IOWA | Health and Human Services

PDL DRUG REVIEW

Proprietary Name: Eohilia®
Common Name: budesonide oral suspension
PDL Category: Glucocorticoids

Comparable Products	Preferred Drug List Status
Dupixent (dupilumab)	Preferred with Conditions
Fluticasone	Preferred

Pharmacology/Usage: Budesonide, the active ingredient of Eohilia®, is a synthetic corticosteroid; it is an anti-inflammatory corticosteroid and has a high glucocorticoid effect and a weak mineralocorticoid effect. Corticosteroids have a wide range of inhibitory activities against multiple cell types (e.g., mast cells, eosinophils, neutrophils, macrophages, and lymphocytes) and mediators (e.g., histamine, eicosanoids, leukocytes, and cytokines) involved in allergic inflammation. However, the exact mechanism of action for its approved indication is not known.

Indication: For 12 weeks of treatment in adult and pediatric patients 11 years of age and older with eosinophilic esophagitis (EoE). A limitation of use includes that Eohilia® has not been shown to be safe and effective for the treatment of EoE for longer than 12 weeks.

There is no pregnancy category for this medication; however, the risk summary indicates that available data from studies with oral budesonide use in pregnant women have not identified a drug-associated risk of major birth defects, miscarriage, or other adverse maternal outcomes. Infants exposed to in-utero corticosteroids, including Eohilia®, are at risk for hypoadrenalism. Based on animal data, advise pregnant women of the potential risk to a fetus. The safety and efficacy of use in the pediatric population less than 11 years of age have not been established.

Dosage Form: Oral Suspension: 2mg/10ml, with cherry flavoring. Available as single-dose stick packs.

Recommended Dosage: The recommended dosage is 2mg PO BID for 12 weeks. Do not take with food or liquid at the time of ingestion. Wait for at least 30 minutes to eat or drink after taking Eohilia®. Administer Eohilia® as follows:

- Do not mix with food or liquid.
- Shake the stick pack for at least 10 seconds prior to opening.
- Squeeze the stick pack from the bottom to the top directly into the mouth. Repeat 2 to 3 times until the Eohilia® stick pack is empty.
- Swallow all the Eohilia® suspension.
- Do not eat or drink for 30 minutes after taking Eohilia®. After 30 minutes, rinse mouth with water and spit out the contents without swallowing.
- Avoid consumption of grapefruit juice for the duration of therapy with Eohilia®.

Patients with moderate to severe hepatic impairment could be at an increased risk of hypercorticism and adrenal axis suppression due to an increased systemic exposure to budesonide. Use is not recommended in patients with severe hepatic impairment. Dosage adjustments are not recommended in patients with mild or moderate hepatic impairment; however, in patients with moderate hepatic impairment, monitor for signs and/or symptoms of hypercorticism.

Drug Interactions: Budesonide is a substrate for CYP3A4. Concomitant use of budesonide with CYP3A4 inhibitors (e.g., ketoconazole, itraconazole, ritonavir, indinavir, saquinavir, erythromycin, cyclosporine, grapefruit juice) can increase systemic budesonide concentrations. Avoid concomitant use of CYP3A4 inhibitors, including grapefruit juice, with Eohilia®.

Box Warning: There is no box warning listed with this product.

Common Adverse Drug Reactions: *Listed % incidence for adverse drug reactions= reported % incidence for drug (Eohilia®) minus reported % incidence for placebo. Please note that an incidence of 0% means the incidence was the same as or less than placebo.* The most frequently reported adverse events included respiratory tract infection (2%), gastrointestinal mucosal candidiasis (6%), headache (3%), gastroenteritis (2%), throat irritation (1%), adrenal suppression (2%), and erosive esophagitis (2%).

Systemic effects, such as hypercorticism and adrenal axis suppression, may occur with use of corticosteroids, including Eohilia®. Monitor patients for signs and symptoms of hypercorticism and adrenal axis suppression and consider reducing the dosage of Eohilia®. In addition, corticosteroids, including Eohilia®, can reduce the response of the hypothalamus-pituitary-adrenal (HPA) axis to stress. In situations where patients are subject to trauma, surgery, infection, or other stress situations, supplementation with a systemic corticosteroid is recommended.

Corticosteroids, including Eohilia®, suppress the immune system and increase the risk of infection with any pathogen, including viral, bacterial, fungal, protozoan, or helminthic pathogens. Monitor patients for the development of infection and consider discontinuation of Eohilia® if the patient develops an infection while on treatment. Refer to the prescribing information for additional information regarding specific infections.

Erosive esophagitis occurred in subjects who received Eohilia® in a 12-week clinical trial. Advise patients or caregivers to report new onset or worsening signs or symptoms of erosive esophagitis to their healthcare provider.

Use of corticosteroids may cause a reduction of growth velocity in pediatric patients. Monitor the growth of pediatric patients on Eohilia®.

Monitor patients who are transferred from corticosteroid treatment with high systemic effects to corticosteroids with lower systemic availability, such as Eohilia®, since symptoms attributed to withdrawal of steroid therapy, including those of acute adrenal axis suppression or benign intracranial hypertension, may develop.

Monitor patients with hypertension, diabetes mellitus, osteoporosis, peptic ulcer, glaucoma, or cataracts, or with a family history of diabetes or glaucoma, or with any other condition where corticosteroids may have unwanted effects.

Kaposi's sarcoma has been reported to occur in patients receiving corticosteroid therapy, most often for chronic conditions. Discontinuation of corticosteroids may result in clinical improvement of Kaposi's sarcoma.

Contraindications: In patients with hypersensitivity to budesonide.

Manufacturer: Takeda Pharmaceuticals America, Inc.

