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New Drug Evaluations: Epidermolysis bullosa

Date of Review: December 2025
Generic Name: beremagene geperpavec, topical gel
Generic Name: prademagene zamikeracel, topical gene-modified cellular sheets
Generic Name: birch triterpenes, topical gel

End Date of Literature Search: 09/12/2025
Brand Name (Manufacturer): Vyjuvek (Krystal Biotech, Inc)
Brand Name (Manufacturer): Zevaskyn (Abeona Therapeutics, Inc)
Brand Name (Manufacturer): Filsuvez (Lichtenheldt GmbH)

Dossier Received: No

Plain Language Summary:

- Epidermolysis bullosa is a condition associated with very fragile skin. In people with epidermolysis bullosa, small bumps and scrapes can cause chronic wounds that do not heal.
- The Food and Drug Administration (FDA) has approved 3 medicines to help wounds heal in people with epidermolysis bullosa. There are many different genetic mutations that cause epidermolysis bullosa, and these therapies have been mostly studied in people with mutations in the collagen type VII alpha 1 chain (COL71A) gene. People with this genetic mutation generally have many long-lasting, non-healing wounds.
    - Birch triterpenes is a medicine that patients apply to non-healing wounds every 1 to 4 days when wound dressings are changed. About 41% of people who applied birch triterpenes had wounds that healed over 45 days compared to 29% of people who had usual wound care. When wound healing was measured at 90 days or with other definitions, birch triterpenes was no different than usual wound care.
    - Beremagene geperpavec is a medicine that is approved by the FDA for people with at least one mutation in the COL71A gene. Providers can apply this medicine to the surface of non-healing wounds. This medicine is designed to correct the underlying genetic mutation that causes the wound, but it must be reapplied every week. In clinical studies, 65% of wounds treated with beremagene geperpavec were completely healed by 6 months compared to 26% of wounds treated with usual care.
    - Prademagene zamikeracel is a medicine that is approved by the FDA for people with at least two mutations in the COL71A gene. It is made from healthy skin cells that are collected from the patient and modified in the lab to correct the underlying genetic mutation. These modified cells are grown into sheets that are sewn onto non-healing wounds. After about 6 months, 16% of wounds treated with these modified skin cells were completely healed compared to 0% of wounds treated with usual care. Unlike other medicines, prademagene zamikeracel was studied in people who had very large and old wounds which could have influenced study results. The average age of non-healing wounds was 5 years (range 6 months to 21 years).
- There is not enough information to determine if one medicine is better than another. Differences in the studied populations (such as wound duration and size) make it difficult to determine if one particular medicine works better than another.
- During clinical studies, the number of people who had serious side effects was generally small for all 3 medicines. However, these medicines have not been studied in very many people, and there are many things that are not known about their long-term safety.

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- We recommend that the Oregon Health Authority pay for birch triterpenes, beremagene geperpavec, or prademagene zamikeracel when the provider documents why someone needs these medicines. This process is called prior authorization.

Research Questions:

1. In people with epidermolysis bullosa (EB), what is the evidence for recent FDA-approved therapies to improve wound healing or symptoms and how does efficacy compare to current standard of care for wound treatment?
2. What is the evidence for safety of FDA-approved treatments for EB?
3. Are there subgroups of patients (based on genetic variation, disease severity, type of EB, or comorbid conditions) for whom these treatments are more effective or associated with more harms?

Conclusions:

- There is low certainty evidence from a single randomized controlled trial (RCT; n=223) that birch triterpenes gel has a small benefit for complete wound closure compared to standard wound care in people with junctional or dystrophic EB with about 45 days of therapy (41.3% vs. 28.9%; difference 12.4%; number-needed-to-treat [NNT] 9; relative risk [RR] 1.44; 95% confidence interval [CI] 1.01 to 2.05; p=0.013).[1] In the subgroup of people with junctional EB, wounds treated with birch triterpenes had less healing compared to standard of care, but the overall number of people with junctional EB was small and the study was not powered to detect differences between subgroups.[1]
- There is insufficient evidence to determine whether birch triterpenes affects EB complications (e.g., skin cancer, infection), quality of life, total wound burden, or re-opening of wounds. When wound closure and severity was evaluated using a variety of other outcomes including time to first complete wound closure, complete wound closure at 90 days, change in total wound burden, and percent of body surface area affected, the differences between groups were not statistically significant.[1] There is no data on efficacy in wounds older than 9 months.[1] For people enrolled in the trial, median wound duration was about 1 month, and 65% of wounds were less than 20 cm^2 in size.[1]
- There in low certainty evidence from a single small trial (n=31) that beremagene geperpavec improves complete wound healing in patients with dystrophic EB compared to usual care over 6 months (65% vs. 26%; difference 39%; 95% CI 14% to 63%; p=0.012; NNT = 3).[2] People enrolled in this trial generally had recessive dystrophic EB (97%) and a wound size less than 20 cm^2 (71%).[2] There is insufficient data to determine whether beremagene geperpavec impacts other symptoms including itching or pain, EB complications (e.g., skin cancer, infection), or quality of life. There is currently insufficient evidence on efficacy beyond 6 months. A long-term extension study documented that some people had wounds remain closed over a median treatment duration of 1.5 years, but evidence is limited by a significant amount of missing data, risk for selection bias, and lack of control groups.[3]
- There is insufficient evidence from a small trial (n=11) that prademagene zamikeracel improves wound healing in patients with recessive dystrophic EB and chronic non-healing wounds compared to usual care.[4] After 24 weeks, more people had treated wounds that were at least 50% healed (81% vs. 16%; difference 67%; 95% CI 50 to 89%) and completely healed (16% vs. 0%; difference 13%; 95% CI 2 to 26%) compared to standard of care.[4] In this trial the median wound age was 5 years (range 6 months to 21 years) and all wounds were larger than 20 cm^2.[4] There is insufficient evidence that prademagene zamikeracel improves pain compared to standard of care, and other clinically relevant outcomes have not been evaluated including total wound burden, complications (e.g., skin cancer, infection), or impacts on quality of life. Prademagene zamikeracel has not been studied in people with an immune response to type VII collagen or people who are more likely to develop an immune response to type VII collagen.[4]
- All 3 therapies were generally well tolerated in short-term studies. The incidence of serious side effects was generally infrequent and not attributed to therapy. Available safety data is limited by small trials, intra-patient study designs, and lack of controlled long-term data. For the gene therapies, it is currently unclear how immunogenicity against viral vectors or collagen type VII might impact long-term safety or efficacy of therapy. Studies of beremagene geperpavec documented development of antibodies for collagen type VII without impacts on short-term efficacy, and studies of prademagene zamikeracel

excluded people who had baseline antibodies for collagen type VII or were likely to develop antibodies. The long-term durability of treatment effects for these gene therapy is currently unknown.

