VYJUVEK- vyjuvek
Krystal Biotech, Inc.

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use VYJUVEK safely and effectively. See full prescribing information for VYJUVEK.

VYJUVEK™ (beremagene geperpavec-svdt) biological suspension mixed with excipient gel for topical application
Initial U.S. Approval: 2023

INDICATIONS AND USAGE

VYJUVEK is a herpes-simplex virus type 1 (HSV-1) vector-based gene therapy indicated for the treatment of wounds in patients 6 months of age and older with dystrophic epidermolysis bullosa with mutation(s) in the *collagen type VII alpha 1 chain (COL7A1)* gene.(1)

DOSAGE AND ADMINISTRATION

For topical application only.

Age Range	Maximum Weekly Dose (plaque forming units; PFU)	Maximum Weekly Volume (milliliter; mL)*
6 months to <3 years old	1.6×10^9	0.8
≥ 3 years old	3.2×10^9	1.6

* Maximum weekly volume is the volume after mixing VYJUVEK biological suspension with excipient gel.

Apply VYJUVEK gel to the selected wound(s) in droplets spaced evenly within the wound, approximately 1cm-by-1cm apart. (2.3)
The table below provides a reference on dose per approximate size of the wound.

Wound Area (cm^2)*	Dose (PFU)	Volume (mL)
<20	4×10^8	0.2
20 to <40	8×10^8	0.4
40 to 60	1.2×10^9	0.6

* For wound area over 60 cm2, recommend calculating the total dose based on this table until the maximum weekly dose is reached.

- Apply VYJUVEK gel on wounds once a week. (2.1)
- See full prescribing information for instructions on preparation and handling, (2.2) and administration (2.3).

DOSAGE FORMS AND STRENGTHS

VYJUVEK is a biological suspension, mixed into excipient gel, for topical application. VYJUVEK biological suspension is supplied as a 1.0 mL extractable volume in a single dose vial at a nominal concentration of 5×10^9 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. (3)
(3)
(3)

CONTRAINDICATIONS

None. (4)

WARNINGS AND PRECAUTIONS

- Accidental Exposure to VYJUVEK: Avoid direct contact with treated wounds and dressings of treated wounds for approximately 24 hours following application. Clean the affected area if accidental exposure occurs. (5.1)

ADVERSE REACTIONS

The most common adverse drug reactions (incidence >5%) were itching, chills, redness, rash, cough, and runny nose. (6)
To report SUSPECTED ADVERSE REACTIONS, contact Krystal Biotech, Inc. at 1-844-557-9782 or FDA at 1-800-FDA-1088 or http://www.fda.gov/medwatch.
See 17 for PATIENT COUNSELING INFORMATION.

Revised: 5/2023

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

VYJUVEK is indicated 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.

2 DOSAGE AND ADMINISTRATION

For topical application on wounds only.

2.1 Dose

- The recommended dose of VYJUVEK gel is based on age (Table 1). VYJUVEK gel is applied topically to wound(s) once a week.

Table 1 Maximum Weekly Dose by Age

Age Range	Maximum Weekly Dose (plaque forming units; PFU)	Maximum Weekly Volume (milliliter; mL)*
6 months to <3 years old	1.6×10^9	0.8
≥ 3 years old	3.2×10^9	1.6

* Maximum weekly volume after mixing VYJUVEK biological suspension with excipient gel.

- It may not be possible to apply VYJUVEK gel to all the wounds at each treatment visit.
- Apply VYJUVEK gel to wounds until they are closed before selecting new wound(s) to treat. Prioritize weekly treatment to previously treated wounds if they re-open. [*see Administration (2.3)*]
- If a dose is missed, apply VYJUVEK gel as soon as possible and resume weekly dosing thereafter.

2.2 Preparation

Important Preparation Instructions

- Prepare VYJUVEK gel at the pharmacy by mixing the VYJUVEK biological suspension into the excipient gel for immediate use within 8 hours of application. [see *Storage and Handling (16.2)]*
- Only a healthcare professional (HCP) should apply VYJUVEK gel either at a healthcare professional setting (e.g., clinic) or the home setting.
- Individuals who are pregnant should not prepare or apply VYJUVEK gel and should

avoid direct contact with the treated wounds or dressings from treated wounds [see *Accidental Exposure to VYJUVEK* (5.1)].

Below is the list of supplies needed for VYJUVEK gel preparation:

- One (1) carton containing one (1) VYJUVEK biological suspension vial and one (1) excipient gel vial (Figure 1)
- Two (2) 18-gauge needles
- Two (2) to four (4) 1mL administration syringes
- One (1) 3mL preparation syringe
- Two (2) to four (4) syringe caps
- Protective gloves
- 70% isopropyl alcohol pads
- Biohazard container
- Labels for administration syringes
- Virucidal agent for clean-up

Follow the steps below for VYJUVEK gel preparation.

