and **21**, respectively. Assuming constant prevalence across the UK, this equates to **61** JEB patients, **569** DEB patients and **18** Kindler syndrome patients in England (**647** in total across the three clinically distinct subtypes). Of this group, the number of treatable patients from the prevalent population is estimated to be around **250 – 300** – which has been validated by EB	Comments noted. The background section is intended to give a brief overview of the overall. The appropriate sections of the scope have been updated to reflect the populations to be considered in the evaluation. NICE will conduct the evaluation of birch bark extract (Filsuvez gel) within its marketing authorisation.

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		clinical experts. Further the incident-population in England is estimated to be under **20** patients per year, of which we expect between 5-10 would be candidates for treatment with Oleogel-S10. Over the 20 years from 1999 to 2019, overall incidence rates are estimated at 6.3 cases per million live births with JEB, 18.4 per million with DEB and 0.7 per million with Kindler syndrome. In certain subgroups, incidence rates have been reported since the inception of the UK EB service in 2002; incidence for JEB-GS fell from 9 to 3.8 per million live births between 2002-2010 and 2011-2019, and numbers with RDEB-GS from 6.8 to 2.9 per million live births. To summarise, we believe that a better starting point for the background section would be to focus on the clinically distinct and rarer forms of EB indicated for potential treatment with Oleogel-S10: JEB, DEB and KS and their relevant incidence and prevalence rates. Please let us know if you would like our number calculations.	
	NHS England and NHS Improvement	The background is comprehensive.	Comment noted. No changes to the scope required.
	DEBRA UK	The background information does not convey the clinical picture or the numbers of EB patients accurately. Whilst the breakdown of subtypes / classification is accurate in its simplest form, the wording does not reflect the reality of living with EB I will start with a quote from a parent “My son [redacted] has generalised severe EB. He was born with no skin on his feet, knees, and hands and even where there was intact skin, it blistered. It was so hard to bond - I did not hold my baby for the first six months. He is the first person in my family to have EB, so it came as an enormous shock. Jamie has a full skin check every day, which involves me lancing all blisters that have occurred overnight. I dress all the	Comments noted. The background section is intended to give a brief overview of the condition. Further details of the impact of EB will be considered by the committee, and stakeholders will have the opportunity to

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		wounds and put protective bandages on before dressing him as well as giving him pain killers. The daily routine is quite structured to ensure he feels safe and secure at all times. He has his large dose of morphine before the evening meal so he is ready for his bath and can cope with more dressing changes. I thought that being a nurse would make caring for Jamie easier. The most difficult thing about EB is seeing your child in pain, knowing that the care you are giving is causing so much distress. I have to draw disability living allowance to help soften the blow of not being able to return to work as I am now a full-time carer." The reality of living with EB is not just simply trauma or friction causing the skin to blister and tear easily, but large areas of skin may simply be missing, raw and bleeding requiring 2-4 hours of dressing changes daily. This invariably worsens with age as the inflammation and scarring associated with this condition take hold. Chronic pain is a key factor with more than 90% experiencing pain every day – specifically at dressing changes. They experience intractable itch with the continued healing, wounding, and scarring process. Patients invariably have mitten hands and feet rendering them useless as the digits are fused together. EB is chronically disabling. The written summary does not convey what images or real-life consultation with a patient can describe. The image below is a common example. REF: Hubail et al. Int J Gen Med Vol 2018:11 This is a rare, complex, multi organ condition. Optimal management requires a multidisciplinary approach as mentioned and revolves around the protection of the skin against slightest injury, use of careful wound care dressings, aggressive nutritional support, and early medical or surgical interventions if needed to manage any complications. The multidisciplinary team consists of a dermatologist, paediatrician, anaesthetist, pathologist, medical geneticist, pain specialist, specialised	include this in their submissions. The appropriate sections of the scope have been updated to reflect the populations to be considered in the evaluation. NICE will conduct the evaluation of birch bark extract (Filsuvez gel) within its marketing authorisation, that is 'for treating partial thickness wounds associated with dystrophic and junctional epidermolysis bullosa (EB) in patients 6 months and older.

