BlueCross BlueShield of Arizona
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PHARMACY COVERAGE GUIDELINES	**ORIGINAL EFFECTIVE DATE: 1/19/17**
SECTION: DRUGS	**LAST REVIEW DATE: 5/16/19**
	LAST CRITERIA REVISION DATE: 5/17/18
	ARCHIVE DATE:

VIBERZI™ (eluxadoline) oral tablet

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. All requested data must be provided. Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

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Criteria:

- **Criteria for initial therapy:** Viberzi (eluxadoline) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Individual is 18 years of age or older
  2. A confirmed diagnosis of moderate to severe irritable bowel syndrome with diarrhea (IBS-D) with symptoms of moderate abdominal pain, discomfort and bloating
  3. The recurrent symptoms are present, on average, at least 1 day per week in the last 3 months associated with 2 or more of the following: related to defecation, associated with a change in stool frequency, associated with a change in stool form/appearance
  4. The abnormal diarrheal bowel movements are Bristol Stool Form Scale (BSFS) type 6 or 7
  5. Failed dietary modification that includes lactose restricted diet, if lactose-intolerant; exclusion of gas-producing foods; low carbohydrate diet and elimination of fermentable oligo-, di-, and monosaccharides and polyols (FODMAPs)
  6. Individual has failure, contraindication or intolerance to **BOTH** dicyclomine **AND** hyoscyamine
  7. Individual has failure, contraindication or intolerance to **EITHER** amitriptyline **OR** nortriptyline
  8. There are **NO** contraindications:
     - Contraindications include:
       - Individual without a gallbladder
       - Known or suspected biliary duct obstruction or sphincter of Oddi disease or dysfunction
       - Alcoholism, alcohol abuse or alcohol addiction, or in patients who drink > 3 alcoholic beverages per day
       - A history of pancreatitis; structural diseases of the pancreas, including known or suspected pancreatic duct obstruction
       - Severe hepatic impairment (Child-Pugh Class C)
       - A history of chronic or severe constipation or sequelae from constipation, or known or suspected mechanical gastrointestinal obstruction
       - Known hypersensitivity reaction to Viberzi

  Initial approval duration: 60 tabs per month for 6 months

- **Criteria for continuation of coverage (renewal request):** Viberzi (eluxadoline) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Individual's condition has responded while on therapy
     - Response is defined as both:
       - Achieved and maintains BSFS type of 3 or 4 on at least 3 or 4 days

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- At least a 50% reduced symptoms of abdominal pain, discomfort, and bloating

2. Individual has been adherent with the medication

3. Individual has not developed any contraindications or other significant level 4 adverse drug effects that may exclude continued use
   - Contraindications as listed in the criteria for initial therapy section
   - Significant adverse effect such as:
     - Liver toxicity
     - Pancreatitis
     - Constipation
     - Hypersensitivity

4. There are no significant interacting drugs

Renewal duration: 60 tabs per month for 12 months

Description:

Viberzi (eluxadoline) is indicated in adults for the treatment of irritable bowel syndrome with diarrhea (IBS-D). Eluxadoline is a mu-opioid receptor agonist. It is also a delta opioid receptor antagonist and a kappa opioid receptor agonist. In animals, eluxadoline interacts with opioid receptors in the gut. Stimulation of the opioid receptors within the gut causes inhibition of gastric emptying, inhibition of peristalsis, increased muscle tone, induction of non-propulsive motility, and a delay in gastrointestinal transit.

Irritable bowel syndrome (IBS) is a chronic, relapsing and often life-long functional bowel disorder in which abdominal pain or discomfort is associated with defecation and/or a change in bowel habits. IBS is characterized by symptoms of abdominal pain or discomfort associated with abnormal stool frequency, abnormal stool form, abnormal stool passage, and/or bloating or abdominal distension, which may or may not be relieved by defecation. Symptoms vary and are often associated with food intake and, characteristically, with defecation. Symptoms interfere with daily life and social functioning in many patients.

IBS may be subtyped on the basis of the patient's stool characteristics: IBS with diarrhea (IBS-D), IBS with constipation (IBS-C), IBS with mixed bowel habits or cyclic pattern (IBS-M), and un-subtyped IBS (IBS-U). Treatment is determined by the predominant symptom. Milder, less frequent episodes may be managed with dietary modifications such as eliminating or minimizing foods that worsen symptoms (such as those that contain caffeine, lactose, or artificial sweeteners for IBS-D) or eating a high-fiber diet (for IBS-C or IBS-D) and increasing fluid intake (for IBS-C).

