Preemptive policy: This is a P&T approved policy and can be used after the drug is FDA approved until it is superseded by an updated policy

CENTENE® Corporation

# Clinical Policy: Prademagene Zamikeracel (EB-101)

Reference Number: CP.PHAR.609
Effective Date: FDA Approval Date
Last Review Date: 02.23
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

**See Important Reminder at the end of this policy for important regulatory and legal information.**



## Description

Prademagene zamikeracel (EB-101®/™) is a COL7A1-directed genetically modified autologous keratinocyte cell-therapy.

## FDA Approved Indication(s) [Pending]

EB-101 is indicated for the treatment of adults and children aged 6 years and older with recessive dystrophic epidermolysis bullosa (RDEB).

Limitation(s) of use: [XXX]

## Policy/Criteria

*Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.*

It is the policy of health plans affiliated with Centene Corporation® that EB-101 is **medically necessary** when the following criteria are met:

### I. Initial Approval Criteria*

**Criteria will mirror the clinical information from the prescribing information once FDA-approved*

**A. Recessive Dystrophic Epidermolysis Bullosa** (must meet all)**:**

1. Diagnosis of RDEB as evidenced by two copies of positive COL7A1 gene mutation by one of the following (a, b, or c; *see Appendix E*):*
   a. Immunofluorescence mapping;
   b. Transmission electron microscopy;
   c. Antigenic mapping;
2. Prescribed by or in consultation with a geneticist, dermatologist, or histopathologist;
3. Age ≥ 6 years;*
4. Provider attestation that member is concomitantly receiving standard of care preventative or treatment therapies for wound care (e.g., polymeric membrane, super-absorbent dressings, soft-silicone foam, enzyme alginogel, protease; *see Appendix F)*;
5. Wound site must be a stage 2 chronic wound with an area of at least 20 $cm^2$ and present for at least 6 months (*see Appendix D)*;
6. Member has no evidence of immune response to COL7 as evidenced by immunofluorescence (e.g., member is not positive for anti-COL7 antibodies at baseline);

7. Member does not have a history of squamous cell carcinoma in the area that will undergo treatment;
8. Dose does not exceed 6 sheets.*

**Approval duration: 3 months *(1 application only)***

**B. Other diagnoses/indications** (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

## II. Continued Therapy*

**Criteria will mirror the clinical information from the prescribing information once FDA-approved*

**A. Recessive Dystrophic Epidermolysis Bullosa**

1. Continued therapy will not be authorized as EB-101 is indicated to be a one-time surgical application.

**Approval duration: Not applicable**

**B. Other diagnoses/indications** (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 2 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

**III. Diagnoses/Indications for which coverage is NOT authorized:**

**A.** Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

**IV. Appendices/General Information**

*Appendix A: Abbreviation/Acronym Key*

DDEB: dominant dystrophic epidermolysis bullosa
DEB: dystrophic epidermolysis bullosa
EB: epidermolysis bullosa
FDA: Food and Drug Administration
RDEB: recessive dystrophic epidermolysis bullosa

*Appendix B: Therapeutic Alternatives*

Not applicable

*Appendix C: Contraindications/Boxed Warnings [Pending]*

- Contraindication(s): pending
- Boxed warning(s): pending

*Appendix D: General Information*

- RDEB is an ultra-rare epidermolysis bullosa (EB) subtype caused by mutations in the COL7A1 gene.
- Inherited EB has four main classifications relating to the affected layer of skin: EB simplex, junctional EB, dystrophic EB, and Kindler's EB.
- Wound staging:
  - Stage 1: Unbroken skin
  - Stage 2: Partial-thickness skin loss with exposed dermis
  - Stage 3: Full-thickness skin loss with exposed adipose
  - Stage 4: Full-thickness skin loss and tissue loss

*Appendix E: Diagnosis Information*

- Per 2017 Best Practice Guidelines for Skin and Wound Care in Epidermolysis Bullosa, definitive diagnosis is most commonly made from analysis of a skin biopsy using positive immunofluorescence, antigenic mapping, and transmission electron microscopy. Due to rarity of expertise and facilities, diagnosis is generally made using immunofluorescence and antigen mapping.

*Appendix F: Recommended Wound Care for DEB*

- Wounds should be dressed with nonadherent silicone dressings, foam dressings that absorb exudates, and nonadherent silicone-based tape. Diluted bleach baths or compresses, topical antiseptics, and topic antibiotics are used as preventative measures against bacterial infections.
- Standard of Care for wound care per 2017 Best Practice Guidelines for skin and wound care in epidermolysis bullosa:

  - First choice of dressing when available:
    - Chronic or acute wounds – PolyMem
    - Super-absorbent – Cutimed Siltec
- Recommended dressings for DEB per 2017 Best Practice Guidelines for skin and wound care in epidermolysis bullosa:

| Dressing Type | Brand | Indication/ Function | Contraindication/ Comments | Wear Time |
|---|---|---|---|---|
| Polymeric membrane | PolyMem | • Where cleansing is required<br>• Chronic wounds | • Stimulates high levels of exudate<br>• Distinct smell does not necessarily indicate infection<br>• Can still be difficult to retain on vertical surfaces | • Change frequently until exudate reduces |
| Super-absorbent dressings | • Cutimed Siltec<br>• Sorbion Sachet S<br>• Filvasorb/ Vilwasorb Pro<br>• Kerramax Care | • High exudate levels | • Can be cut between super-absorbent crystals, which appear in rows (as opposed to cutting across the crystal lattice) | |
| Soft silicone mesh | • Mepitel<br>• Mepitel One<br>• Adaptic Touch<br>• Cuticell Contact | • Moist wound<br>• Contact layer | | |
| Lipido-colloid | • Urgo Tul | • Moist wound, drier wounds and protection of vulnerable healed areas<br>• Used as an alternative to soft silicon (see above) in the presence of over-granulation | • Where retention is difficult (e.g., vertical surfaces) | |
| Soft silicone foam | • Mepilex<br>• Mepilex Lite<br>• Mepilex Transfer | • Absorption of exudate<br>• Protection | • Over-heating<br>• May need to apply over recommended | |

| Dressing Type | Brand | Indication/ Function | Contraindication/ Comments | Wear Time |
|---|---|---|---|---|
| | | • Lightly exuding wounds<br>• To transfer exudate to absorbent dressing<br>• Where conformability is required (e.g., digits, axillae) | atraumatic primary dressing | |
| Foam | • Allevyn<br>• UrgoTul Absorb<br>• Aquacel Foam | • Absorption and protection | • May adhere if placed directly on wound bed, use alternative contact layer | |
| Bordered foam dressings | • Mepilex Border/ Mepliex Border Lite<br>• Biatain Silicone Border/ Biatain Border Lite<br>• Allevyn Gentle Border<br>• Allevyn Border Lite<br>• Kerrafoam<br>• UrgoTul Absorb Border | • Isolated wounds<br>• DDEB and mild RDEB | • Bordered dressings may require removal with SMAR to avoid skin stripping<br>• May require primary contact layer<br>• Poor absorption of highly viscous exudate | • Up to 4 days depending on personal choice |
| Keratin | • Keragel | • Chronic wounds | • Dilute with blend emollient if stinging occurs | • Reapply with dressing changes |



- First choice of treatment when available: PolyMem, Flaminal Hydro/Forte
- Treatment of choice for chronic wounds based on consensus opinion per 2017 Best Practice Guidelines for skin and wound care in epidermolysis bullosa:

| Dressing Type | Brand | Indications | Contraindication/ Comments | Wear Time |
|---|---|---|---|---|
| Polymeric membrane | • PolyMem<br>• PolyMem Max | • Infected wounds | • Can provide initial increase in exudate resulting in further skin | • Change when wet to avoid hypothermia |

| Dressing Type | Brand | Indications | Contraindication/ Comments | Wear Time |
|---|---|---|---|---|
| | • PolyMem WIC (under a secondary dressing or further layer of PolyMem) | • Recalitrant wounds | damage if not properly controlled<br>• Distinct smell does not necessarily indicate infection<br>• Protect periwound skin | |
| Enzyme alginogel | • Flaminal Hydro<br>• Flaminal Forte | • Low exudate<br>• High exudate | • Debrides, de-sloughs and antimicrobial<br>• Has some action in modulating excess proteases<br>• Can be used on all wounds apart from third degree burns<br>• Do not use if patient has sensitivity to alginates or polyethylene glycol | • Re-apply at each dressing change at least 2mm thick |
| Honey | | • Sensitive wounds | • Can cause transient stinging or pain due to its acidity and high osmotic 'pull'<br>• In turn this will contribute to high levels of exudate | |
| Protease modulator | • UrgoTul Start range<br>• Promogran<br>• Promogran Prisma (with silver) | • When excess protease may be present | • Promogran/Promogran Prisma may cause initial transient stinging<br>• Excess product cannot be saved once opened as it degrades on contact with air<br>• A secondary dressing required and the product may provoke initial heavy exudate | • Frequent dressing changes may be required to avoid maceration |



## V. Dosage and Administration [Pending]

| Indication | Dosing Regimen | Maximum Dose |
|---|---|---|
| RDEB* | Pending | Pending |

## VI. Product Availability [Pending]

Pending*

## VII. References

1. Denyer J, Pillay E, Clapham J. Best practice guidelines for skin and wound care in epidermolysis bullosa. An International Consensus. Wounds International, 2017.
2. Mariath LM, Santin JT, Schuler-Faccini L, Kiszewski AE. Inherited epidermolysis bullosa: update on the clinicaland genetic aspects. An Bras Dermatol. 2020;95:551---69.
3. ClinicalTrials.gov. Phase 3, open-label clinical trial of EB-101 for the treatment of recessive dystrophic epidermolysis bullosa (RDEB). Available at: https://clinicaltrials.gov/ct2/show/NCT04227106. Accessed November 23, 2022.

| Reviews, Revisions, and Approvals | Date | P&T Approval Date |
|---|---|---|
| Policy created pre-emptively. | 12.06.22 | 02.23 |

**Important Reminder**

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

**Note:**
**For Medicaid members**, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.