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		nurses, psychiatrist, ophthalmologist, gastroenterologist, dentist, otolaryngologist, and endocrinologist. DEBRA UK helped fund the Rare Disease Unit at St Thomas Hospital a few years ago and has been closely involved in supporting the specialist teams that manage this incredibly challenging group of patients. The background suggests that treatments help ease and control symptoms, however there are no EB-specific treatments. Patients are treated with polypharmacy to manage the complexity of EB and its manifestations. The most accurate patient numbers should be taken from the clinicians themselves and the focus should be on the severe sub types – DEB, JEB and KS. The numbers are likely to be in the region of 100-150 based on discussions with the clinicians. To quote the number of 5000 being affected in the UK creates a false impression of the range of severity and actual numbers within each subtype. Because of the specialism involved, patients are treated at 4 centres in the UK only – 2 adult and 2 paediatric centres. This level of expertise is required with complete specialism of the managing clinicians. DEBRA UK part funds NHS nurses at these centres and it is a specialist role requiring training and years of clinical experience with patients	
The technology/ intervention	Amryt Pharma	Yes	Comment noted. The product now has a marketing authorisation in Great Britain and is referred to as birch bark extract with the brand name Filsuvez gel. The

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			scope has been updated to reflect this.
	NHS England and NHS Improvement	The description of the technology is accurate.	Comment noted. The product now has a marketing authorisation in Great Britain and is referred to as birch bark extract with the brand name Filsuvez gel. The scope has been updated to reflect this.
	DEBRA UK	From my reading / scientific meeting presentations from the manufacturer of Oleogel S10 the basic description appears accurate.	Comment noted. The product now has a marketing authorisation in Great Britain and is referred to as birch bark extract with the brand name Filsuvez gel. The scope has been updated to reflect this.
Population	Amryt Pharma	Yes	Comment noted. The product now has a marketing authorisation in Great Britain for treating partial thickness wounds associated with dystrophic and junctional epidermolysis

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			bullosa (EB) in patients 6 months and older. The population in the scope has been updated to reflect this.
	NHS England and NHS Improvement	The population is appropriately defined.	Comment noted. The product, now referred to as birch bark extract (brand name Filsuvez gel), has a marketing authorisation in Great Britain for treating partial thickness wounds associated with dystrophic and junctional epidermolysis bullosa (EB) in patients 6 months and older. The population in the scope has been updated to reflect this.
	DEBRA UK	From my reading / scientific meeting presentations from the manufacturer of Oleogel S10 the population included in the clinical trial appears accurate	Comment noted. This product, now referred to as birch bark extract (brand name Filsuvez gel), has a marketing authorisation in Great Britain for treating partial thickness wounds associated with

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			dystrophic and junctional epidermolysis bullosa (EB) in patients 6 months and older. The population in the scope has been updated to reflect this.
Comparators	Amryt Pharma	There are no approved pharmacological treatments for EB; the potential comparators listed are a range of off-label and experimental treatments which lack robust evidence of clinical effectiveness. Current management should be described as best supportive care (BSC) with a range of bandages, emollients, and treatments for symptoms rather than established clinical management as there are currently no licensed and/or approved treatments. Oleogel-S10 would be a step change in terms of active management of the EB sub-types in question on top of current BSC, with the potential to displace some of it.	Comments noted. The comparator wording in the scope has been updated as follows: 'Current clinical management without birch bark extract (including, but not limited to, treatments which can help ease and control infections, pain and other aspects of EB).'
	NHS England and NHS Improvement	The comparators are appropriate.	Comment noted. The comparator wording in the scope has been updated as follows: 'Current clinical management without birch bark extract (including, but not limited to, treatments which can help ease

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			and control infections, pain and other aspects of EB).'
	DEBRA UK	There are no approved treatments for EB and patients are managed using polypharmacy (oral and topical medicines), washes, emollients, dressings etc DEBRA UK have supported research projects over the last 40 years, part of which has been understanding EB and looking for opportunities for improved management and increased quality of life. One project over the last 7 years has been looking at the natural history of EB and the heterogeneity of patients New strategies are desperately required, and new topical agents would be a replacement for or addition to existing treatments a patient uses	Comments noted. The comparator wording in the scope has been updated as follows: 'Current clinical management without birch bark extract (including, but not limited to, treatments which can help ease and control infections, pain and other aspects of EB).'
Outcomes	Amryt Pharma	Yes, although we suggest the addition of the following outcome measure: • incidence and severity of wound infection	Comment noted. The suggested outcome has been added to the scope.
	NHS England and NHS Improvement	The outcomes are appropriate	Comment noted. No changes to the scope required.
	DEBRA UK	The outcomes as defined are all relevant to patients, what are harder to define are the qualitative improvements and impact on the wider family	Comments noted. The NICE committee will consider if all relevant health benefits are captured in any