Recommendations:

- Implement prior authorization for high cost treatments for epidermolysis bullosa including birch triterpenes, beremagene geperpavec and prademagene zamikeracel.
- After review of costs in executive session, make all 3 therapies non-preferred.

Background:

Epidermolysis bullosa (EB) is a condition affecting skin integrity in which minor trauma can cause blistering and chronic, non-healing wounds. It can be inherited (i.e., caused by genetic mutations in proteins essential to skin structure) or autoimmune-mediated.[5] Inherited forms of EB are broadly categorized into 4 types based on the location blisters form in the skin. In epidermolysis bullosa simplex, blisters originate in the epidermis; in junctional epidermolysis bullosa, blisters originate within part of the basement membrane called the lamina lucida; in dystrophic epidermolysis bullosa, blisters originate within the sublamina densa; and in Kindler epidermolysis bullosa blisters can originate at any layer of the epidermis.[5] Both junctional and dystrophic disease can be associated with severe symptoms, whereas EB simplex typically has more mild symptoms. Dystrophic epidermolysis bullosa can be further categorized as autosomal dominant or recessive depending on the inheritance pattern of mutations in the COL7A1 gene.[5] This gene is responsible for formation of the collagen type VII protein which forms anchoring fibrils that hold the epidermis and dermis together. In dominant dystrophic EB the amount of functional collagen VII protein is reduced, whereas recessive dystrophic EB is usually associated with absence of functional collagen VII and more severe symptoms.[5] Without collagen VII, when a blister forms, it is easier for skin layers to separate creating chronic non-healing wounds. It is estimated that 1 in 125,000 people live with some form of EB in the United States, and about 5-25% of patients have dystrophic EB.[5].

Diagnosis is based on clinical presentation of symptoms, evaluation of family history, skin biopsy to determine the level at which blisters form, and genetic testing. Laboratory diagnosis is typically recommended to rule out other skin conditions such as bullous pemphigoid, other inherited skin conditions, skin infections, and friction blisters. Inherited disease typically presents in neonates as skin blistering, most commonly on extremities or from diapers.[5] Blisters can be associated with pain, itching, scarring, and milia (e.g., small cysts caused by build-up of keratin in the skin).[5] More severe forms of the disease can be associated with nail dystrophy or loss, infection, alopecia, mucosal involvement resulting in growth failure or malnutrition, and scaring causing partial fusion of fingers and toes.[5] Long-term repeated blistering and scarring can increase risk for severe infections and squamous-cell carcinoma.[2] Both junctional and recessive dystrophic EB are associated with early mortality. Junctional EB has an estimated mortality of 50% by 2 years of age. In people with recessive dystrophic epidermolysis bullosa, squamous cell carcinoma is the most common cause of death with an estimated cumulative risk of 70% by 45 years of age.[5]

Management of EB is primarily supportive and focuses on wound management, skin care, and treatment of complications. Until recently, there have been no targeted treatments for EB. Pain and itching are some of the most common symptoms associated with open or partially healed wounds. Pain treatments could include cognitive behavioral therapy, topical analgesics and systemic analgesics.[5] Common treatments for pruritus could include antihistamines, tricyclic antidepressants, and gabapentinoids.[5] Wound care includes lancing and draining blisters, using soft, non-traumatic dressings with adhesive removers to remove adherent dressings, and monitoring for infection.[5,6] Because of the rarity of the conditions, much of the evidence for specific topical medications for wound management is based on case reports and expert opinion.[6] Choice of topical therapies and dressings should address specific wound characteristics considering need for wound debridement to remove dry or necrotic skin cells, infection or critically colonized wounds, or need moisturizers and exudate management.[6] Since 2023, the FDA has approved 3 therapies for treatment of wounds in people with certain types of EB (**Table 1**).

Table 1. FDA-approved indications for newer EB therapies

Generic Name (Brand)	Mechanism	FDA Indication	Gene mutation	Route and Frequency	How Supplied
birch triterpenes (FILSUVEZ)[7]	Decreases inflammation and promotes wound healing	Junctional and Dystrophic EB	Junctional: LAMA3, LAMB3, LAMC2, ITGB4, ITGA6, COL17A1, ITGA3 Dystrophic: COL7A1	Topical gel applied with dressing changes every 1-4 days	Single-use, sterile tubes
beremagene geperpavec (VYJUVEK)[8]	Gene therapy that delivers a functional COL7A1 gene to cells in existing wounds; COL7A1 is not incorporated into cellular DNA	Dystrophic EB	COL7A1	Topical gel applied weekly	Single-use vials of cryopreserved drug product intended to be mixed with excipient gel immediately before administration
prademagene zamikeracel (ZEVASKYN)[9]	Gene therapy in which the patient's cell have been collected and modified to produce a functional COL7A1 gene	Recessive Dystrophic EB	COL7A1	Topical sheets applied during surgery	Skin cells collected from biopsy, modified with retrovirus, and grown into sheets
Abbreviations: COL71A = collagen type VII alpha 1 chain; DNA = deoxyribonucleic acid; EB = epidermolysis bullosa					

Clinically relevant outcomes for patients with EB include improvements in wound healing, pain, or itching and prevention of complications like infection, scarring, and skin cancer. For patients with severe disease, wound management can present a significant burden and impact on quality of life. There is no broadly accepted definition for clinically meaningful differences in these outcomes.[10] For adults, wound closure for at least 3 months may represent a clinically significant benefit, and for people with severe disease, more than a 50% improvement in wound burden may be needed to lead a more normal life.[10] However, even closure of a small number of wounds may result in clinically meaningful improvement in pain, itching, or quality of life.[10]

Beginning in January 2026, the Oregon Health Authority is proposing that high cost, rarely used medications be carved out of Coordinated Care Organization (CCO) payments and billed directly to fee-for-service (FFS). Medications can be included in this carve-out if they meet the following criteria:

1. Estimated acquisition cost of more than $500,000 per member over a 12-month period
2. Are indicated for rare conditions, and
3. Have few alternatives, as determined by the Oregon Health Authority

The medications listed in **Table 1** are currently included in the list of medications proposed to be carved-out of CCO budgets. Over a 1 year period from 4/1/24 to 3/31/25, 7 members had a diagnosis of dystrophic EB in their medical claims.

