Vyjuvek (beremagene geperpavec-svdt) biological suspension

Policy Number: MC/PC 050
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Instructions for Use

Table of Contents **Page**

Coverage Rationale 1
Applicable Codes 2
Background 2
Clinical Evidence 2
U.S. Food and Drug Administration 3
References 4
Policy History/Revision Information 4
Instructions for Use 4

Related Policies

- n/a

Coverage Rationale

Wound care in dystrophic epidermolysis bullosa

For initial coverage of Vyjuvek 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, the following will be required:

- Diagnosis of dystrophic epidermolysis bullosa (DEB) **and**
- Patient has mutation(s) in the collagen type VII alpha 1 chain (*COL7A1*) gene **and**
- Medication is being used for the treatment of wounds **and**
- Patient is 6 months of age or older **and**
- Medication will be applied by a healthcare professional **and**
- Wound(s) being treated meet all of the following criteria:
    - Adequate granulation tissue
    - Excellent vascularization
    - No evidence of active wound infection in the wound being treated
    - No evidence or history of squamous cell carcinoma in the wound being treated
- Prescribed by or in consultation with a specialist with expertise in wound care

For reauthorization coverage of Vyjuvek 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, the following will be required:

- Documentation of positive clinical response (e.g., decrease in wound size, increase in granulation tissue, complete wound closure) **and**
- Wound(s) being treated meet all of the following criteria:
    - Adequate granulation tissue

- Excellent vascularization
- No evidence of active wound infection in the wound being treated
- No evidence or history of squamous cell carcinoma in the wound being treated

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS Code	Description
J3401	Beremagene geperpavec-svdt for topical administration, containing nominal 5 x 10^9 pfu/ml vector genomes, per 0.1 ml

ICD-10 Code	Description
Q81.2	Epidermolysis bullosa dystrophica

Background

Epidermolysis bullosa (EB) is a rare, genetic disorder characterized by skin fragility, blistering, and wounds due to minimal trauma. EB is a heterogeneous group of disorders that arise from structural anomalies within the epidermis of the skin. Based on skin cleavage location, EB is classified into 4 major groups: epidermolysis bullosa simplex (EBS), junctional epidermolysis bullosa (JEB), Kindler epidermolysis bullosa (KEB), and DEB (Laimer et al 2024). The United States (U.S.) prevalence of EB is 11.07 per 1 million population (Fine 2016).

Dystrophic epidermolysis bullosa (DEB) affects the dermal layer of the skin and nails and typically presents at birth (Has et al 2020, Laimer et al 2024). It is caused by genetic mutations in the *COL7A1* gene that encodes COL7 which is the main component of the anchoring fibrils located below the lamina densa in the epidermal basement membrane zone. Recessive DEB (RDEB) is generally more severe in presentation due to the complete absence of COL7 protein compared to dominant DEB (DDEB); however, there is large phenotypic overlap between the types. Patients with DEB have reduced or little to no functional anchoring fibrils to connect the epidermis to the dermis which results in skin fragility, blistering, scarring, nail changes, and milia formation in response to minimal friction or trauma. COL7 is also expressed in mucous membranes and the upper third of the esophagus so these tissues may also be impacted. Large blisters in the oropharyngeal mucosa or in the esophagus can lead to acute feeding inability in infants or acute esophageal obstruction with dysphagia due to blisters in the esophagus or worsening of esophageal strictures. Both scenarios may require hospitalization (Mellerio et al 2020).

Clinical Evidence

Vyjuvek (beremagene geperpavec-svdt) biological suspension
The efficacy and safety of beremagene geperpavec-svdt (B-VEC) were established in GEM-3, a Phase 3, double-blind (DB), multi-center (MC), placebo-controlled (PC), intra-patient randomized trial of 31 patients aged 6 months of age and older with genetically confirmed DEB (Guide et al 2022). Each patient served as their own control by contributing a primary wound pair to be randomized to receive weekly topical application of B-VEC or placebo. Wounds were matched

in size, appearance, and anatomical locations and were clean, with adequate g
vascularization, and did not appear infected. A total of 30 patients had RDEB a
patients had previously participated in the Phase 1/2 trial but were treated for different wounds in this trial. The primary endpoint was complete wound closure at 6 months, which was defined as complete wound closure at weeks 22 and 24 or weeks 24 and 26. The key secondary endpoints were complete wound closure at 3 months and pain severity.