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			evidence presented. Health-related quality of life of caregivers, where relevant, can be considered by the committee as outlined in the NICE methods guide. No changes to the scope required.
Economic analysis	Amryt Pharma	In the clinically distinct and rare EB patient populations that Oleogel-S10 is expected to be licensed in, the impact of the treatment compared to best supportive care (BSC) on patient HRQoL through reduction in wound burden and symptoms such as itch and pain will be captured, and impact on mortality through reduction in risk of complications such as infection/ sepsis and squamous cell carcinoma (SCC) modelled. As EB is a life-long condition, the appropriate time horizon for the base case in the economic model is lifetime, and natural history data will be compared to the disease course of patients treated with Oleogel-S10 to capture the long-term effects of the treatment. As well as patient QALY gain, it is intended that the model will also capture caregiver/ parent QALY impact.	Comments noted. Health-related qualify of life of caregivers, where relevant, can be considered by the committee as outlined in the NICE methods guide. No changes to the scope required.
	NHS England and NHS Improvement	The economic analysis is appropriate	Comment noted. No changes to the scope required.
	DEBRA UK	I am unable to comment on the economic analysis per se however the costs of EB are far more reaching than the cost of skin and complex patient management. The cost of drugs, medical tests and interventions,	Comments noted. Relevant costs will be considered by the committee. Health-related qualify of life of

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		hospitalisations, dressings, and practical aspects of daily life are only part of the whole which also includes carers, social support, and productivity loss. REF: Angelis European Health Economic Journal 2016	caregivers, where relevant, can be considered by the committee as outlined in the NICE methods guide. No changes to the scope required
Equality and Diversity	Amryt Pharma	We are not aware of any potential equality issues	Comment noted. No changes to the scope required.
	NHS England and NHS Improvement	The scope seems appropriate with respect to addressing equality issues	Comment noted. No changes to the scope required.
	DEBRA UK	There are no equality issues that align with legislation however there are huge cultural issues where a disabled child is not welcome or treated equally. There are also financial and educational issues specifically in EB because of the specialist nature of the condition, families who resource can support a child / adult living with EB far more effectively. The impact on the family as a whole is devastating, especially the impact on siblings who are side-lined and possibly rolled into caring At DEBRA UK we provide hardship grants – examples include a washing machine to manage the additional burden of multiple bedding changes, it's a stark reality that EB patients with end stage EB-related cancer need dark coloured bedding to help manage the issues with extreme wounds and fungating cancer at the end of life DEBRA UK has a community support team that provide help in helping families gain the correct financial state benefits and supporting with school	Comment noted. No changes to the scope required but the NICE committee will consider any potential equality issues raised during this appraisal.

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		applications. Equality for patients with EB impacts hardest on those that have least and who may be culturally disadvantaged. We can provide examples as required	
Other considerations	Amryt Pharma	None.	Comment noted. No changes to the scope required.
	NHS England and NHS Improvement	No additional considerations	Comment noted. No changes to the scope required.
	DEBRA UK	None	Comment noted. No changes to the scope required.
Innovation	Amryt Pharma	We consider the technology to be potentially innovative. If approved, it will be the first treatment to receive marketing authorisation in EB. It has the potential to significantly improve quality of life of patients as well as their siblings and parents. By reducing infection, the technology also has the potential to change the course of the condition reducing the number of patients that go on to develop squamous cell carcinoma, therefore improving length of life. Most of the benefits can be captured within the QALY and we will be attempting to quantify the impact on HRQoL and utility for the caregiver/ parent. However, there are likely to be further benefits that are not captured - in particular, impacts of EB on wider family (e.g. sibling) utility have been identified in published literature, as well as reduced levels of engagement with school and work.	Comments noted. The appraisal committee will consider whether birch bark extract (brand name, Filsuvez gel) is innovative.

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		The Phase III EASE study (BEB-13) collects data using several patient-reported outcome measures that provides patient relevant granular information that goes beyond that captured by the QALY value, including: - Itch Man scale (4-13yrs) / Leuven Itch Scale (14+yrs) - FLACC scale (<4yrs) / Wong Baker - FACES scale (4+yrs) for pain (background and procedural) - W-QoL (wound impact on sleep) (14+yrs) - Questions on number of days missed from school or work - Treatment satisfaction questionnaire (14+yrs) - IScoreEB and EQ5D (open-label phase only) Given the wide-ranging impact of the condition for both patients and their families/caregivers, it may be appropriate and possible to complement trial data with evidence from external sources such as registry data, cross-sectional studies, or patient/carer utility studies.	
	NHS England and NHS Improvement	Yes, EB is a severe life limiting condition with few treatments currently available. Those that are limited to symptom control.	Comments noted. The appraisal committee will consider whether birch bark extract (brand name, Filsuvez gel) is innovative.
	DEBRA UK	There are no EB specific treatments Currently academic centres across the world and a number of pharmaceutical/biotechnology companies are working on treatments and cures for EB. This has been a recent advance. The challenges of running clinical trials in EB cannot be underestimated with the heterogeneity of the population and the requirements of meeting defined clinical endpoints in a trial	Comments noted. The appraisal committee will consider whether birch bark extract (brand name, Filsuvez gel) is innovative.