See **Appendix 1** for **Highlights of Prescribing Information** from the manufacturer, including Boxed Warnings and Risk Evaluation Mitigation Strategies (if applicable), indications, dosage and administration, formulations, contraindications, warnings and precautions, adverse reactions, drug interactions and use in specific populations. Pharmacology and Pharmacokinetic Properties are listed in **Appendix 2**.

Clinical Efficacy:

Filsuvez (birch triterpenes)

FDA approval for birch triterpenes was based on a single, phase 3 RCT evaluating topical application of birch bark extract with vehicle control in people with dystrophic or junctional EB (**Table 2**). The exact mechanism of triterpenes is unknown but it is thought to decrease inflammation and promote wound healing.[1] People enrolled in the clinical trial were primarily pediatric patients with recessive dystrophic EB with partial thickness wounds that had been present for at least 21 days.[1] At the initial treatment visit, one wound meeting eligibility criteria was selected as the target wound. Patients were excluded if they had local skin infections, recent antibiotic use, or EB simplex (which generally has less severe symptoms), and wounds older than 9 months.[1,11] The median wound size was 15.6 cm^2 and average age was 35.5 days.[1] The primary outcome was complete closure of the target wound within 45 days defined as re-epithelialization without drainage. In alignment with FDA guidance for wound outcomes, the first evaluation of wound closure was re-confirmed by a second observation within 7 days.[1] More patients treated with birch triterpenes had complete wound closure before 45 days compared to vehicle control (41.3% vs. 28.9%; RR 1.44; 95% CI 1.01 to 2.05; p=0.013).[1] However, data was limited by large and differential amounts of missing data for the follow-up observational visit (33% in treatment and 61% in placebo lacked confirmation after 7 days).[1] Additionally, none of the secondary outcomes evaluating wound healing or symptom improvement achieved statistical differences between groups. Secondary outcomes included the time to first complete closure of the target wound, complete wound closure at 90 days, incidence and severity of wound infection, change in total wound burden, percent of body surface area affected, pain and itch intensity.[1]

Evidence limitations and unknowns:

- Evidence from the phase 3 trial has risk for selection bias based on differences between groups in baseline characteristics (e.g., wound age and subtype of EB) and risk for attrition bias (with differential attrition between groups). FDA analyses to account for missing data using multiple imputation methods indicated high risk for attrition bias.[12] The treatment group enrolled more people with recessive dystrophic EB (83.5% vs. 73.7% with placebo).[1] Treatment effects were also more prominent in this subtype, and people with junctional or dominant dystrophic EB did not have trends favoring treatment over control.[1] In people with junctional EB, wound closure was more common in people treated with placebo (26.7%) compared to treatment (18.2%), but the total number of people treated was small (n=26) and the trial was not designed to detect differences between subgroups.[1]
- There is insufficient evidence to evaluate efficacy of birch triterpenes in specific subtypes of EB, and no data evaluating birch triterpenes in EB simplex (a less severe form of the disease).
- There is inadequate evidence to evaluate whether birch triterpenes improves sustained wound closure compared to placebo or assists with healing of chronic wounds. People with EB have inherently fragile skin, and it is common to have minor trauma re-open wounds after partial or complete healing. At 90 days, the difference between groups was smaller and not statistically significant.[1] While initially patients with wounds older than 9 months were eligible for trial enrollment, they were subsequently excluded from the study, and FDA analyses suggest that clinical activity of birch triterpenes is more relevant to promoting closure of acute wounds compared to healing older, chronic wounds.[12] There is no evidence that birch triterpenes prevents wounds from re-opening.
- There is insufficient evidence to evaluate other outcomes including total wound burden, other symptoms (like pain and itch severity), and prevention of infections or other long-term complications.

Beremagene geperpavec

Beremagene geperpavec is a topically administered gene therapy composed of a herpes simplex virus-type 1 (HSV-1) vector. It is intended to deliver a non-mutated copy of COL7A1 gene to the nucleus of skin cells without integration of DNA into the host cell chromosome. The delivered DNA results in formation of functional COL7 protein, but because the DNA is not integrated into the host genome, re-application is needed for ongoing efficacy. The drug was FDA approved based on results of a phase 3 trial which enrolled people with dystrophic EB (primarily recessive) caused by mutations in the COL7A1 gene (**Table 2**).[2] For each

enrolled patient, 2 matching wounds were identified and randomized to either treatment or placebo. Wounds were matched based on size, region and appearance. Median size was 10.6 cm^2 and most wounds were less than 40 cm^2 in size.[2] Age of wounds at baseline was not reported. Patients with active infection or history of squamous cell carcinoma were excluded. The primary endpoint was complete wound healing at 6 months defined as skin re-epithelialization without drainage for at least 2 weeks.[2] A key secondary endpoint was complete wound healing at 3 months. Compared to placebo, more wounds treated with beremagene geperpavec were completely healed by 3 months (68% vs. 23%; difference 45%; 95% CI 23 to 69%) and 6 months (65% vs. 26%; difference 39%; 95% CI 14 to 63%).[8,13] Pain severity during dressing changes for wounds receiving treatment or placebo was also evaluated as a secondary endpoint. However, changes from baseline were generally small for both groups (<1 point change on a 0-10 point visual analogue scale),[2] and methodological limitations make interpretation of these results unclear.[13] There was no pre-specified statistical analysis plan for pain severity endpoints, no methods documented to handle missing data, and rescue pain medication use was not documented.[13]

Data is limited by unclear risk of selection bias as randomization methods were not reported. The trial also included 5 patients (16%) who were previously enrolled in earlier trials for beremagene geperpavec which is a population likely to have had benefit from beremagene geperpavec based on prior treatment experience. There is insufficient data to evaluate differences in specific subgroups or populations. The trial was adequately blinded and enrolled a wide variety of races. The majority of data is applicable to people with recessive dystrophic EB who have wounds smaller than 40 cm^2. Wound age was not reported which make indirect comparisons to other treatment options difficult. Most people either tested positive for HSV antibodies at baseline or developed antibodies over the course of the study.[2] However, post-hoc subgroup analyses did not identify any differences in efficacy among people who tested seropositive or seronegative for anti-HSV-1 or anti-COL7 antibodies for the duration of the study.[2] Long-term data are needed to confirm these findings, and there is currently insufficient data to evaluate long-term efficacy and durability of response. Of the 24 patients in the phase 3 trial who enrolled in the long-term extension study, there was available efficacy data for 16 to 18 members who had consistent follow-up visits after 12 to 18 months of treatment.[3] In these members, 10 to 14 had complete wound closure (41.6% to 58.3%) after a treatment duration of 1 to 1.5 years.[3] However, long-term efficacy data is limited by a significant amount of missing data, risk for selection bias, and lack of control groups.

