Highly Specialised Technologies (HST) criteria checklist

Beremagene geperpavec for treating wounds associated with dystrophic epidermolysis bullosa [ID3959]

**Introduction:** The NICE HST criteria checklist is to highlight where a technology meets/partially meets or does not meet the criteria for routing to the HST programme. Its purpose is to show the details of why a technology may not be appropriate for HST evaluation, but also where it has been identified as suitable.

### Key – does the technology meet the criteria? Please use the colour key to advise if the technology meets the criteria

|  |  |
| --- | --- |
| Met | There is clear and strong evidence that this criterion is met |
| Not met | There is no evidence or limited evidence that the criterion is met. |

### MA wording: \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*

| **Number** | **Criterion** | **Description of how the technology meets the criteria** | **Does the technology meet the criteria?** |
| --- | --- | --- | --- |
|  | The condition is very rare defined by 1:50,000 in England | Epidermolysis Bullosa is thought to affect 1 in 17,000 births. Around 5,000 people are affected in the UK. (BMJ Best Practice, [Epidermolysis bullosa](https://bestpractice.bmj.com/topics/en-gb/744), March 2019 & Patient UK, [Epidermolysis Bullosa](https://patient.info/doctor/epidermolysis-bullosa-pro#nav-2), February 2016)  However, only ~25% of EB is DEB (dystrophic EB), which would mean ~1 in 68,000 if using the above source. Using other sources might change this ratio, for example the [Horn et al 1998](https://pubmed.ncbi.nlm.nih.gov/9155958/) – which estimates a prevalence rate in Scotland as 28.6 per million for EB simplex, the most common EB subgroup (or ~1.43 per 50,000), and dystrophic EB 20.4 per million (or 1.02 ~50,000). Petrof et al (2022), a registry study conducted in England, estimates a prevalence of DEB of 10.7 per million, which equates to 0.535 per 50,000.  DEB is caused by mutations in the COL7A1 gene. Beremagene geperpavec aims to provide a working copy of the human COL7A1 gene directly to skin cells, using a modified virus (herpes simplex virus-1) as a carrier. It is not anticipated that beremagene geperpavec would provide clinical benefit to other forms of EB as only DEB is caused by COL7A1 mutations.  The Topic Oversight Panel (TSOP) noted that there were significant histological differences between the different subtypes and was aware that mutations in the COL7A1 gene are only seen in DEB. DEB can also be diagnosed through genetic testing, so can clinically distinguished from other forms of EB. Prognosis and symptoms are expected to differ for DEB compared to other types of EB.  It concluded that the condition in this instance was dystrophic EB, due to the reasons outlined, and that the Petrof et al 2020 study was preferred to estimate prevalence, given advancements in genetic diagnosis of DEB since the Horn et al 1998 publication. Therefore this criterion was considered met. | Met |
|  | Normally no more than 300 people in England are eligible for the technology in its licensed indication and no more than 500 across all its indications | The anticipated license wording covers all people with \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Using EB registry data, ID1505 (HST28) estimated the prevalence of relevant subgroups of EB in England to be 569 (DEB). This aligns with the information in a recent publication: <https://onlinelibrary.wiley.com/doi/10.1111/bjd.20958>.  DEB would need to be confirmed by genetic testing, all those with DEB who have a mutation in the COL7A1 gene may be eligible for treatment. Severity can vary in DEB, and need for treatment over a lifetime can change – wounds can appear and heal and appear again elsewhere.  DEB comprises of two main subgroups – Dominant DEB (DDEB) and Recessive DEB (RDEB) – with RDEB being the most severe subgroup. At the scoping workshop, clinician experts stated that diagnosis of RDEB is usually clear due to the severity of symptoms but there is uncertainty in some cases between DDEB and RDEB.  The company cite clinical expert opinion that treatment with beremagene geperpavec would be mostly reserved for use in the recessive subgroup (RDEB) – which includes around 200 people in England (with 362 estimated to have DDEB). They also note that 31/32 people in the GEM-3 trial had RDEB. The clinical experts at the scoping workshop also stated that RDEB had the most severe wounds and that while beremangene geperpavec would be an option for all DEB, they estimated ~60% uptake/use amongst the DEB population. The company estimate ~230 people in England would be considered for treatment. The company noted further clinical opinion that considered ~80% of those with RDEB and ~20% of DDEB (those with the more severe cases) would have beremagene geperpavec were it recommended. This would result in less than 300 people being eligible for the technology.  TSOP was aware of clinical feedback given to NHS England that suggested some clinicians would likely offer beremagene geperpavec to all people with DEB and therefore uptake estimates would likely be higher than those estimated by the company.  TSOP concluded that the eligible population was the marketing authorisation population and that NICE would normally consider the technology within its marketing authorisation for this criterion. \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*.  TSOP considered if flexibility could be applied for this criterion but decided that as the eligible population within the anticipated marketing authorisation was substantially above 300 people, it was not persuaded that flexibility could be applied.  TSOP concluded that this criterion is not met. | Not Met |
|  | The very rare disease for which the technology is indicated significantly shortens life or severely impairs quality of life | Epidermolysis bullosa (EB) cause the skin to become very fragile. Any trauma or friction can cause the skin to blister and tear easily. EB can manifest internally affecting areas such as the eye, mouth or stomach. This can lead to vision loss, disfigurement, and other serious complications including the development of aggressive skin cancers, dental problems, or nutritional compromise.  DEB is one of the most severe forms of EB, and can severely impair its quality however severity and symptoms vary across the affected population. Overall, TSOP considered that DEB severely impairs quality of life and may reduce life expectancy also. Therefore, TSOP considered that this criterion was met. | Met |
|  | There are no other satisfactory treatment options, or the technology is likely to offer significant additional benefit over existing treatment options. | Birch bark extract (BBE) was recommended by NICE in September 2023 as an option for treating skin wounds associated with junctional and dystrophic epidermolysis bullosa (HST28).  TSOP considered that birch bark extract was a satisfactory treatment approved by NICE as an option for DEB. The TSOP panel considered that conditions with a NICE recommended treatment option normally would not meet this HST criterion. But, it agreed that beremagene geperpavec, as a gene therapy, would likely offer significant additional benefits over birch bark extract, given the difference in mechanisms of action between the treatments. TSOP noted that there was some uncertainty, due to limited long term clinical outcomes, but overall it concluded that this criterion was met. | Met |