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		This piece of work therefore carried out across the world in a significant number of patients against the backdrop of a rare, complex condition should not be underestimated. This would be a major and significant step forward in both understanding how to plan and run trials in this population, providing EB patients with a product that has been studied specifically in the patient population and a path forward for EB management in the future Improving wound healing leads to reduced pain, itch, a change in pattern of dressing changes and perhaps longer-term benefits such as less inflammation. With reduced pain comes less anxiety and potentially other tangible benefits. In experimental situations we have been able to see some of these more qualitative benefits; “The general improvement to skin condition, together with increase in skin resilience in trauma, enabled the children to participate more fully in play and family life. One parent reported a one-fifth reduction in the child’s oral morphine analgesia requirement.” “Some parents reported a reduction in the amount of the time required to provide skin care for their children. The amount of dressings required has also reduced. A parent reported about 50% reduction in dressings. One parent described he often needed to return home to assist with his child’s skin care - he saw a reduction in unscheduled absence from work as his child’s skin condition improved. One parent reported that the improvement to her child’s skin condition was one of the key factors that enabled her to take up part-time employment.” “The improvement to the children’s RDEB has led to improved quality of family life” REF: Petrof et al, J Investigative Derm 2015	

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		Oleogel S10 is the first product to achieve positive clinical study results rather than anecdotal or experimental evidence. This should not be underestimated.	
Questions for consultation	Amryt Pharma	***How many people would be expected to be considered for Oleogel-S10 treatment in clinical practice in England?*** This question has been answered in the Consultation Response Form. However, for the avoidance of doubt, we estimate between 250-300. ***Are the subgroups suggested in 'other considerations' appropriate?*** For completeness, we would suggest adding Kindler Syndrome. **Are there any other subgroups of people in whom Oleogel-S10 is expected to be more clinically effective and cost effective or other groups that should be examined separately?** No. There are no other subgroups. ***Do you consider Oleogel-S10 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)?*** Yes. We believe that Oleogel-S10 has the potential to make a significant and substantial impact on the quality of life of patients and their caregivers. We believe that we have addressed this adequately elsewhere in the Consultation Response Form, but for the avoidance of doubt these rare and severe EB subtypes have a significant deleterious impact on all aspects of life for the patient, their caregivers, and immediate family to the extent that even marginal improvements in pain, itch and dressing time for example could have a transformational impact on their combined quality of life.	This topic meets the criteria for consideration as a highly specialised treatment. The scope has been amended to reflect this Birch bark extract (brand name, Filsuvez gel) has a marketing authorisation in Great Britain for treating partial thickness wounds associated with dystrophic and junctional epidermolysis bullosa (EB) in patients 6 months and older. Comments noted. please refer to relevant responses in other sections of this document.

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		Do you consider that the use of Oleogel-S10 can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation? We belief most health-related benefits will be captured in the QALY calculation, however there are number of potential benefits that may not be i.e. sibling and wider family disutility. Also the potential hope and impact value that the approval of the first licensed treatment of EB will have on patients, their families, and the wider clinical community should not be underestimated, although this value cannot readily be captured within the QALY.. ***Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.*** We are not aware of any specific data although we are certain these benefits would be validated by the clinical and patient community. **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 **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** We believe that Oleogel-S10 should be appraised through the HST and not the STA process. We feel that Oleogel-S10 meets all 7 of the HST criteria. However, we are aware that the Topic Selection Panel had concerns about meeting two of these criteria. Their first concern related to population size and the risk that Oleogel-SI0 could be used in a much larger population as a consequence of a broader license that could be interpreted to include the much larger group of EB Simplex patients.	