<u>Prademagene zamikeracel</u>

Prademagene zamikeracel is FDA approved for people with recessive dystrophic EB. It is manufactured from autologous skin cells collected from the patient, modified with a retrovirus to contain the COL7A1 gene, and grown in the laboratory into cellular sheets which are then sewn onto wounds.[9] Each cellular sheet is about 41 cm^2 and up to 12 sheets can be made from 2 skin biopsies.[9] All manufactured sheets are intended to be applied during a single surgery. In the phase 3 clinical trial, the average time between skin biopsy and application of cellular sheets was about 25 days.[4]

Prademagene zamikeracel was evaluated in an open-label, phase 3, intra-patient trial containing 11 people.[4] The study included people with recessive dystrophic EB and at least 2 large (≥20 cm^2) chronic (≥ 6 month) wounds.[4] Median wound duration was 5 years (range 6 months to 21 years).[4] Wounds were matched based on size, location and duration whenever possible and randomized to treatment or standard of care. After 24 weeks, more people had treated wounds that were at least 50% healed compared to standard of care (81% vs. 16%; difference 67%; 95% CI 50 to 89%).[4] The trial also reported pain improvement using 11-point visual analogue scale in treated wounds compared to untreated wounds (-3.07 vs. -0.9; MD -2.23; 95% CI -3.45 to -0.66) and more wounds with complete healing at 24 weeks (16% vs. 0%; difference 13%; 95% CI 2 to 26%).[4]

Due to the nature of the intervention, blinding was not possible. Data are limited by the open-label study design which increases risk of performance and detection bias, particularly for subjective outcomes like pain reduction. Wound healing was not evaluated by blinded assessors, and differences in treatment between groups (such as debridement and cauterization of wounds in the treatment arm) may account some of the differences between groups. Very few

patients were enrolled, and it is unclear whether 50% of wound healing represents a clinically meaningful outcome for patients. Only 16% of treated wounds were completely healed after 24 weeks.[4] However, unlike other drugs evaluated to promote wound healing in EB, the people enrolled in this trial had wounds that were generally larger and older than other trials of drugs to treat EB, making comparisons between agents difficult. There is insufficient data to determine if treated wounds continued to heal beyond 24 weeks, or if this gene therapy prevents wounds from re-opening or reforming. Re-treatment with prademagene zamikeracel has not been evaluated. People enrolled in the trial had to lack an immune response to type VII collagen and have expression of the amino-terminal NC1 fragment of type VII collagen, which decreases risk of developing an immune response. Because there is no data in other populations, it is unclear how an immune response to collagen VII would impact efficacy of prademagene zamikeracel.

In conclusion, there is no direct data to evaluate comparative efficacy or safety of therapies recently approved by the FDA for treatment of EB. All three therapies demonstrated improvements in wound healing compared to standard of care, though none of the trials described the specific interventions provided as standard of care. Studies of birch triterpenes enrolled the largest number of patients with a variety of EB subtypes, but studied wounds for the shortest duration. By comparison, both beremagene geperpavec and prademagene zamikeracel were studied in a much smaller population with primarily recessive dystrophic EB. The median wound size was smallest in patients treated with beremagene geperpavec and largest in patients treated with prademagene zamikeracel.

	Birch triterpenes[1]	Beremagene geperpavec[2]	Prademagene zamikeracel[4]
EB type	Recessive dystrophic (79%) Junctional (12%) Dominant dystrophic (9%)	Recessive Dystrophic (97%)	Recessive dystrophic (100%)
Number of patients enrolled	223	31	11
Median wound size	15.6 cm^2	10.4 cm^2	Not reported; all were ≥ 20 cm^2
Median wound age	35 days	Not reported	5 years
Trial duration	45 days	24 weeks	24 weeks
Study design	RCT	Intra-patient RCT	Intra-patient RCT

Abbreviations: cm = centimeters; EB = epidermolysis bullosa; RCT = randomized controlled trial.

Clinical Safety:

Filsuvez (birch triterpenes)

During the phase 3 study and open-label extension period, 223 people with inherited EB were exposed to birch triterpenes for a duration of 24 months.[7] The most common adverse event was application site reactions (e.g., pain, pruritus) which occurred at similar rates as placebo gel (7.3% vs. 6.1%).[7] Squamous cell carcinoma, which is a common complication in recessive dystrophic EB, was reported for 4 people, 2 of whom had applied birch triterpenes to the area that developed carcinoma.[7] However, animal studies do not indicate carcinogenic risk and overall systemic absorption is low.[7] There is no data on use in specific populations including those that are pregnant or lactating. Birch triterpenes was studied in people as young as 6 months of age but has not been evaluated in people over 65 years. Local hypersensitivity reactions have been reported in post-marketing data including urticaria and dermatitis.[7]

Beremagene geperpavec

During the phase 3 clinical trial, 31 people with dystrophic EB were exposed to beremagene geperpavec for a median duration of 25 weeks. The most common adverse events observed in 2 or more patients in the phase 3 study were itching (n=3; 10%), chills (n=3; 10%), redness, rash, cough, and runny nose (n=2; 6%).[8]

The intra-patient design of the phase 3 trial confounds the systemic safety evaluation, and the exact location of localized skin reactions was not documented.[13] However, only 3 patients experienced serious adverse events during the treatment period (e.g., asymptomatic bacteremia, cellulitis, diarrhea, and anemia) and none of the adverse events appeared to be related to treatment. There were no discontinuations due to adverse events. FDA-approved labeling includes warnings for accidental exposure. While beremagene geperpavec is not designed to be integrated into cellular DNA, general precautions include avoiding direct contact with treated wounds for 24 hours following application, wearing gloves during dressing changes, and flushing eyes or mucous membranes for 15 minutes in the case of accidental exposure.[8] There is insufficient long-term data to evaluate the impact of developing immunogenicity on adverse events related to treatment.