PREPARE THE PREPARATION SYRINGE

1. Wash hands and put on protective gloves.
2. Remove both vials from the carton and thaw the VYJUVEK biological suspension vial and the excipient gel vial at room temperature for AT LEAST 20 minutes (Figure 1).

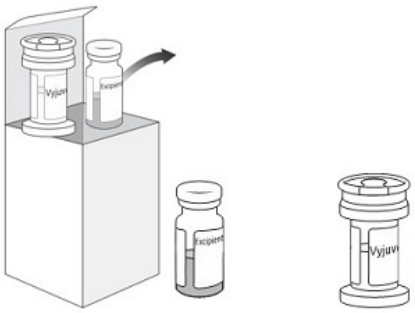


Figure 1 Carton containing the VYJUVEK biological suspension vial and excipient gel vial

Note: Visually inspect the vials to ensure both are in liquid form and completely thawed. Excipient gel is more viscous and will take longer to thaw (Figure 2).

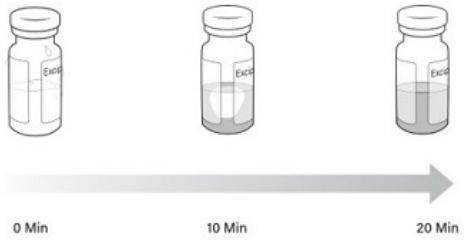


Figure 2 Timelapse of excipient gel thaw from 0 minutes to 20 minutes

Note: Once either the VYJUVEK biological suspension or the excipient gel is thawed, do not refreeze.

3. Invert the VYJUVEK biological suspension vial 4-5 times. Do not invert the excipient gel vial.
4. Remove the caps from the vials and clean each vial stopper with a 70% isopropyl alcohol pad. Allow them to dry.
5. Aseptically connect an 18-gauge needle to the 3 mL preparation syringe.
6. Remove the needle cap and puncture the VYJUVEK biological suspension vial stopper.
7. Hold the vial at 45 to 90 degrees and withdraw 1 mL of VYJUVEK biological suspension into the preparation syringe (Figure 3).
8. Remove the preparation syringe (still connected to the needle) containing 1 mL of VYJUVEK biological suspension from the vial. Do NOT engage the safety lock.

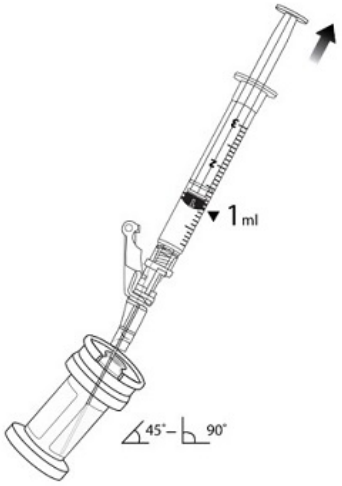


Figure 3 The removal of 1 mL of biological suspension using the preparation syringe

9. Discard the VYJUVEK biological suspension vial in the biohazard waste.
10. Puncture the clean excipient gel stopper and transfer the VYJUVEK biological suspension into the excipient gel vial (Figure 4).

Figure 4 Transferring VYJUVEK biological suspension to excipient gel vial

11. WITHOUT REMOVING THE NEEDLE from the excipient gel vial, lift the bevel of the needle above the liquid (Figure 5)and pull the plunger back to the 1 mL mark (Figure 6).

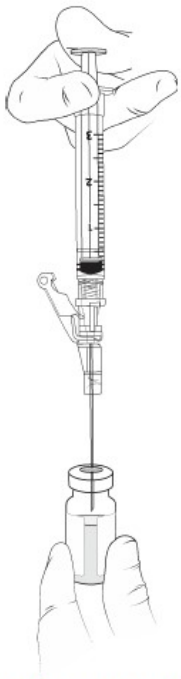


Figure 5 The needle above the liquid without removal any material

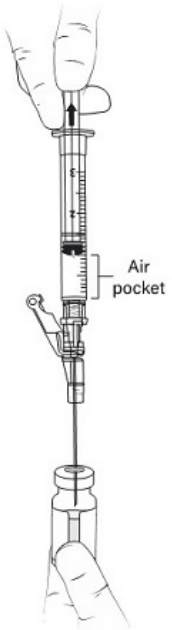


Figure 6 Pulling the plunger back to the 1 mL mark to remove air

12. Remove the preparation syringe with the 1 mL of air and engage the safety lock.
13. Discard the preparation syringe and needle into the biohazard waste.
14. Place a 70% isopropyl alcohol pad on top of the excipient gel stopper and hold it tightly in place.
15. Shake VIGORIOUSLY for 10 SECONDS (Figure 7).