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		Having explored the literature, examined data from the UK PEBLES registry and discussed the patient population issue extensively with KOLs we believe the HST criterion relating to population size and treatment restricted to a very small number of specialist centres is met. Our calculations show that the population of the clinically distinct rare EB subtypes is small such that patients eligible for Oleogel-S10 would be treated in a very small number of specialist centres. As a result of our calculations relating to this criterion, we estimate the total treatable population to be around 250-300. For the avoidance of doubt: - EB Simplex patients were not included in the pivotal EASE trial. The trial included JEB, DEB and Kindler syndrome patients only - The MA will categorically not include EB Simplex patients We would be happy to present further details of the data and modelling used regarding this criterion. Furthermore, we would be happy to discuss measures that could be put in place to minimise any risk or uncertainty, no matter how small, around the prescribing of Oleogel-S10 beyond its intended population. The second concern of the Topic Selection Panel related to the potential for the use of Oleogel-S10 in partial thickness wounds due to a historic marketing authorisation. It is important to stress that Amryt do not currently market Oleogel-S10 for the treatment of partial thickness wounds and will not for the reasons below. Amryt are exclusively an orphan drug/rare disease company focused on serving patients with very high unmet need and a lack of treatment alternatives. If Oleogel-S10 receives European marketing authorisation in DEB, JEB, and Kindler syndrome we will withdraw the MA for adult partial thickness wounds immediately. For the voidance of doubt, Oleogel-S10 would	

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		therefore be marketed and used exclusively in the DEB, JEB, and Kindler syndrome subtypes. We would be happy to provide whatever reassurance needed in regard to this. Otherwise, we believe the Topic Selection Panel were satisfied that all of the other HST criteria were met. We would stress that we are completely supportive of the HST criteria and respectful of the intent behind each one. We would not suggest that we should be appraised through the HST process unless we were convinced that we met the criteria and had the evidence to support this.	
	NHS England and NHS Improvement	No additional comments	Comment noted. No changes to the scope required.
	DEBRA UK	How many people would be expected to be considered for oleogel-S10 treatment in clinical practice in England? The clinicians should provide the best estimate – my comment would be 100-150 having discussed the scoping workshop with them Have all relevant comparators for oleogel-S10 been included in the scope? See previous section	This topic meets the criteria for consideration as a highly specialised treatment. The scope has been amended to reflect this Comments noted. please refer to relevant responses in other sections of this document.

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		Which treatments are considered to be established clinical practice in the NHS for epidermolysis bullosa? There are no EB specific treatments, wound healing nis managed on a case by case basis with a range of options (washes/emollients/barrier creams etc) which change if the skin becomes more sore or infected accordingly Please describe how treatment differs by disease subgroups. Are the outcomes listed appropriate? Are the subgroups suggested in 'other considerations' appropriate? Are there any other subgroups of people in whom oleogel-S10 is expected to be more clinically effective and cost effective or other groups that should be examined separately? The product has been studied in DEB, JEB and KS and these are the sub groups that should be considered, please see the earlier section where I have expanded on and created a more realistic clinical picture in these patients. 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. Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts. Please see the section where I have commented on equality Do you consider oleogel-S10 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)? Please see my comment that the challenge of achieving positive data in this challenging population should not be underestimated	

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		Do you consider that the use of oleogel-S10 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. Please see my comments in this section, whilst the QALY calculation can take into account most of the individual benefits, the impact of a positive change in treatment firstly on the individual but then proportionately on family and siblings is of critical importance Please take a look at the theory also of minimally important clinical differences – where even a small incremental or numerical change can have a large meaningful change to an individual. This is well documented in a number of disease areas but very relevant here – considering the severity of impact on daily life 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 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).	

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		I would advocate that this be appraised through the Highly specialised technology route (HST). EB is rare, incredibly complex, devastating in its more severe and rarer forms for which this product will be used. The patients are only managed at 4 UK centres -2 adult and 2 children by a very small, highly trained group of clinicians and nurses. Having been involved in the funding of the rare disease centre in London and seen first-hand the patients, their care, and the specialist nature of such the route should match the existing commissioning of the National Epidermolysis Bullosa service with its defined service specification	
Additional comments on the draft scope	Amryt Pharma	We have no additional comments.	Comment noted. No changes to the scope required.
	NHS England and NHS Improvement	No additional comments	Comment noted. No changes to the scope required.
	DEBRA UK	I would urge NICE to include formal patient representation within the scoping process – patients can be suggested by both the clinical teams and DEBRA UK.	Comment noted. NICE aim to include all relevant stakeholders in appraisals of new health technologies. No changes to the scope required.

The following consultees/commentators indicated that they had no comments on the draft remit and/or the draft scope

None