Prademagene zamikeracel

Package labeling for prademagene zamikeracel includes potential for retroviral vector-mediated insertional oncogenesis, and lifelong monitoring is recommended for the development of malignancies.[9] It is also manufactured using human and bovine-derived products which, like all human and animal-derived products, carry risk for infectious disease transmission or hypersensitivity reactions.[9] The most common adverse event in the phase 3 trial was procedural pain (n=3; 27%).[9]

None of the patients in the phase 3 trial developed antibodies against collagen type VII over the 6 month study.[9] However, the trial was small and excluded people at risk for development of antibodies. There is overall insufficient data evaluating the incidence or clinical importance of anti-collagen type VII antibodies in people treated with prademagene zamikeracel.[9]

Comparative Endpoints:

Clinically Meaningful Endpoints:

1) Complete wound closure
2) Total wound burden (e.g., number, frequency, or severity of wounds)
3) Pain or Itching
4) Quality of life, missed work or school days
5) Skin infection or skin cancer
6) Serious adverse events
7) Study withdrawal due to an adverse event

Primary Study Endpoint(s):

1) Complete wound closure
2) 50% wound closure
3) Pain improvement

Table 2. Comparative Evidence Table.

Ref./ Study Design	Drug Regimens/ Duration	Patient Population	N	Efficacy Endpoints	ARR/ NNT	Safety Outcomes	ARR/ NNH	Risk of Bias/ Applicability
1. Kern, et al. 2022.[1] DB, PC, phase 3 RCT NCT03068780	1. birch triterpenes 10% gel applied at least every 4 days 2. Placebo vehicle gel Administered in conjunction with standard of care dressings Duration: 90 day double-blind phase followed by 24 month open-label extension study	Demographics: - Median patient age: 12 years (95% CI 14.8-18.5) - Dystrophic EB Recessive: 79% 1. 83.5% 2. 73.7% Dominant: 9% 1. 5.5% 2. 12.3% - Junctional EB: 12% 1. 10.1% 2. 13.2% - Wound Size 10 to <20 cm^2: 65% 20 to <30 cm^2:21% 30-50 cm^2: 14% - Median wound age: 1. 39 days 2. 32 days Key Inclusion Criteria: - Dystrophic, junctional, Kindler EB - Partial-thickness wound lasting between 21 days and 9 months - Wound size 10-50 cm^2 Key Exclusion Criteria: - EB Simplex - Signs of local infection or antibiotic use within 7 days - Systemic or topical steroids - Immunosuppressive or cytotoxic chemotherapy - Prior gene therapy or stem cell transplant - Basal or squamous cell carcinoma	ITT: 1. 109 2. 114 PP: 1. 100 2. 99 Attrition 1. 9 (8%) 2. 15 (13%)	Primary Endpoint: Complete wound closure in 45 days 1. 45 (41.3%) 2. 33 (28.9%) Difference: 12.4% (95% CI 0.8 to 25.6%); RR 1.44 (95% CI 1.01 to 2.05); p=0.013 Secondary Endpoints: Time to first complete closure of target wound 1. 37.7 days (95% CI 31.9 to 43.6) 2. 44.5 days (95% CI 37.1 to 51.9) P=0.302 Complete wound closure in 90 days 1. 50.5% 2. 43.9% RR 1.16 (95% CI 0.88 to 1.52); P=0.296 All secondary endpoints were non-significant and considered exploratory based on the pre-specified testing plan	12.4%/ 9 NA NA	Serious AE: 1. 7 (6.4%) 2. 6 (5.3%) Withdrawal due to AE: 1. 3 (2.8%) 2. 2 (1.8%) Overall Infections & infestations: 1. 37 (33.9%) 2. 36 (31.6%) Wound-related infection: 1. 8 (7.3%) 2. 10 (8.8%)	NA	**Risk of Bias (low/high/unclear)**: Selection Bias: HIGH. Randomized using blinded and computer-generated allocation tables with concealment for treatment group. Stratification included EB subtype and size of the target wound. More patients randomized to treatment had recessive dystrophic subtype (83.5% vs. 73.7%) and median wound age was 7 days older in the treatment group. Performance Bias: LOW. Blinded with identical vehicle control made from sunflower oil, cera flava/yellow wax and carnauba wax. Detection Bias: UNCLEAR. Blinding of assessors not reported. Blinded patients initially notified clinic of wound closure which was confirmed by clinic assessment upon the next visit. Unblinded interim analysis was conducted to determine whether estimated sample size was sufficient. Attrition Bias: HIGH. All patients randomized were included in the analysis. Differential attrition (5%) between groups. Missing data was defined as not achieving complete closure for the primary endpoint and censored at the date last known to have not achieved complete closure for the key secondary endpoint. Patients (n=2 in control arm) were withdrawn from the study because the target wound worsened or developed infection. Analyses to account for missing data using multiple imputation and tipping point analyses show that results "were fragile to these sensitivity analyses".[12] Reporting Bias: UNCLEAR. Primary and secondary outcomes reported as pre-specified. Multiple subgroup analyses and secondary outcomes evaluated at a variety of time-points. Other Bias: UNCLEAR. Funded by Amryt Research Limited. **Applicability**: Patient: Subgroup analyses indicate improvement was primarily driven by changes in people with recessive dystrophic EB, though the proportion of people with other types of EB was small. Rate of wound closure was higher in people with junctional EB who were prescribed placebo. Intervention: Applied in 1 mm layer to wound dressing at least every 4 days. At baseline, 43% changed dressings daily and 41% applied dressings every 2 days. Frequency of dressing changes decreased slightly in the treatment group over the course of the study. Comparator: Placebo gel appropriate to determine efficacy. Specifics Outcomes: Wound healing is a clinically relevant outcome. None of the secondary outcomes evaluating wound closure achieved differences from placebo; and magnitude of benefit is likely small. Re-opening of wounds is common in EB and re-confirmation within 7 days of initial assessment was planned. These results are supportive of the primary analysis but were limited by a significant amount of missing data; 33% in treatment and 61% in placebo lacked confirmation after 7 days.