Figure 7 Manually mixing the excipient gel vial

Note: The mixture of VYJUVEK biological suspension and excipient gel is referred to as VYJUVEK gel.

PREPARE THE ADMINISTRATION SYRINGES

16. Aseptically connect an 18-gauge needle to the first 1 mL administration syringe and remove the needle cap.
17. Insert the 18-gauge needle into the excipient vial containing VYJUVEK gel (Figure 8).

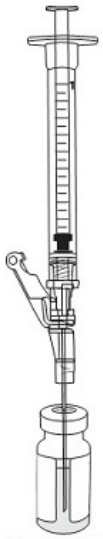


Figure 8 Needle within VYJUVEK gel prior to withdraw

18. Tilt the vial 45 to 90 degrees and withdraw 0.4 mL of VYJUVEK gel (Figure 9).

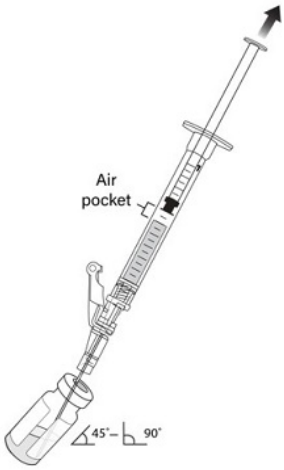


Figure 9 Administration syringe withdrawing 0.4 mL of VYJUVEK gel with air pocket visible

Note: An air pocket may form near the plunger when extracting VYJUVEK gel.

19. DO NOT REMOVE THE NEEDLE FROM THE VIAL; lift the bevel of the needle above the VYJUVEK gel and disconnect the administration syringe containing 0.4 mL of mixed VYJUVEK (Figure 10).

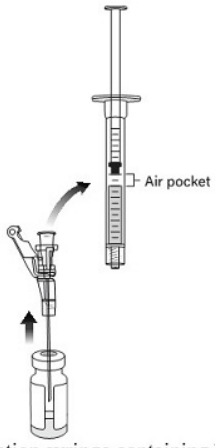


Figure 10 Disconnecting the administration syringe containing VYJUVEK gel with air pocket visible

Note: Leave the needle in the excipient gel vial stopper.

20. DO NOT flick the syringe to remove the air pocket. Manipulate the plunger up and down, until all air pockets have been removed (Figure 11)

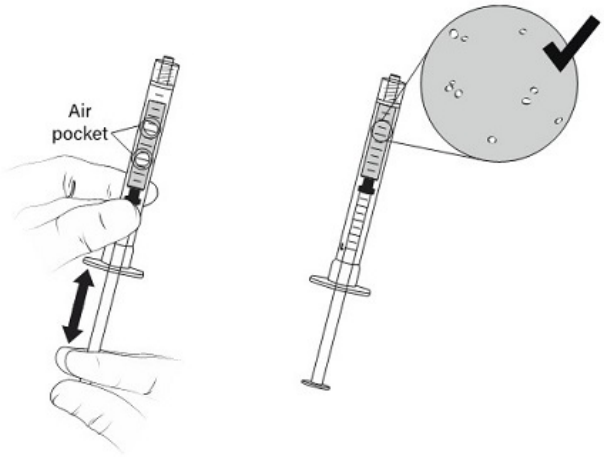


Figure 11 Manipulation of administration syringe plunger to remove air pockets

21. Cap the administration syringe and set aside (Figure 12).

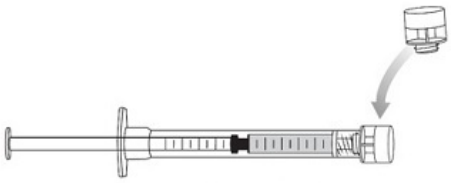


Figure 12 Capped syringe

22. Connect a new 1 mL administration syringe to the needle that remains in the excipient gel vial stopper (with the bevel of the needle ABOVE the VYJUVEK gel) (Figure 13).

