Clinical Policy Bulletin: Palifermin (Kepivance)

Number: 0851

Policy

Aetna considers palifermin (Kepivance) medically necessary to prevent and treat severe oral mucositis in members with hematologic malignancies undergoing high-dose chemotherapy requiring hematopoietic cell transplantation using preparative regimens predicted to result in WHO grade 3 or 4 oral mucositis in the majority of patients (see Table 4 in appendix).

Aetna considers palifermin experimental and investigational for gastrointestinal mucositis and all other indications.

Background

Effective oral hygiene, appropriate analgesia, oral cryotherapy, infection management and parenteral nutrition are considered to be standard of care for oral mucositis.

Kepivance has been approved by the FDA to decrease the incidence and duration of severe oral mucositis in patients with hematologic malignancies receiving myelotoxic therapy requiring hematopoietic stem cell support. Kepivance is indicated as supportive care for preparative regimens predicted to result in ~WHO Grade 3 mucositis in the majority of patients. The FDA labeling states that the safety and efficacy of Kepivance have not been established in patients with non-hematologic malignancies. The labeling states that Kepivance is not recommended for use with melphalan 200 mg/m2 as a conditioning regimen.

Guidelines from the European Society for Medical Oncology (Peterson, et al., 2011) state that palifermin is recommended in a dose of 60 µg/kg/day for 3 days before conditioning treatment and for 3 days posttransplant for the prevention of oral mucositis in patients with hematological malignancies.
receiving high-dose chemotherapy and total body irradiation with autologous stem cell transplantation.

Guidelines from the American Society for Clinical Oncology (ASCO, 2008) state that palifermin is recommended for use in patients undergoing autologous stem-cell transplantation for a hematologic malignancy with a total body irradiation conditioning regimen to decrease the incidence of severe mucositis. The ASCO guidelines state that there are insufficient data to recommend the routine use of palifermin for patients undergoing autologous stem-cell transplantation for a hematologic malignancy where the conditioning regimen is chemotherapy only. The ASCO guidelines also state that palifermin may be considered for use in patients undergoing myeloablative allogeneic hematopoietic stem-cell transplantation with a total body irradiation–based conditioning regimen; there are insufficient data to recommend its use in myeloablative conditioning regimens consisting of chemotherapy alone in this setting. The ASCO guidelines state that palifermin should be administered intravenously at 60 g/kg daily for 3 days preceding the start of the conditioning regimen and 60 g/kg daily for 3 days beginning on the day of stem-cell infusion; it should not be administered within 24 hours of the initiation of the conditioning regimen.

ASCO guidelines state that there are insufficient data to recommend the use of palifermin in the non–stem-cell transplantation setting, or for use in the treatment of solid tumors.

Appendix

Table 1: Routine Oral Hygiene Care

Toothbrushing. [Note: Electric and ultrasonic toothbrushes are acceptable if the patient is capable of using them without causing trauma.]

Soft nylon-bristled brush (2-3 rows).

Brush 2 to 3 times daily with Bass sulcular scrub method.
Rinse frequently.
Foam toothbrushes:

Use only when use of a regular toothbrush is not feasible.
Use with antimicrobial rinses when possible.
Brush teeth and mucosal surfaces 2 to 3 times a day.
Rinse frequently.

Dentifrice:

Patient preference as tolerated.
Fluoride recommended.
Use 0.9% saline or water if toothpaste causes irritation.

Flossing:

Once daily.
Atraumatic technique with modifications as needed.

Bland Rinses:

Varieties:
0.9% saline.  
Sodium bicarbonate solution.  

0.9% saline plus sodium bicarbonate solution.  

Use 8 to 12 oz of rinse, hold and expectorate; repeat every 2 to 4 hours or as needed for pain.  

Fluoride:  
1.1% neutral sodium fluoride gel.  
0.4% stannous fluoride gel. Brush on gel for 2 to 3 minutes. Expectorate and rinse mouth gently.  

Apply once a day.  

Topical antimicrobial rinses:  
0.12% to 0.2% chlorhexidine oral rinse.  
Povidone iodine oral rinse.  
Rinse, hold 1 to 2 minutes, expectorate.  

Repeat 2 to 4 times a day depending on severity of periodontal disease.  

**Guidelines for Management of Dentures and Orthodontic Appliances in Patients Receiving High-Dose Cancer Therapy**  
Minimize denture use during first 3 to 4 weeks posttransplant.  
Wear dentures only when eating.  
Discontinue use at all other times.  
Clean twice a day with a soft brush and rinse well.  
Soak in antimicrobial solutions when not being worn.  
Perform routine oral mucosal care procedures 3 to 4 times a day with the oral appliances out of the mouth.  
Leave appliances out of mouth when sleeping and during periods of significant mouth soreness.  
Dentures may be used to hold medications needed for oral care (e.g., antifungals).  
Discontinue use of removable  
Discontinue use of removable appliances until oral mucositis has healed.  
Remove orthodontic appliances (e.g., brackets, wires, retainers) prior to conditioning.  

**Table 2: Mucositis Management**  

**Table 3: Summary of Clinical Practice Guidelines for Care of Patients with Oral Mucositis**  

**Basic Oral Care and Good Clinical Practices**
I. The panel suggests multidisciplinary development and evaluation of oral care protocols, and patient and staff education in the use of such protocols to reduce the severity of oral mucositis from chemotherapy and/or radiation therapy (Level III evidence, grade B suggestion). As part of the protocols, the panel suggests the use of a soft toothbrush that is replaced on a regular basis. Elements of good clinical practice should include the use of validated tools to regularly assess oral pain and oral cavity health. The inclusion of dental professionals is vital throughout the treatment and follow-up phases.

