## Vyjuvek™ (beremagene geperpavec-svdt) – New orphan drug approval

- On May 19, 2023, the FDA announced the approval of Krystal Biotech's Vyjuvek (beremagene geperpavec-svdt), for the treatment of wounds in patients 6 months of age and older with dystrophic epidermolysis bullosa (DEB) with mutation(s) in the *collagen type VII alpha 1 chain (COL7A1)* gene.

- DEB is a rare skin disorder that results from mutation(s) in the *COL7A1* gene. This gene encodes type VII collagen (COL7), which is an essential protein that helps strengthen and stabilize the outer and middle layers of the skin. When COL7A1 is deficient, skin layers can separate, causing painful and debilitating blisters and wounds. DEB usually presents itself at birth and is divided into two major types depending on the inheritance pattern: recessive dystrophic epidermolysis bullosa (RDEB) and dominant dystrophic epidermolysis bullosa (DDEB).

    — Symptoms can vary widely among affected people. Individuals with DDEB typically have mild cases with blistering primarily affecting the hands, feet, knees, and elbows. RDEB cases can be painful and debilitating, often involving widespread blistering that can lead to vision loss, disfigurement, and other serious medical complications, which could be fatal.

- Vyjuvek is a herpes-simplex virus type 1 vector-based gene therapy that delivers normal copies of the *COL7A1* gene to the wounds. Vyjuvek has also been modified to eliminate its ability to replicate in normal cells.

    — Vyjuvek is the first FDA approved therapy for DEB.

- The efficacy of Vyjuvek was established in a randomized, double-blind, intra-subject placebo-controlled study in 31 patients with DEB. Two comparable wounds in each subject were selected and randomized to receive either topical application of Vyjuvek gel or the placebo (excipient gel) weekly for 26 weeks. Efficacy was established on the basis of improved wound healing defined as the difference in the proportion of complete (100%) wound closure at 24 weeks confirmed at two consecutive study visits 2 weeks apart, assessed at weeks 22 and 24 or at weeks 24 and 26, between the Vyjuvek gel-treated and the placebo gel-treated wounds.

    — Complete wound closure at 24 weeks was achieved for 65% of wounds treated with Vyjuvek vs. 26% with placebo (treatment difference 39%, 95% CI: 14, 63; p = 0.012).

- A warning and precaution for Vyjuvek is accidental exposure to Vyjuvek.

- The most common adverse reactions (> 5%) with Vyjuvek use were itching, chills, redness, rash, cough, and runny nose.

- The recommended dose of Vyjuvek is based on age and is applied topically to wound(s) once a week.

| Age range | Maximum weekly dose (plaque forming units; PFU) | Maximum weekly volume |
|---|---|---|
| 6 months to < 3 years old | $1.6 \times 10^9$ | 0.8 mL |
| ≥ 3 years old | $3.2 \times 10^9$ | 1.6 mL |

    — It may not be possible to apply Vyjuvek gel to all the wounds at each treatment visit.

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  - — Vyjuvek should be applied to wounds until they are closed before selecting new wound(s) to treat. Weekly treatment to previously treated wounds if they re-open should be prioritized.
  - — Only a healthcare professional should apply Vyjuvek gel either at a healthcare professional setting (eg, clinic) or the home setting.

- Krystal Biotech plans to launch Vyjuvek in the third quarter of 2023. Vyjuvek will be available as a biological suspension, mixed into excipient gel.
  - — Vyjuvek biological suspension is supplied as a 1.0 mL extractable volume in a single dose vial at a nominal concentration of $5\times10^{9}$ PFU/mL.
  - — The excipient gel is supplied as a 1.5 mL fill volume in a separate single use vial. Vyjuvek biological suspension (1 mL) is mixed into the excipient gel vial prior to administration as Vyjuvek gel.