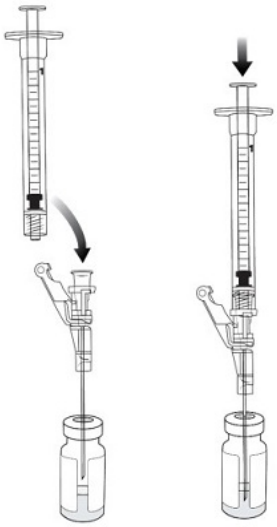


Figure 13 Connecting an administration syringe to the needle within the excipient gel vial stopper

23. Place the bevel of the needle in the VYJUVEK gel, tilt the vial 45 to 90 degrees and withdraw 0.4 mL of VYJUVEK gel into the administration syringe [see steps 17 and 18: Figure 8 and Figure 9)].
24. Complete steps 19, 20, and 21 above to disconnect the administration syringe and remove the air pockets, prior to capping the administration syringe (Figure 10, Figure 11, and Figure 12).
25. Repeat steps 22, 23, and 24 if two (2) additional administration syringes are required (each containing 0.4 mL of VYJUVEK gel).
    Note: Administration syringes are labeled as syringe #1, #2, #3, and #4.
26. Discard the excipient gel vial (with the needle within the vial stopper) into the biohazard container.
27. Clean all surfaces that may have come in contact with VYJUVEK biological suspension or gel and treat all spills with a virucidal agent such as 70% isopropyl alcohol, 6% hydrogen peroxide or <0.4% ammonium chloride. Blot using absorbent materials.
28. Dispose all materials (e.g., vial, syringe, needle, cleaning materials) that may have come in contact with VYJUVEK biological suspension or gel into a biohazard bag or container.
29. Place the capped administration syringes containing the VYJUVEK gel in a sealable plastic bag.
30. Place the sealable plastic bag with administration syringes into an appropriate insulated secondary container at 2º to 8ºC (35.6º to 46.4ºF) for transport from the preparation site to the administration site.

2.3 Administration

Below is the list of supplies needed for VYJUVEK gel administration:

- The administration syringes
- Non-adherent hydrophobic dressing
- Scissors
- Standard dressing
- Protective gloves
- Biohazard container
- Virucidal agent for clean-up

Use the VYJUVEK gel in the administration syringes immediately after preparation. If immediate use is not possible, please refer to section [*seeStorage and Handling (16.2)*].

VYJUVEK GEL ADMINISTRATION

Follow the steps below for VYJUVEK gel administration.

1. Apply VYJUVEK gel to the selected wound(s) in droplets spaced evenly within the wound, approximately 1cm-by-1cm apart. The resulting droplet pattern should loosely resemble a grid. Avoid touching the administration syringe to the skin (Figure 14).

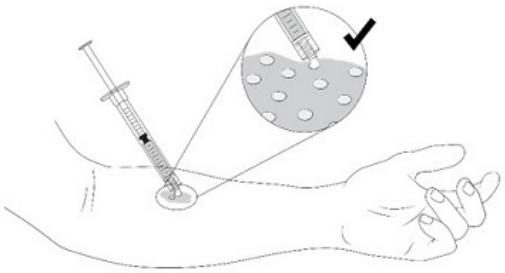


Figure 14 Application of VYJUVEK gel to the wound

Table 2 below provides a reference on dose per approximate size of the wound.
Table 2 by Wound Size

Wound Area (cm^2)	Dose (PFU)	Volume (mL)
< 20	4×10^8	0.2
20 to < 40	8×10^8	0.4
40 to 60	1.2×10^9	0.6

* For wound area over 60 cm^2, recommend calculating the total dose based on Table 2 until the maximum weekly dose in Table 1 is reached.

2. Use the clean scissors to cut the non-adherent hydrophobic dressing to a size slightly larger than the wound and place the dressing atop the VYJUVEK gel droplets (Figure 15).

Figure 15 Placing the non-adherent hydrophobic dressing over the treated wound

3. Use the scissors to cut the standard dressing used by the patient to a size slightly larger than the hydrophobic dressing and place the standard dressing atop the hydrophobic dressing (Figure 16).

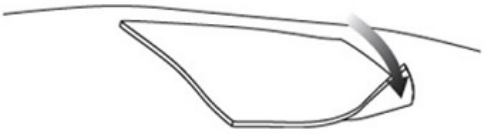


Figure 16 Placing the standard dressing over the hydrophobic dressing

4. Clean all surfaces that may have come in contact with VYJUVEK gel and treat all spills with a virucidal agent such as 70% isopropyl alcohol, 6% hydrogen peroxide or <0.4% ammonium chloride. Blot using absorbent materials.
5. Dispose all materials (e.g., syringe, cleaning materials) that may have come in contact with VYJUVEK biological suspension or gel into a biohazard bag or container.
6. Discard unused administration syringes containing the VYJUVEK gel after preparation into a biohazard bag or container [*see Storage and Handling (16.2)]*.
7. Do not change wound dressing within approximately 24 hours after VYJUVEK gel application.

3 DOSAGE FORMS AND STRENGTHS

VYJUVEK is an opalescent yellow to colorless biological suspension, mixed into excipient gel, for topical application. VYJUVEK biological suspension is supplied as a 1.0 mL extractable volume in a single-use vial with a green cap, at a nominal concentration of 5×10^9 PFU/mL. The excipient gel is a clear viscous solution supplied as a 1.5 mL fill

volume in a separate single-use vial with a blue cap.

