

Budesonide (UCERIS) Extended-release Tablets (Multimatrix [MMX] Formulation) for Ulcerative Colitis

Criteria for Use

July 2015

VA Pharmacy Benefits Management Services, Medical Advisory Panel, and VISN Pharmacist Executives

The following recommendations are based on medical evidence, clinician input, and expert opinion. The content of the document is dynamic and will be revised as new information becomes available. The purpose of this document is to assist practitioners in clinical decision-making, to standardize and improve the quality of patient care, and to promote cost-effective drug prescribing. **THE CLINICIAN SHOULD UTILIZE THIS GUIDANCE AND INTERPRET IT IN THE CLINICAL CONTEXT OF THE INDIVIDUAL PATIENT. INDIVIDUAL CASES THAT ARE EXCEPTIONS TO THE EXCLUSION AND INCLUSION CRITERIA SHOULD BE ADJUDICATED AT THE LOCAL FACILITY ACCORDING TO THE POLICY AND PROCEDURES OF ITS P&T COMMITTEE AND PHARMACY SERVICES.**

The Product Information should be consulted for detailed prescribing information.

See the VA National PBM-MAP-VPE Monograph on this drug at www.pbm.va.gov or <http://vawww.pbm.va.gov> for further information.

Exclusion Criteria *If the answer to ANY item below is met, then the patient should NOT receive budesonide ER tablets*

- Hypersensitivity to budesonide or any of the tablet ingredients (anaphylactic reactions have occurred)
- Concomitant therapy with CYP3A4 inhibitors (e.g., ketoconazole, itraconazole, ritonavir, indinavir, saquinavir, and erythromycin); these agents may increase systemic exposure to budesonide and increase glucocorticoid effects.
- Acute, severe ulcerative colitis
- Glucocorticoid-refractory ulcerative colitis, defined as no meaningful clinical response to induction therapy using the equivalent of prednisone 30 to 60 mg/day for 2 weeks (then tapering over the next 2 weeks) for oral therapy or 1 to 1.5 weeks for intravenous therapy. (There is a lack of evidence that budesonide 9-mg ER tablets provide benefit in this situation.)
- Stable quiescent ulcerative colitis without evidence of a recent exacerbation (budesonide should not be used for maintenance of remission)
- Untreated or uncontrolled fungal, bacterial, systemic viral or parasitic infections
- Crohn's disease or microscopic / collagenous colitis (i.e., currently available evidence supports using budesonide enteric-coated capsules [ENTOCORT equivalent] for these indications)

Inclusion Criteria *The answers to ALL of the following must be fulfilled in order to meet criteria.*

- Received/receiving VA care or consultation and the initial prescription for budesonide ER tablets from a gastroenterologist or other expert in the treatment of ulcerative colitis

AND

- Intolerance or relative contraindication (e.g., unstable or uncontrolled diabetes mellitus, hypertension, heart failure, osteoporosis) to orally administered prednisone, prednisolone, methylprednisolone or other glucocorticoids known to have higher systemic bioavailability than budesonide

AND one of the following:

- Require treatment to induce remission in patients with newly diagnosed or recurrence of active mild to moderate ulcerative colitis

OR

- Require rapid-onset treatment for recurrence of active, mild to moderate ulcerative colitis as an adjunct to 5-ASA maintenance therapy

Dosage and Administration

Refer to Product Information.

Initial and Subsequent Dosages: 9 mg orally once daily in the morning with or without food (excluding grapefruit and grapefruit juice) for up to 8 weeks.

Tablets should not be chewed, crushed or broken.

Avoid ingestion of grapefruit and grapefruit juice in connection with administration of budesonide ER tablets (may result in hypercorticism).

Discontinuation: Tapering of doses is not required and the Prescribing Information makes no recommendations for tapering. A clinical decision to taper doses should take into account that only one tablet-strength (9 mg) is available.