II. The panel recommends patient-controlled analgesia with morphine as the treatment of choice for oral mucositis pain in patients undergoing hematopoietic stem cell transplantation (HSCT) (Level 1 evidence, grade A recommendation). Regular oral pain assessment using validated instruments for self-reporting is essential.

Radiotherapy: Prevention

I. The panel recommends the use of midline radiation blocks and 3-dimensional radiation treatment to reduce mucosal injury. (Level 2 evidence, grade B recommendation)

II. The panel recommends benzydamine for prevention of radiation-induced mucositis in patients with head and neck cancer receiving moderate-dose radiation therapy. (Level I evidence, grade A recommendation)

III. The panel recommends that chlorhexidine not be used to prevent oral mucositis in patients with solid tumors of the head and neck who are undergoing radiotherapy. (Level II evidence, grade B recommendation)

IV. The panel recommends that antimicrobial lozenges not be used for the prevention of radiation-induced oral mucositis. (Level II evidence, grade B recommendation)

Radiotherapy: Treatment

I. The panel recommends that sucralfate not be used for the treatment of radiation-induced oral mucositis. (Level II evidence, grade A recommendation)

Standard-Dose Chemotherapy Prevention

I. The panel recommends that patients receiving bolus 5-fluorouracil (5-FU) chemotherapy undergo 30 minutes of oral cryotherapy to prevent oral mucositis. (Level II evidence, grade A recommendation)

II. The panel suggests the use of 20 to 30 minutes of oral cryotherapy to decrease mucositis in patients treated with bolus doses of edatrexate. (Level IV evidence, grade B suggestion)

III. The panel recommends that acyclovir and its analogues not be used routinely to prevent mucositis. (Level II evidence, grade B recommendation)

Standard-Dose Chemotherapy: Treatment

I. The panel suggests that chlorhexidine not be used to treat established oral mucositis. (Level III evidence, grade C recommendation)

High-Dose Chemotherapy With or Without Total Body Irradiation Plus HCST: Prevention

I. In patients with hematologic malignancies who are receiving high-dose chemotherapy and total body irradiation with autologous stem cell transplantation, the panel recommends the use of keratinocyte growth factor-1 (palifermin) in a dose of 60 micrograms/kg per day for 3 days prior to conditioning treatment and for 3 days posttransplantation for the prevention of oral mucositis. (Level 1 evidence, grade A recommendation)
II. The panel suggests the use of cryotherapy to prevent oral mucositis in patients receiving high-dose melphalan. (Level II evidence, grade A recommendation)

III. The panel does not recommend the use of pentoxifylline to prevent mucositis in patients undergoing HSCT. (Level II evidence, grade B recommendation)

IV. The panel suggests that granulocyte macrophage colony-stimulating factor (GM-CSF) mouthwashes not be used for the prevention of oral mucositis in patients undergoing HSCT. (Level II evidence, grade C recommendation)

V. The panel suggests the use of low-level laser therapy (LLLT) to reduce the incidence of oral mucositis and its associated pain in patients receiving high-dose chemotherapy or chemoradiotherapy before HSCT if the treatment center is able to support the necessary technology and training, because LLLT requires expensive equipment and specialized training. Because of interoperator variability, clinical trials are difficult to conduct, and their results are difficult to compare; nevertheless, the panel is encouraged by the accumulating evidence in support of LLLT. (Level II evidence, grade B recommendation)

Key: HSCT: hematopoietic stem cell transplantation; 5-FU: 5-fluorouracil; TBI: total-body irradiation; LLLT: low-level laser therapy.

Table 4: WHO Classification of Oral Mucositis

<table>
<thead>
<tr>
<th>Grade 0</th>
<th>No oral mucositis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1</td>
<td>Soreness +/- erythema</td>
</tr>
<tr>
<td>Grade 2</td>
<td>Erythema and ulcers</td>
</tr>
<tr>
<td>Grade 3</td>
<td>Extensive erythema, ulcers and inability to swallow solid food</td>
</tr>
<tr>
<td>Grade 4</td>
<td>Mucositis that prevents any form of alimentation, including swallowing liquids</td>
</tr>
</tbody>
</table>

Bland Rinses:

- 0.9% saline solution
- Sodium bicarbonate solution
- 0.9% saline/sodium bicarbonate solution.

Topical anesthetics:

- Lidocaine: viscous, ointments, sprays.
- Benzocaine: sprays, gels.
- 0.5% or 1.0% dyclonine hydrochloride (HCl).
- Diphenhydramine solution.

Mucosal coating agents:

- Amphojel.
- Kapectate.
- Hydroxypropyl methylcellulose film-forming agents (e.g., Zilactin).
- Cyanoacrylate mucoadherent film.

Analgesics:

- Benzydamine HCl topical rinse. (not approved in the United States)
Opioid drugs: oral, intravenous (IV) (e.g., bolus, continuous infusion, patient-controlled analgesia [PCA]), patches, transmucosal.

CPT Codes / HCPCS Codes / ICD-9 Codes

CPT codes covered if selection criteria are met:

38240 Hematopoietic progenitor cell (HPC); allogeneic transplantation per donor
38241 autologous transplantation
38242 HPC boost

HCPCS codes covered if selection criteria are met:

J2425 Injection, palifermin, 50 micrograms

ICD-9 codes covered if selection criteria are met:

528.01 Mucositis (ulcerative) due to antineoplastic therapy

The above policy is based on the following references:


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