B-VEC and placebo were applied weekly for 26 weeks in a DB manner. Maximum weekly dosing was based on age. Dosing of each wound was based on wound surface area. Secondary wounds were selected in each patient to receive B-VEC in a controlled, OL manner, if the maximum weekly dosage had not been exceeded by the primary wound pair. Unmatched secondary wounds contributed to the safety evaluation. A total of 62 wounds were randomized to B-VEC or placebo; wound size ranged from 2.3 to 57.3 cm2. Median area of wounds was 10.6 cm2 treated with B-VEC and 10.4 cm2 treated with placebo. Complete wound closure at 6 months was achieved in 20 (65%) wounds treated with B-VEC vs 8 (26%) wounds treated with placebo (difference, 39%, 95% confidence interval [CI], 14 to 63, p = 0.012).

The pain severity endpoint was not interpretable due to the use of different pain scales for patients age < 6 years and aged ≥ 6 years, lack of documentation of pain medication use, and lack of pain medication protocol. Serious adverse effects (AEs) were deemed unrelated to therapy. The most common AEs were pruritus, chills, and squamous cell carcinoma (SCC). All 3 cases of SCC occurred at locations that had not had exposure to B-VEC or placebo. Baseline anti-HSV antibodies were positive in 14/22 (64%) of patients. By week 26, 6/8 (75%) of patients seroconverted against HSV-1. One patient (1/22, 5%) was positive for anti-COL7 antibodies at baseline. By week 26, 13/18 (72%) patients had anti-COL7 antibodies who previously did not at baseline. Treatment response was not associated with baseline HSV-1 serostatus or COL7 seroconversion.

Place in Therapy

Currently, no guidelines address the role of B-VEC in the treatment of wounds in patients with DEB.

Numerous consensus statements recommend comprehensive, multi-disciplinary, supportive care for patients with DEB. Wound care is the cornerstone of supportive care and generally requires various topical applications and dressings. Pain management is also critical. Special care to reduce the risk of further skin trauma and blistering should be implemented. Patients with severe RDEB may require nutritional support through a gastrostomy tube (G-tube). Management of anemia may be required due to chronic inflammation, blood loss from wounds, and malabsorption of iron and other micronutrients. Screening for SCC in patients with EB should be performed on a regular basis beginning in adolescence (*El Hachem et al 2014, Goldschneider et al 2014, Has et al 2021, Liy-Wong et al 2023, Murrell 2024*).

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

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.

References

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Policy History/Revision Information

Date	Summary of Changes
04/17/2024	Approved by OptumRx P&T Committee
8/21/2025	Annual Review. Updated references

Instructions for Use

This Medical Benefit Drug Policy provides assistance in interpreting standard benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard plan. In the event of a conflict, the member specific benefit plan document governs. Before using this policy, please check the member specific benefit plan document and any applicable federal or state mandates. The insurance reserves the right to modify its Policies and Guidelines as necessary. This Medical Benefit Drug Policy is provided for informational purposes. It does not constitute medical advice.

OptumRx may also use tools developed by third parties to assist us in administering health benefits. OptumRx Medical Benefit Drug Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.

Archived Policy Versions (Internal Only)

Effective Date	Policy Number	Policy Title
mm/dd/yyyy – mm/dd/yyyy	######	Title of Policy Hyperlinked to KL or Other Internal Location

Nondiscrimination & Language Access Policy

Discrimination is Against the Law. Aspirus Health Plan, Inc. complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability, or sex, (including sex characteristics, including intersex traits; pregnancy or related conditions; sexual orientation, gender identity and sex stereotypes), consistent with the scope of sex discrimination described at 45 CFR § 92.101(a)(2). Aspirus Health Plan, Inc. does not exclude people or treat them less favorably because of race, color, national origin, age, disability, or sex.

Aspirus Health Plan, Inc.:
Provides people with disabilities reasonable modifications and free appropriate auxiliary aids and services to communicate effectively with us, such as:

- Qualified sign language interpreters.
- Written information in other formats (large print, audio, accessible electronic formats, other formats).

Provides free language assistance services to people whose primary language is not English, which may include:

- Qualified interpreters.
- Information written in other languages.

If *you* need reasonable modifications, appropriate auxiliary aids and services, or language assistance services, contact the Nondiscrimination Grievance Coordinator at the address, phone number, fax number, or email address below.