Other lifestyle measures IBS include stress management and dietary interventions such as a diet low in fermentable oligo-, di-, and monosaccharides and polyols (FODMAP). FODMAPs are incompletely absorbed in the small intestine and ferment in the colon. They include foods with fructose (such as apples, pears, honey, high-fructose corn syrup), lactose (milk), fructans or galactans (wheat, onions), and polyols (some fruits and vegetables, artificial sweeteners such as sorbitol). Individuals with IBS may see symptom improvement with gluten restriction. This may be due to the fact that gluten is found in wheat, a high FODMAP food. Recent data

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confirms a role for probiotics in IBS, but also makes it clear that the effects of probiotics in IBS are highly strain-specific.

Small intestinal bacterial overgrowth (SIBO) occurs with greater frequency in patients who have been diagnosed with IBS compared to healthy controls. The classical features of SIBO are those of digestive problems and malabsorption. SIBO is most common in IBS-D but also occurs in IBS-C. Symptoms of SIBO include bloating, abdominal pain, diarrhea or constipation among others and the symptoms of SIBO overlap with those of IBS, which suggests that SIBO is related to IBS. Some researchers believe that SIBO may lead to IBS. Statistically significant reduction in IBS symptoms occurs following antibiotic therapy for SIBO. However, more research is needed to show a link between SIBO and IBS. SIBO is rare unless the patient has a primary or secondary motility disorder, has had surgery, such as ileocecal resection or bariatric surgery, or has impaired immunity (such as immunoglobulin A deficiency). Also recent research has shown that the lactulose hydrogen breath test does not actually measure SIBO, and that SIBO is unlikely to be the cause of IBS.

Guidelines recommend non-pharmacologic and over-the-counter therapy as first line therapy for IBS-D. Antispasmodics such as dicyclomine and hyoscyamine reduce abdominal spasms and cramps through reduced smooth muscle contractions. They may improve pain and global symptoms. Their efficacy is based on continuous use and the effect is rated as modest. Tricyclic antidepressants (amitriptyline, nortriptyline) improve abdominal pain and GI symptoms. Modest improvements may not be seen for several weeks. Loperamide may improve abdominal pain, stool consistency & frequency, but may require continuous use. Ondansetron blocks vagal stimulation of the gut, reducing motility & secretions, may reduce loose stools, frequency, and urgency. Lotronex (alosetron) also blocks vagal stimulation of the gut, reducing motility & secretions, it improves pain & stool consistency. Use is associated with a high risk for constipation and rarely, idiopathic ischemic colitis. It is FDA-approved for use in women with IBS-D who have failed conventional treatment. Xifaxan (rifaximin), a semi-synthetic, non-aminoglycoside, non-systemic antibiotic and is structural analog of rifampin, modestly improves abdominal pain and stool consistency. It is limited to a maximum of three 14-day courses of therapy using 550 mg three times a day. Viberzi (eluxadoline) may also modestly improves abdominal pain & loose stool.

Definitions:

Irritable Bowel Syndrome (Rome IV criteria)
Recurrent abdominal pain, on average, at least one day per week in the last three months with two or more of the following:

Related to defecation
Associated with a change in frequency of stool
Associated with a change in form (appearance) of stool

Irritable bowel syndrome with predominant diarrhea (IBS-D)
Abnormal bowel movements are usually diarrhea (BSFS type 6 and 7)
More than 25% of BM with BSFS types 6 or 7 and less than 25% of BM with BSFS types 1 or 2

Bristol Stool Form Scale (BSFS)
Seven types of stool are:

- Type 1: Separate hard lumps, like nuts (hard to pass); also known as *goat feces*
- Type 2: Sausage-shaped, but lumpy

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- Type 3: Like a sausage but with cracks on its surface
- Type 4: Like a sausage or snake, smooth and soft
- Type 5: Soft blobs with clear cut edges (passed easily)
- Type 6: Fluffy pieces with ragged edges, a mushy stool
- Type 7: Watery, no solid pieces, entirely liquid

Types 1 & 2 indicate constipation
Types 3 & 4 indicate the ideal stools (especially the latter)
Types 5, 6 & 7 specify diarrheal stools

Resources:

Viberzi (eluxadoline) product information accessed 04-26-18 at DailyMed: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=7821bd40-4c84-4984-951b-6436ae20421a

Viberzi (eluxadoline). Package Insert. Revised by manufacturer 11/2017. Accessed 03-14-2018.