VYJUVEK biological suspension (1.0 mL) is mixed into the excipient gel vial prior to administration.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Accidental Exposure to VYJUVEK

VYJUVEK is a genetically modified, herpes-simplex virus type 1 vector-based, replication-deficient, non-integrating gene therapy. VYJUVEK will not replicate in the subject's cells and does not integrate into the subject cells' native genetic material. For precautions,

- Avoid direct contact with treated wounds (e.g., touching or scratching) and dressings of treated wounds for approximately 24 hours following treatment.
- Wear protective gloves when assisting subjects with changing wound dressings and handling the disposal.
- In the event of an accidental exposure (e.g., through a splash to the eyes or mucous membranes), flush with clean water for at least 15 minutes.

6 ADVERSE REACTIONS

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

6.1 Clinical Trials Experienc

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The safety data described in this section primarily reflect exposure to VYJUVEK gel in a randomized, intra-subject placebo-controlled study. A total of 31 subjects with dystrophic epidermolysis bullosa (DEB), including 30 subjects with autosomal recessive DEB and one subject with autosomal dominant DEB received topical administration of VYJUVEK gel to their wounds. The age of the subjects ranged from 1 year to 44 years (mean age 17 years). Of the 31 subjects, 19 (61%) were pediatric subjects (less than 17 years of age), and 11 (36%) were females. Each subject received weekly topical application of VYJUVEK gel at one or more wound sites and placebo at a matching wound site as an intra-subject comparator. The median duration of exposure to VYJUVEK gel was 25 weeks. The most frequent adverse reactions (incidence >5%) observed in the study are summarized in Table 3. There were no discontinuations due to adverse reactions.

Table 3 Adverse Reactions (incidence >5%) Following Treatment with VYJUVEK gel (n =31)

Adverse Reactions	Subjects n (%)
Itching	3 (10)
Chills	3 (10)
Redness	2 (6)
Rash	2 (6)
Cough	2 (6)
Runny Nose	2 (6)

In addition, the safety profile of VYJUVEK in two subjects with autosomal recessive DEB (RDEB) of six and seven months of age, respectively, who received topical VYJUVEK gel weekly in an open-label study was similar to the safety profile of VYJUVEK observed in the randomized, intra-subject placebo-controlled study described above.

7 DRUG INTERACTIONS

No drug interaction studies have been performed.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no data with VYJUVEK gel use in pregnant women to inform a drug-associated risk. Animal developmental and reproductive toxicity studies have not been conducted with VYJUVEK.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. In the U.S. general population, the estimated background risks of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

Clinical Considerations

If the patient becomes pregnant while being administered VYJUVEK gel, the patient should be apprised of the potential hazards to the fetus and neonate. Women of childbearing potential should be advised to use an effective method of contraception to prevent pregnancy during treatment with VYJUVEK gel.

8.2 Lactation

Risk Summary

There is no information available on the presence of VYJUVEK in human milk, the effects on the breastfed infant, or the effects on milk production. Animal lactation studies have not been conducted with VYJUVEK.

The developmental and health benefits of breastfeeding should be considered along with the mother’s clinical need for VYJUVEK and any potential adverse effects on the breastfed child from VYJUVEK or from the underlying maternal condition.

8.3 Females and Males of Reproductive Potential

No nonclinical or clinical studies were performed to evaluate the effect of VYJUVEK on fertility.

8.4 Pediatric Use

The safety and effectiveness of VYJUVEK gel was studied in pediatric patients. The safety and efficacy findings of VYJUVEK gel in pediatric patients were similar to safety and efficacy findings in adult patients. [*see Clinical Studies (14)*].

8.5 Geriatric Use

Clinical studies of VYJUVEK gel did not include geriatric patients aged 65 years and over.

11 DESCRIPTION

VYJUVEK (beremagene geperpavec-svdt) is a suspension of a HSV-1 vector-based gene therapy, mixed with the supplied sterile excipient gel for topical application on wounds. VYJUVEK is a live, replication defective HSV-1-based vector that has been genetically modified to express the human type VII collagen (COL7) protein. The parental virus for VYJUVEK was a primary isolate, which was subsequently altered using recombinant methods to result in gene deletions and insertions.

VYJUVEK is an opalescent yellow to colorless biological suspension following thaw from its frozen state. Each 1 mL VYJUVEK vial contains 5×10^9 PFU/mL of VYJUVEK in a solution of 100.0 mL/L Glycerol, 8.0 mg/mL Sodium Chloride, 2.16 mg/mL Sodium Phosphate Dibasic, 0.2 mg/mL Potassium Chloride, 0.2 mg/mL Potassium Phosphate Monobasic.