If *you* believe that Aspirus Health Plan, Inc. has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability, or sex, *you* can file a *grievance* with:

Nondiscrimination Grievance Coordinator
Aspirus Health Plan, Inc.
PO Box 1890
Southampton, PA 18966-9998
Phone: 1-866-631-5404 (TTY: 711)
Fax: 763-847-4010
Email: customerservice@aspirushealthplan.com

You can file a *grievance* in person or by mail, fax, or email. If *you* need help filing a *grievance*, the Nondiscrimination Grievance Coordinator is available to help *you*.

You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights, electronically through the Office for Civil Rights Complaint Portal, available at https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at:

U.S. Department of Health and Human Services
200 Independence Avenue, SW
Room 509F, HHH Building
Washington, D.C. 20201
1.800.368.1019, 800.537.7697 (TDD)

Complaint forms are available at http://www.hhs.gov/ocr/office/file/index.html. This notice is available at Aspirus Health Plan, Inc.'s website: https://aspirushealthplan.com/webdocs/70021-AHP-NonDiscrim_Lang-Assist-Notice.pdf.

Language Assistance Services

Albanian: KUJDES: Nëse flitni shqip, për ju ka në dispozicion shërbime të asistencës gjuhësore, pa pagesë.Telefononi në 1-800-332-6501 (TTY: 711).

Arabic تنبيه: إذا كنت تتحدث اللغة العربية، فإن خدمات المساعدة اللغوية متاحة لك مجاناً. اتصل بن اعلى رقم الهاتف1-800-332-6501(رقم هاتف الصم والبك : 711)

French: ATTENTION: Si vous parlez français, des services d'aide linguistique vous sont proposés gratuitement. Appelez le 1-800-332-6501 (ATS: 711).

German: ACHTUNG: Wenn Sie Deutsch sprechen, stehen Ihnen kostenlos sprachliche Hilfsdienstleistungen zurVerfügung. Rufnummer: 1-800-332-6501 (TTY: 711).

Hindi: _यान द_: य_द आप ि हंदी बोलते ह_ तो आपके ि लए मु_त म_ भाषा सहायता सेवाएं उपल_ध ह_।1-800-332-6501 (TTY: 711) पर कॉल कर_।

Hmong: LUS CEEV: Yog tias koj hais lus Hmoob, cov kev pab txog lus, muaj kev pab dawb rau koj. Hu rau 1-800-332-6501 (TTY: 711).

Korean: 주의: 한국어를 사용하시는 경우, 언어 지원 서비스를 무료로 이용하실 수 있습니다.1-800-332-6501 (TTY: 711)번으로 전화해 주십시오.

Polish: UWAGA: Jeżeli mówisz po polsku, możesz skorzystać z bezpłatnej pomocy językowej. Zadzwoń pod numer1-800-332-6501 (TTY: 711).

Russian: ВНИМАНИЕ: Если вы говорите на русском языке, то вам доступны бесплатные услуги перевода.Звоните 1-800-332-6501 (телетайп: 711).

Spanish: ATENCIÓN: si habla español, tiene a su disposición servicios gratuitos de asistencia lingüística. Llame al1-800-332-6501 (TTY: 711).

Tagalog: PAUNAWA: Kung nagsasalita ka ng Tagalog, maaari kang gumamit ng mga serbisyo ng tulong sa wika nangwalang bayad. Tumawag sa 1-800-332-6501 (TTY: 711).

Traditional Chinese: 注意：如果您使用繁體中文， 您可以免費獲得語言援助服務。請 致電 1-800-332-6501 (TTY: 711)

Vietnamese: CHÚ Ý: Nếu bạn nói Tiếng Việt, có các dịch vụ hỗ trợ ngôn ngữ miễn phí dành cho bạn. Gọi số 1-800-332-6501 (TTY: 711).

Pennsylvania Dutch: Wann du Deitsch (Pennsylvania German / Dutch) schwetzscht, kannscht du mitaus Koschte ebbergricke, ass dihr helft mit die englisch Schprooch. Ruf selli Nummer uff: Call 1-800-332-6501 (TTY: 711).

Lao: ໂປດຊາບ: ຖ້າວ່າ ທ່ານເວົ້າພາສາ ລາວ, ການບໍລິການຊ່ວຍເຫຼືອດ້ານພາສາ,ໂດຍບໍ່ເສັງຄ່າ, ແມ່ນມີພ້ອມໃຫ້ທ່ານ. ໂທຣ 1-800-332-6501 (TTY: 711).

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