								Setting: April 2017 to June 2020 in 26 countries (Asia, Europe, Americas)
2. Guide, et al. 2022.[2] FDA Clinical Review[13] DB, phase 3, PC, intra-patient RCT NCT04491604 For each patient, 2 wounds were matched based on size, region and appearance and randomized to treatment or placebo	1. Beremagene geperpavec applied topically weekly (at a dose of $4x10^8$ to $1.2x10^9$ plaque forming units depending on baseline wound size) 2. Placebo Duration: 26 weeks Dose was determined by size of the wound at baseline and applied in drops about 1 cm apart; any remaining dose could be applied to up to 4 additional wounds.	Demographics: - Median patient age: 16 years - Recessive dystrophic EB: 97% - Male: 65% - White: 65% - Asian: 19% - American Indian/Alaskan Native: 16% - Hispanic: 52% - Median wound size: 10.6 cm^2 (range 2.3-57.3) <20cm^2: 71% 20 to <40 cm^2: 26% Key Inclusion Criteria: - Patient age ≥ 6 months - Clinical and genetically confirmed dystrophic EB - 2 wounds of similar size, location, appearance Key Exclusion Criteria: - Current immuno- or chemotherapy - Active infection or current or historical squamous cell carcinoma in the treatment area - Active substance use disorder - Skin graft in the past 3 months	ITT: 1. 31 PP: 1. 28 Attrition 1. 3 (10%)	Primary Endpoint: Complete wound healing for at least 2 weeks at ~24 weeks (6 months) 1. 20 (65%) 2. 8 (26%) Difference: 39%; 95% CI 14 to 63%; p=0.012 Secondary Endpoints: Complete wound healing at ~12 weeks (3 months) 1. 21 (68%) 2. 7 (23%) Difference 45%; 95% CI 22 to 69%; p=0.003	NA	Serious AE: 1. 3 (10%) Withdrawal due to AE: 1. 0 Pruritus: 1. 3 (10%) Chills: 1. 3 (10%)	NA	**Risk of Bias (low/high/unclear)**: Selection Bias: UNCLEAR. Primary wound pair matched based on size, region, appearance and randomized to treatment or placebo. Randomization method was not reported. Pairing only controls for known confounding factors, and the similarity between wounds was not reported. Intra-patient design limits ability to evaluate systemic AEs. Wound age was not reported. Performance Bias: LOW. Patients, investigators, site staff and sponsor were blinded with matching placebo (with the same viscosity, appearance and volume). Open-label treatment was allowed for up to 4 additional wounds which may increase risk of potential unblinding. Detection Bias: LOW. Site staff evaluating wound closure were blinded with use of matching placebo. Attrition Bias: LOW. Overall attrition 10% (n=3) with ITT analysis. Missing data were imputed with a mixed model approach assuming data was missing at random and using a worst case scenario strategy with similar magnitude of effect. Reporting Bias: HIGH. Pain scores were reported at multiple time points and other secondary outcomes were not reported. Because the primary outcome was assessed over 2 consecutive weeks, it was evaluated twice for each patient (e.g., at 22 and 24 weeks or 24 and 26 weeks), leading to potential bias if the outcome was not consistent for all 3 weeks. However, the number of wounds in each group that had closed wounds that reopened at 26 weeks was similar between groups.[13] Other Bias: UNCLEAR. Funded by Krystal Biotech. Study sponsor was involved in data collection, monitoring, statistical analyses, and writing the manuscript. **Applicability**: Patient: Data is most applicable to patients with recessive dystrophic EB; only 1 patient had dominant dystrophic EB. Potentially enriched study population; 5 patients (16%) had been enrolled in the phase 1/2 trial for this treatment. Intervention: Cryopreserved drug product is mixed with excipient gel immediately before administration and applied to the wound in drops 1 cm apart each week until wound closure. Five wounds that closed at weeks 22 to 24 re-opened at week 26 indicating that weekly administration is needed to maintain treatment effects. Comparator: Placebo controlled appropriate to determine efficacy. Outcomes: Wound healing is a clinically relevant outcome. Only wounds that remained closed for at least 2 weeks were defined as completely healed. Setting: Three sites in the United States from August 2020 to April 2021.

Tang, et al. 2025.[4] Open-label, phase 3, intra-patient RCT NCT04227106	1. prademagene zamikeracel 2. standard of care Duration: 24 weeks Maximum of 6 wounds could be treated per patient. Non-matched wounds could receive open-label treatment Long-term follow-up is planned for a total of 15 years in NCT05708677	Demographics: - Median patient age: 21 years - Female: 64% - White 91% - Hispanic/Latino: 18% - Median wound duration: 5 years (range 0.5 to 21) - Subtype Severe: 36% Intermediate: 64% Key Inclusion Criteria: - Patient age ≥ 6 years - Clinical and genetically confirmed recessive dystrophic EB - At least 2 chronic wounds present for ≥6 months & ≥ 20 cm^2 - Expression of the amino-terminal NC1 fragment of type VII collagen - No immune response to type VII collagen Key Exclusion Criteria: - Current or historical squamous cell carcinoma - Hypersensivity to vancomycin or amikacin	ITT: 11 enrolled 1. 43 wounds 2. 43 wounds Attrition 0	Primary Endpoint: Proportion of wounds with ≥ 50% healing at week 24 1. 35 (81%) 2. 7 (16%) difference 67%; 95% CI 50 to 89%; p<0·0001 Pain reduction at week 24 (range 0-10 VAS) 1. -3.07 2. -0.90 MD -2.23; 95% CI -3.45 to -0.66; p=0.0002 Secondary Endpoints: Complete wound healing at 12 weeks 1. 6 (14%) 2. 0 (0%) Difference 19%; 95% CI 3 to 42; p=0·032 Complete wound healing at 24 weeks 1. 7 (16%) 2. 0 (0%) Difference 13%; 95% CI 2 to 26; p=0·016	NA	Serious AE: 2 (18%) Withdrawal due to AE: 0 Wound infection Patients 8 (73%) Wounds 1. 12/57 (21%) 2. 4/43 (9%) Procedural pain Patients 6 (55%) Wounds 1. 10/57 (18%) 2. 3/43 (7%)	NA	**Risk of Bias (low/high/unclear)**: Selection Bias: HIGH. Wounds were paired based on chronicity, location and size and wound pairs were randomized to treatment or standard of care with a computer randomization and an electronic data capture system. No allocation concealment. Pairing only accounts for known confounding factors and there is potential for mismatched wounds and selection bias. More control wounds were located on the back. Performance Bias: HIGH. Open-label design without blinding as wounds had visible sheets sutured to wounds. Lack of blinding could have influenced frequency of wound dressing changes impacting healing and incidence of wound infections. Treated wounds were debrided and cauterized under general anesthesia and untreated wounds were not debrided. In the absence of treatment, debridement may increase wound size. Detection Bias: HIGH. Outcomes for wound healing were not conducted by independent or blinded assessors. Open-label design without blinding increases risk of bias particularly for subjective outcomes like pain in which there is typically a large placebo response. Attrition Bias: UNCLEAR. Amount of missing assessments was not reported. ITT analysis with use of last observation carried forward for missing data. Responses for each wound pair were averaged to get a single measure per patient, then averaged for the population. Reporting Bias: LOW. Protocol available. Outcomes reported as prespecified. Other Bias: UNCLEAR. Funded by Abeona therapeutics who was involved in study design, data review, interpretation, analysis and writing the manuscript. **Applicability**: Patient: Applicable to members with recessive dystrophic EB and large, chronic non-healing wounds that have been present for at least 6 months (with a median duration of 5 years). Enrolled patients had no immune response to type VII collagen and were unlikely to form an immune response based on expression of amino-terminal NC1 fragment of type VII collagen. Intervention: Non-blistered skin was collected from two 8 mm punch biopsies. Isolated keratinocytes were transduced with retrovirus carrying COL7A1 gene and cultured to form autologous 40 cm^2 sheets. About 25 days after the biopsy under general anesthesia, treated wounds were debrided and cauterized to fit the size of the 40 cm^2 sheet. Sheets were sutured onto wounds and covered with non-adhesive protective dressings. Patients remained hospitalized for 7 days to protect sheets from pressure and friction. Median number of sheets administered was 6 (range 3-6). Comparator: Supportive standard of care appropriate to determine efficacy.