The excipient gel is a clear viscous solution, following thaw from its frozen state. Each 1.5mL Excipient Gel vial contains 44 mg/mL Hydroxypropyl Methylcellulose in a solution of 0.91 mg/mL Tromethamine, 9.0 mg/mL Sodium Chloride, 0.726 mg/mL Sodium Phosphate Dibasic, 0.21 mg/mL Potassium Phosphate Monobasic.

VYJUVEK biological suspension is mixed into excipient gel prior to administration. After mixing, VYJUVEK gel consists of 5.0×10^9 PFU in a volume of 2.5 mL.

Neither VYJUVEK biological suspension nor the excipient gel contains preservatives.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Dystrophic epidermolysis bullosa (DEB) is caused by mutation(s) in the *COL7A1* gene, which results in reduced or absent levels of biologically active COL7.

Upon topical application to the wounds, VYJUVEK can transduce both keratinocytes and fibroblasts. Following entry of VYJUVEK into the cells, the vector genome is deposited in the nucleus. Once in the nucleus, transcription of the encoded human *COL7A1* is initiated. The resulting transcripts allow for production and secretion of COL7 by the cell in its mature form. These COL7 molecules arrange themselves into long, thin bundles that form anchoring fibrils. The anchoring fibrils hold the epidermis and dermis together and are essential for maintaining the integrity of the skin. Patients with autosomal dominant DEB (DDEB) have lower than normal functional anchoring fibrils, and patients with RDEB have no functional anchoring fibrils.

12.2 Pharmacodynamics

The pharmacodynamic activity (expression and localization of COL7 transgene) of VYJUVEK gel was demonstrated in an initial clinical study (n=6 subjects). Linear deposition of the non-collagenous domain 1 (NC1) and domain 2 (NC2) of COL7 were observed at the dermal-epidermal junction in skin biopsies harvested after VYJUVEK treatment.

12.3 Pharmacokinetics

In an initial clinical study, viral vector DNA was detected in skin swab samples in all nine treated subjects, with maximum level ranging from 5.1×10^4 to 4.1×10^8 vector genomes. In 6 out of 9 subjects (67%), negative shedding was confirmed with three measurements below limit of detection within 8 weeks of treatment with VYJUVEK. No viral vector DNA was detected in blood or urine.

In the 31-subject randomized, double-blind, intra-subject placebo-controlled trial, systemic and potential environmental exposure assessments were conducted at weekly clinical site visits via quantification of VYJUVEK genomes in blood, urine, skin swabs, and bandage samples (vector shedding) using a validated qPCR assay, and detection of infectious viral particles in skin swabs (infectivity) using a validated plaque titer assay.

All blood samples and all but one urine sample collected throughout the study were below the limit of detection. Skin swabs from 19 of the 31 subjects (61%) were positive for viral vector following treatment with VYJUVEK. Negative shedding from skin swabs was achieved in 16 of the 19 subjects (84%) within six weeks following treatment with VYJUVEK. Most wound dressings (94%, 29/31) contained a range of detectable vector genomes. However, no extracellular infectious particles were detected on the skin surface of any subject at any timepoint tested, after topical VYJUVEK application.

12.6 Immunogenicity

There was minimum potential for systemic exposure to VYJUVEK. Antibodies against the viral vector (HSV-1) and transgene protein (COL7) were evaluated in a subset of subjects in the randomized, intra-subject placebo--controlled clinical study. A total of 64% of evaluated subjects (14/22) were anti-HSV-1 antibody positive at baseline. Six of the 8 anti-HSV-1 seronegative subjects seroconverted by Week 26 following treatment with VYJUVEK. For subjects with available matched baseline and end-of-study serum samples, anti-drug antibodies (ADAs) to COL7 were detected in 72% (13/18) of subjects treated with VYJUVEK for up to 26 weeks. Data are limited to perform correlative assessment on the impact of ADA on pharmacodynamic activity.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

No animal studies have been conducted to evaluate the effects of VYJUVEK on carcinogenesis, mutagenesis, or impairment of fertility.

14 CLINICAL STUDIES

The efficacy of VYJUVEK gel in subjects one year of age and older with dystrophic epidermolysis bullosa (DEB) with mutation(s) in the *COL7A1* gene was evaluated in one randomized, double-blind, intra-subject placebo-controlled trial. All study subjects had clinical manifestations consistent with DEB and genetically confirmed mutation(s) in the *COL7A1* gene. 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.