Analysis: The safety and efficacy of Eohilia® were assessed in two multicenter, randomized, double-blind, placebo-controlled, parallel-group studies (Study 1 and Study 2). Eligible subjects had esophageal inflammation, defined as ≥15 eosinophils/high-power field (hpf) from at least 2 levels of the esophagus at baseline following a treatment course of a proton pump inhibitor (PPI) either prior to or during screening and at least 4 days of dysphagia as measured by the Dysphagia Symptom Questionnaire (DSQ) over a 2-week period prior to randomization. Concomitant use of stable doses of inhaled or intranasal steroids (for conditions other than EoE), PPIs, H2-receptor antagonists, antacids, antihistamines or anti-leukotrienes, and maintenance immunotherapy was allowed.

In Study 1, subjects were enrolled after maintaining a stable diet for at least 3 months prior to screening and were instructed to maintain a stable diet throughout the study. In Study 2, subjects were instructed to maintain a stable diet throughout the study. In both studies, subjects were instructed to not eat or drink for 30 minutes after taking the drug and then to rinse the mouth with water and spit out the contents without swallowing prior to resuming normal oral intake.

In Study 1, subjects (N=318; 277 adults and 41 pediatrics) were randomized and received at least one dose of study drug. The mean age of the study population was 34 years (range 11 to 56 years), while 66% were male and 95% were white. Greater than 80% were on concomitant PPI therapy, and the mean DSQ combined scores at baseline were 30.3 and 30.4 in the Eohilia® and placebo groups, respectively.

In Study 2, subjects (N=92; 58 adults and 34 pediatrics) were randomized and received at least one dose of study drug (Eohilia® or placebo). The mean age of the study population was 22 years (range 11 to 42 years), while 68% were male and 95% were white. Greater than 65% of the subjects were on concomitant PPI therapy, and the mean DSQ combined scores at baseline were 30.7 and 29.0 in the Eohilia® and placebo groups, respectively.

Both studies assessed efficacy endpoints of histologic remission (defined as a peak eosinophil count of ≤6/hpf across all available esophageal levels) and the absolute change from baseline in subject-reported DSQ combined score after 12 weeks of treatment. Efficacy results are presented in the table below, which was adapted from the prescribing information.

	Study 1			Study 2		
	Eohilia® BID (N=213)	Placebo (N=105)	Treatment difference	Eohilia® BID (N=50)	Placebo (N=42)	Treatment difference
Proportion achieving histological remission[1]	53.1%	1%	52.4%	38%	2.4%	35.8%
NNT *calculated by CHC*	2			3		
Absolute change from baseline in DSQ combined score, LS mean	-10.2	-6.5	-3.7	-14.5	-5.9	-8.6

[1]peak esophageal intraepithelial eosinophil count ≤6eos/hpf LS-least square

During the last 2 weeks of the 12-week treatment periods in Study 1 and Study 2, a greater proportion of subjects randomized to Eohilia® experienced no dysphagia or only experienced dysphagia that 'got better or cleared up on its own' compared to placebo, as measured by the subject-reported DSQ.

After completing Study 1, 48 subjects from the Eohilia® 2mg treatment arm entered a double-blind randomized withdrawal extension study. These subjects received Eohilia® 2mg BID or placebo for up to an additional 36 weeks. Treatment with Eohilia® did not demonstrate a statistically significant difference compared to subjects re-randomized to placebo for prespecified efficacy endpoints based on eosinophil count and/or clinical symptoms measured by the DSQ at week 36.

Place in Therapy: Eohilia® is an oral budesonide suspension indicated for 12 weeks of treatment in adult and pediatric patients 11 years of age and older with eosinophilic esophagitis (EoE). A limitation of use includes that Eohilia® has not been shown to be safe and effective for the treatment of EoE for longer than 12 weeks. The safety and efficacy of use were assessed in two multicenter, randomized, double-blind, placebo-controlled, 12 week studies that compared Eohilia® with placebo in patients with esophageal inflammation. Per the full text study by Dellon et al[2] (Study 2), significantly more in the Eohilia® group achieved histologic response endpoint as compared with placebo ($p<0.0001$). Per the full-text study by Hirano et al[3] (Study 1), significantly more achieved histologic response with Eohilia® ($p<0.001$). While

dietary modification, PPIs, and topical glucocorticoids are generally utilized for this diagnosis as initial treatment,[4] Eohilia® is the first FDA approved oral treatment for EoE, to be used for 12 weeks in patients 11 years and older. Budesonide oral suspension is suggested if topical glucocorticoid therapy is to be utilized.[4]

Summary

There is no evidence at this time to support that Eohilia® is safer or more effective than the other currently preferred, more cost-effective medications. It is therefore recommended that Eohilia® remain non-preferred and require prior authorization and be available to those who are unable to tolerate or who have failed on preferred medications.

PDL Placement: ☐ **Preferred**
☒ **Non-Preferred**

References

[1] Eohilia® [package insert]. Lexington, MA: Takeda Pharmaceuticals America, Inc; 2024.
[2] Dellon ES, Katzka DA, Collins MH, et al. Budesonide oral suspension improves symptomatic, endoscopic, and histologic parameters compared with placebo in patients with eosinophilic esophagitis. *Gastroenterology*. 2017; 152(4): 776-786.
[3] Hirano I, Collins MH, Katzka DA, et al. Budesonide oral suspension improves outcomes in patients with eosinophilic esophagitis: Results from a phase 3 trial. *Clin Gastroenterol Hepatol*. 2022; 20(3): 525-534.
[4] UpToDate online. Treatment of eosinophilic esophagitis (EoE). Accessed June 2024.