								Outcomes: Unclear whether 50% improvement in wound healing is clinically significant. Complete wound healing defined as re-epithelization without visible drainage or erosions and with only the presence of minor crusting, confirmed on a subsequent visit. Setting: Two sites in the United States from January 2020 to March 2022.

Abbreviations: AE = adverse events; ARR = absolute risk reduction; DB = double blind; CI = confidence interval; cm2 = square centimeters; EB = epidermolysis bullosa; FDA = Food and Drug Administration; ITT = intention to treat; MD = mean difference; N = number of subjects; NA = not applicable; NNH = number needed to harm; NNT = number needed to treat; PC = placebo controlled; PP = per protocol; RCT = randomized controlled trial; RR = relative risk; VAS = visual analog scale

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Appendix 1: Prescribing Information Highlights

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

----------RECENT MAJOR CHANGES----------

Indications and Usage (1)	09/2025
Dosage and Administration, Dose (2.1)	09/2025

INDICATIONS AND USAGE

VYJUVEK is a herpes-simplex virus type 1 (HSV-1) vector-based gene therapy indicated for the treatment of wounds in adult and pediatric patients 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 (PFU)	Maximum Weekly Volume (mL)*
<3 years old	2×10^9	1
≥ 3 years old	4×10^9	2

PFU=plaque forming unit; mL=milliliter
*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)

- 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 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)

CONTRAINDICATIONS

None. (4)

WARNINGS AND PRECAUTIONS

- Accidental Exposure to VYJUVEK: Avoid direct contact with treated wounds and dressings of treated wounds until the next dressing change, 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: 09/2025

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use ZEVASKYN™ safely and effectively. See full prescribing information for ZEVASKYN.

ZEVASKYN (prademagene zamikeracel), gene-modified cellular sheets, for topical use
Initial U.S. Approval: 2025

----------INDICATIONS AND USAGE----------

ZEVASKYN is an autologous cell sheet-based gene therapy indicated for the treatment of wounds in adult and pediatric patients with recessive dystrophic epidermolysis bullosa (RDEB). (1)

----------DOSAGE AND ADMINISTRATION----------

For autologous topical application on wounds only

- The recommended dose of ZEVASKYN is based on the surface area of the wound(s). One sheet of ZEVASKYN covers an area of 41.25 cm^2. (2.1)
- Up to twelve ZEVASKYN sheets may be manufactured from the patient biopsies and supplied for potential use. (2.1)
- Verify the patient's identity prior to ZEVASKYN application. (2.2)
- See full prescribing information for ZEVASKYN preparation, and administration instructions. (2.2, 2.3)

----------DOSAGE FORMS AND STRENGTHS----------

ZEVASKYN is supplied as a single-dose of up to twelve cellular sheets each measuring 41.25 cm^2 (5.5 cm x 7.5 cm) and consisting of patient's own, viable, gene-modified cells that contain functional copies of the *COL7A1* gene, which express collagen 7 (C7) protein. (3)

----------CONTRAINDICATIONS----------

None.

----------WARNINGS AND PRECAUTIONS----------

- Hypersensitivity reactions to vancomycin, amikacin, or product excipients may occur with ZEVASKYN application. (5.1)
- Retroviral vector (RVV)-mediated insertional oncogenesis may potentially occur after treatment with ZEVASKYN. (5.2)
- Transmission of Infectious Agents may occur because ZEVASKYN is manufactured using human- and bovine-derived reagents. (5.3)

----------ADVERSE REACTIONS----------

The most common adverse reactions (incidence ≥5%) were procedural pain and pruritus. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Abeona Therapeutics Inc. at 1-844-888-2236 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION

Revised: 4/2025

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

FILSUVEZ® (birch triterpenes) topical gel
Initial U.S. Approval: 2023

INDICATIONS AND USAGE

FILSUVEZ topical gel is indicated for the treatment of wounds associated with dystrophic and junctional epidermolysis bullosa in adult and pediatric patients 6 months of age and older. (1)

DOSAGE AND ADMINISTRATION

- Apply a 1 mm layer of FILSUVEZ to the affected wound surface and cover with wound dressing or apply FILSUVEZ directly to dressing so that the topical gel is in direct contact with the wound. Do not rub in the topical gel. (2)
- Apply FILSUVEZ at wound dressing changes until the wound is healed. (2)
- Each tube of FILSUVEZ is for one-time use only. (2)
- For topical use; not for oral, intravaginal, intra-anal, or ophthalmic use. (2)

DOSAGE FORMS AND STRENGTHS

Topical gel: 10% birch triterpenes w/w supplied in 25 mL sterile tubes (3)

CONTRAINDICATIONS

None (4)

WARNINGS AND PRECAUTIONS

- *Hypersensitivity Reactions:* If signs or symptoms of hypersensitivity occur, discontinue use immediately and initiate appropriate therapy. (5.1)

ADVERSE REACTIONS

The most common (incidence ≥2%) adverse reactions are application site reactions. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Amryt Pharmaceuticals DAC at 1-855-303-2347 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling

Revised: 12/2023

Appendix 2. Pharmacology and Pharmacokinetic Properties.