Switching Glucocorticoids and Dosage Equivalents. Patients switching from other systemic glucocorticoids with higher systemic effects to budesonide ER tablets should be tapered slowly off the other glucocorticoid to reduce the risk of adrenal insufficiency. Clinically equivalent glucocorticoid doses for budesonide ER have not been determined in ulcerative colitis; therefore, dosage equivalents are uncertain when switching glucocorticoid therapy.

Monitoring

- Increased signs and/or symptoms of hypercorticism, particularly in patients
 - With moderate to severe liver disease (consider discontinuing therapy in these patients).
 - Who are taking CYP3A4 inhibitors; consider discontinuation of budesonide or the CYP3A4 inhibitor.
- Signs and/or symptoms of adrenal insufficiency or benign intracranial hypertension, particularly in patients
 - Who are switching from more glucocorticoids with higher systemic effects to budesonide ER tablets
 - Who are subjected to surgery or other stress situations; supplementation with systemic glucocorticoid is recommended.
- Although budesonide has lower systemic bioavailability than other glucocorticoids, general warnings about glucocorticoids should be followed. Monitor patients for potential complications from long-term use of glucocorticoids, such as
 - Hypothalamic-pituitary-adrenal (HPA) axis suppression
 - Cushing's syndrome
 - Hyperglycemia
 - New infections and exacerbation, dissemination or reactivation of latent infection; masking of signs and symptoms of infection
 - Increased blood pressure
 - Sodium and water retention
 - Hypokalemia
 - Gastrointestinal perforation (signs and symptoms may be masked)
 - Behavioral and mood disturbances
 - Decreased bone density
 - Cataracts, eye infections, glaucoma
 - Weight gain

Issues for Consideration

- **FDA Indication:** the induction of remission in patients with active, mild to moderate ulcerative colitis.
- **Use for Active Mild to Moderate Isolated Ulcerative Proctitis:** Budesonide ER tablets were not evaluated in patients with isolated ulcerative proctitis. Budesonide (UCERIS) rectal foam is FDA-approved for this purpose; i.e., for induction of remission in patients with active mild to moderate distal ulcerative colitis extending up to 40 cm from the anal verge.
- **Pregnancy Category C:** Use budesonide during pregnancy only if the potential benefit justifies the potential risk to the fetus.
- **Nursing Mothers:** Budesonide is secreted in human milk and may cause serious adverse effects in nursing infants; either discontinue nursing or discontinue budesonide, taking into account the clinical importance of the drug therapy to the mother.
- **Elderly:** Use caution. There is insufficient data to determine whether there are different age-related responses.
- **Gastric acid reducing agents** (e.g., proton pump inhibitors, H₂-receptor antagonists and antacids) may affect the pH-dependent dissolution of the coating of budesonide ER tablets and result in altered release and uptake of budesonide. The film coating breaks down at or above pH 7.0. There are no specific recommendations for management of this drug interaction.
- **Liver Impairment:** Liver cirrhosis causes a 2.5-fold increase in the systemic bioavailability of orally administered budesonide. The effects of severe liver dysfunction have not been studied. Mild liver disease causes minimal effects on the systemic bioavailability of budesonide.
- **Treatment for Tuberculosis:** Patients with active or latent tuberculosis (TB) infection should receive concomitant anti-TB therapy.
- **Potential Formulation Confusion with Budesonide Enteric-coated Capsules (ENTOCORT):** UCERIS with MMX technology releases drug throughout the colon and is indicated for treatment of active, mild to moderate ulcerative colitis. ENTOCORT with controlled ileal release (CIR) technology releases drug in the ileum and/or ascending colon and is FDA-approved for the treatment of Crohn's disease. ENTOCORT may also be used off-label for microscopic / collagenous colitis.

Renewal Criteria

- Each course of therapy with budesonide ER tablets should be limited to 8 weeks.
- Patients who have an inadequate response to budesonide within 4 weeks may have steroid-refractory disease and require alternative therapies.

Prepared: July 2015

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