The study enrolled 31 subjects (20 males and 11 females), including 30 subjects with autosomal recessive DEB and one subject with autosomal dominant DEB. The size of the VYJUVEK gel-treated wounds ranged from 2 to 57 cm^2, with 74% of wounds < 20 cm^2

VYJUVEK gel-treated wounds ranged from 2 to 57 cm^2, with 74% of wounds < 20 cm^2 and 19% from 20 to < 40 cm^2. The size of the placebo gel-treated wounds ranged from 2 to 52 cm^2, with 71% of wounds < 20 cm^2 and 26% from 20 to < 40 cm^2. The mean age of the subjects was 17 years (1 year to 44 years), including 61% pediatric subjects (n=19, age from 1 year to <17 years). Sixty-four percent of subjects were White; 19% were Asian, and the remainder were American Indian or Alaska Native.

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. Efficacy was supported by the difference in the proportion of complete wound closure assessed at Weeks 8 and 10 or at Weeks 10 and 12 between the VYJUVEK gel-treated and the placebo gel-treated wounds. Complete (100%) wound closure was defined as durable wound closure evaluated at two consecutive visits two weeks apart. The efficacy results are summarized in Table 4.

Table 4 Summary of the efficacy results for VYJUVEK gel (ITT Population)

Wound Closure Assessment Timepoints	Complete Wound Closure, n (%) VYJUVEK gel (N=31)	Complete Wound Closure, n (%) Placebo gel (N=31)	Treatment Difference (95% CI)	p value
Weeks 22 & 24 or Weeks 24 & 26	20 (65)	8 (26)	39% (14, 63)	0.012
Weeks 8 & 10 or Weeks 10 & 12	21 (68)	7 (23)	45% (22, 69)	0.003

16 HOW SUPPLIED/ STORAGE AND HANDLING

16.1 How Supplied

Each carton of VYJUVEK (NDC 82194-510-02) contains one single-dose vial of VYJUVEK biological suspension and one single-dose vial of excipient gel.

VYJUVEK biological suspension (inner NDC 82194-501-01), green cap, is supplied as a 1.0 mL extractable volume in a single-use, single-dose vial containing 5×10^9 PFU/mL.

Excipient gel (inner NDC 82194-001-01), blue cap, is supplied as a 1.5 mL fill volume in a separate single-use, single-dose vial.

16.2 Storage and Handling

Store the VYJUVEK carton at -15°C to -25°C (5°F to -13°F). If a freezer is not available, the carton can be refrigerated (2º to 8ºC (35.6º to 46.4ºF)) for up to 1 month.

Prior to use, VYJUVEK requires mixing into excipient gel.

Administration syringes containing the VYJUVEK gel may remain at room temperature (20 to 25°C (68° to 77°F)) for up to 8 hours. If immediate use is not possible, administration syringes can be stored for up to 48 hours in the refrigerator (2º to 8ºC (35.6º to 46.4ºF)) .

Discard material if it falls out of the parameters described above.

VYJUVEK is replication deficient HSV-1-based gene therapy. See *Dosage and Administration (2)* for appropriate handling, preparation, application, and disposal of materials. Follow universal biohazard precautions for handling.

17 PATIENT COUNSELING INFORMATION

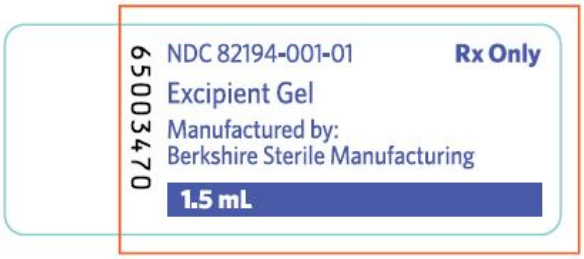
Advise patients or caregivers of the following precautions prior to and during treatment with VYJUVEK gel:

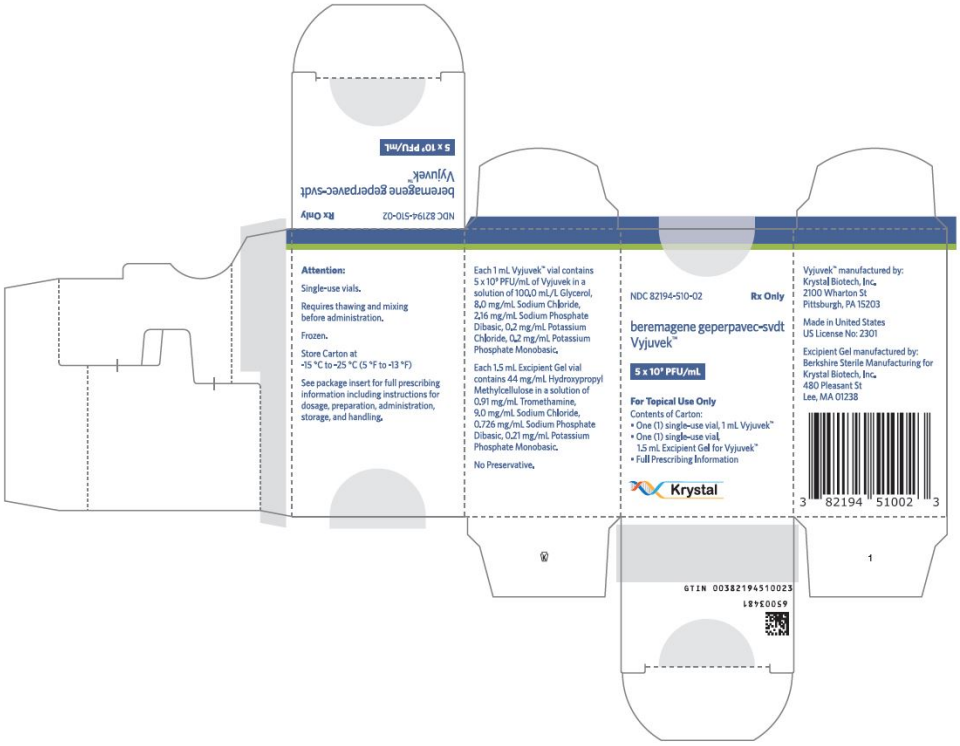
- Avoid direct contact with treated wounds (e.g., touching and scratching) and dressings of treated wounds for approximately 24 hours following VYJUVEK gel application. In the event of accidental exposure, instruct patients and exposed individuals to clean the affected area. [see *Warnings and Precautions* (5.1)]
- Wash hands and wear protective gloves when changing wound dressings. [see *Preparation* (2.2)]
- Disinfect bandages from the first dressing change with a virucidal agent, such as 70% isopropyl alcohol, 6% hydrogen peroxide or <0.4% ammonium chloride, and dispose of the disinfected bandages in a separate sealed plastic bag in household waste. Dispose of the subsequent used dressings and cleaning materials into a

sealed plastic bag and dispose in household waste. [see *Administration* (2.3)]

Manufactured by:
Krystal Biotech, Inc.
2100 Wharton Street, Suite 701
Pittsburgh, PA 15203
U.S. License No. 2301

VYJUVEK™ is a trademark of Krystal Biotech, Inc. having a pending application for registration at the United States Patent and Trademark Office.





VYJUVEK
vyjuvek kit

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:82194-510

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:82194-510-02	1 in 1 CARTON; Type 0: Not a Combination Product	05/19/2023	

Quantity of Parts		
Part #	**Package Quantity**	**Total Product Quantity**
Part 1	1 VIAL	1 mL
Part 2	1 VIAL	1.5 mL

Part 1 of 2

VYJUVEK BIOLOGICAL SUSPENSION

beremagene geperpavec suspension

Product Information	
Item Code (Source)	NDC:82194-501
Route of Administration	TOPICAL

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
BEREMAGENE GEPERPAVEC (UNII: AQN7K24KQU) (BEREMAGENE GEPERPAVEC - UNII:AQN7K24KQU)	BEREMAGENE GEPERPAVEC	5000000000 [PFU] in 1 mL

Inactive Ingredients	
Ingredient Name	**Strength**
GLYCERIN (UNII: PDC6A3C0OX)	
SODIUM CHLORIDE (UNII: 451W47IQ8X)	
SODIUM PHOSPHATE DIBASIC DIHYDRATE (UNII: 94255I6E2T)	

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:82194-501-01	1 mL in 1 VIAL; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA125774		

Part 2 of 2

EXCIPIENT GEL

excipient gel

Product Information	
Item Code (Source)	NDC:82194-001
Route of Administration	TOPICAL

Inactive Ingredients

Ingredient Name	Strength
HYPROMELLOSE, UNSPECIFIED (UNII: 3NXW29V3WO)	1 mL in 1 mL
TROMETHAMINE (UNII: 023C2WHX2V)	
SODIUM CHLORIDE (UNII: 451W47IQ8X)	
SODIUM PHOSPHATE DIBASIC DIHYDRATE (UNII: 94255I6E2T)	
POTASSIUM PHOSPHATE, MONOBASIC (UNII: 4J9FJ0HL51)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:82194-001-01	1.5 mL in 1 VIAL; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA125774		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA125774	05/19/2023	

Labeler - Krystal Biotech, Inc. (021814762)

Establishment

Name	Address	ID/FEI	Business Operations
Krystal Biotech, Inc.		021814762	manufacture(82194-510, 82194-501, 82194-001)

Revised: 7/2023 Krystal Biotech, Inc.