Parameter	Birch triterpenes	Beremagene geperpavec-svdt	Prademagene zamikeracel
Mechanism of Action	Unknown; contains various triterpenes refined from birch bark including betulin (72-88%). Triterepenes are thought to decrease inflammation and enhance keratinocyte migration and differentiation.	HSV-1 viral vector delivers a copy of the COL7A1 gene to the nucleus of both keratinocytes and fibroblasts. This DNA is transcribed to form the collagen type VII protein which is secreted and forms anchoring fibrils that hold the epidermis and dermis together.	A retroviral vector is used to insert a functional COL7A1 gene in skin cells collected from the patient. Modified cells are grown into cellular sheets and applied topically to wounds during surgery.
Distribution and Protein Binding	protein binding >99.9%	N/A	N/A
Elimination	Following topical administration, 68% of people had undetectable betulin blood levels. The average exposure was a mean 12% BSA treated or wound surface area of 0.11m^2 over 90 days.	N/A. No systemic exposure of viral vector following topical application	N/A
Half-Life	N/A	About 61% of patients had skin swabs that were positive for viral vector following treatment. Negative shedding from skin swabs was achieved in 16 of the 19 patients (84%) within six weeks following treatment.	N/A
Metabolism	Not fully characterized; primarily metabolized via CYP3A enzymes	N/A	N/A

Abbreviations: BSA = body surface area; COL7A1 = collagen type VII alpha 1 chain; DNA = deoxyribonucleic acid; HSV = herpes simplex virus; m^2 = square meters; N/A = not applicable; ng/mL= nanograms per milliliter

Appendix 3: Proposed Prior Authorization Criteria

Epidermolysis Bullosa

Goal(s):

- Approve wound treatments in people with epidermolysis bullosa when supported by the evidence.
- Incorporate 2-step review process for drugs on the high-cost drug carve-out list.

Length of Authorization:

- Up to 12 months

Requires PA: pharmacy or provider administered claims

- Birch triterpenes (Filsuvez)
- Beremagene geperpavec (Vyjuvek)
- Prademagene zamikeracel (Zevaskyn)

Covered Populations: FFS and CCO patients beginning 1/1/26

Covered Alternatives:

- Current PMPDP preferred drug list per OAR 410-121-0030 at www.orpdl.org
- Searchable site for Oregon FFS Drug Class listed at www.orpdl.org/drugs/

Table 1. FDA-approved indications and dose

Drug	Maximum dose	Indication	Pathogenic gene mutation
Birch triterpenes (Filsuvez)	1 tube (25 mL) per day	Junctional or dystrophic epidermolysis bullosa	Junctional: LAMA3, LAMB3, LAMC2, ITGB4, ITGA6, COL17A1, ITGA3 Dystrophic: COL7A1
Beremagene geperpavec (Vyjuvek)	1 mL weekly for ages < 3 years 2 mL weekly for ages ≥ 3 years	Dystrophic epidermolysis bullosa	At least one pathogenic mutation in COL7A1
Prademagene zamikeracel (Zevaskyn)	12 sheets per dose	Recessive dystrophic epidermolysis bullosa	2 pathogenic mutations in the COL7A1 gene with recessive inheritance pattern (biallelic)

Approval Criteria	
1. What diagnosis is being treated?	Record ICD10 code.

Approval Criteria		
2. Is the request for a patient with a prior FFS approval for the requested drug?	**Yes:** Go to **Renewal Criteria**	**No:** Go to #3
3. Is this an FDA approved indication (Table 1)?	**Yes**: Go to #4	**No:** Pass to RPh. Deny; medical appropriateness
4. Is there documentation of genetic testing to support the diagnosis?	**Yes:** Go to #5	**No:** Pass to RPh. Deny; medical appropriateness
5. Is the request prescribed by, or in consultation with, a dermatologist or provider with experience in epidermolysis bullosa management or wound care?	**Yes:** Go to #6	**No:** Pass to RPh. Deny; medical appropriateness
6. Is the request for birch triterpenes in a patient with junctional epidermolysis bullosa? Note: In junctional epidermolysis bullosa, people treated with standard of care had better wound healing compared to people who used birch triterpenes.	**Yes:** Pass to RPh. Deny; Refer request to medical director for manual review, assessment of clinical severity, and goals of therapy.	**No:** Go to #7
7. Is there documentation of current open chronic wounds including baseline wound size and estimated duration?	**Yes:** Go to #8	**No:** Pass to RPh. Deny; medical appropriateness
8. Is the request for re-treatment of a wound or location previously treated with prademagene zamikeracel?	**Yes:** Pass to RPh. Deny; Refer request to medical director for manual review, assessment of clinical severity, and goals of therapy.	**No:** Go to #9

Approval Criteria		
9. Is the request for an FDA-approved quantity (Table 1)?	**Yes:** Pass to RPh. Pend; Refer to DMAP for secondary review. Approval durations: Filsuvez for 3 months. Vyjuvek for 3 months. Zevaskyn for up to 12 months. Notify DMAP of approved Zevaskyn requests for care coordination.	**No:** Pass to RPh. Deny; medical appropriateness.

Renewal Criteria		
1. Is the request for an FDA-approved quantity (Table 1)?	**Yes:** Go to #2	**No:** Pass to RPh. Deny; medical appropriateness.
2. Is the request for re-treatment of a wound or location previously treated with prademagene zamikeracel?	**Yes:** Pass to RPh. Deny; Refer request to medical director for manual review of prior therapy, assessment of clinical severity, and goals of therapy.	**No**: Go to #3
3. Is there documentation that treated wound(s) have improved (e.g., decrease in size, closed, or healed)?	**Yes:** Pass to RPh. Refer to DMAP for secondary review. Approval duration: 12 months.	**No:** Pass to RPh. Deny; medical appropriateness