Viberzi (eluxadoline). Package Insert. Revised by manufacturer 04/2017. Accessed 5-08-2017.

Viberzi (eluxadoline). Package Insert. Revised by manufacturer 01/2016. Accessed 12-09-2016.

World Gastroenterology Organization Global Guidelines: Irritable Bowel Syndrome: A global Perspective Update September 2015

Weinberg DS, Smalley W, Heidelbaugh JJ, and Sultan S.: American Gastroenterological Association Institute Guideline on the Pharmacological Management of Irritable Bowel Syndrome. Gastroenterology 2014; 147:1146-1148

Ford AC, Moayyedi P, Lacy BE, et al.: American College of Gastroenterology Monograph on the Management of Irritable Bowel Syndrome and Chronic Ideopathic Constipation. Am J Gastroenterol 2014; 109 Aug Suppl 1:S2-S26

UpToDate: Treatment of irritable bowel syndrome in adults. Current through Mar, 2018. https://www-uptodate-com.mwu.idm.oclc.org/contents/treatment-of-irritable-bowel-syndrome-in-adults?search=irritable%20bowel%20syndrome%20with%20diarrhea&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1

UpToDate: Clinical manifestations and diagnosis of irritable bowel syndrome in adults. Current through Mar, 2018. https://www-uptodate-com.mwu.idm.oclc.org/contents/clinical-manifestations-and-diagnosis-of-irritable-bowel-syndrome-in-adults?search=irritable%20bowel%20syndrome&source=search_result&selectedTitle=2~150&usage_type=default&display_rank=2#H2263560866

UpToDate: Pathophysiology of irritable bowel syndrome. Current through Mar, 2018. https://www-uptodate-com.mwu.idm.oclc.org/contents/pathophysiology-of-irritable-bowel-

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syndrome?search=irritable%20bowel%20syndrome&source=search_result&selectedTitle=3~150&usage_type=default&display_rank=3

UpToDate: Small intestinal bacterial overgrowth: Clinical manifestations and diagnosis. Current through Mar, 2018. https://www-uptodate-com.mwu.idm.oclc.org/contents/small-intestinal-bacterial-overgrowth-clinical-manifestations-and-diagnosis?sectionName=Jejunal%20aspirate%20culture&topicRef=2629&anchor=H894085110&source=see_link#H894085110

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Fax completed prior authorization request form to 602-864-3126 or email to pharmacyprecert@azblue.com.
Call 866-325-1794 to check the status of a request.
All requested data must be provided. **Incomplete forms or forms without the chart notes will be returned.**
Pharmacy Coverage Guidelines are available at www.azblue.com/pharmacy.

Pharmacy Prior Authorization Request Form

Do not copy for future use. Forms are updated frequently.
REQUIRED: Office notes, labs, and medical testing relevant to the request that show medical justification are required.

Member Information

Member Name (first & last):	Date of Birth:	Gender:	BCBSAZ ID#:
Address:	City:	State:	Zip Code:

Prescribing Provider Information

Provider Name (first & last):	Specialty:	NPI#:	DEA#:
Office Address:	City:	State:	Zip Code:
Office Contact:	Office Phone:	Office Fax:	

Dispensing Pharmacy Information

Pharmacy Name:	Pharmacy Phone:	Pharmacy Fax:

Requested Medication Information

Medication Name:	Strength:		Dosage Form:
Directions for Use:	Quantity:	Refills:	Duration of Therapy/Use:

☐ Check if requesting **brand** only ☐ Check if requesting **generic**

☐ Check if requesting continuation of therapy (prior authorization approved by BCBSAZ expired)

Turn-Around Time For Review

☐ Standard ☐ Urgent. Sign here: _____ ☐ Exigent (requires prescriber to include a written statement)

Clinical Information

1. **What is the diagnosis? Please specify below.**

   ICD-10 Code: _____ **Diagnosis Description:** _____

2. ☐ Yes ☐ No **Was this medication started on a recent hospital discharge or emergency room visit?**

3. ☐ Yes ☐ No **There is absence of ALL contraindications.**

4. **What medication(s) has the individual tried and failed for this diagnosis? Please specify below.**
Important note: Samples provided by the provider are not accepted as continuation of therapy or as an adequate trial and failure.

Medication Name, Strength, Frequency	Dates started and stopped or Approximate Duration	Describe response, reason for failure, or allergy

5. **Are there any supporting labs or test results? Please specify below.**

Date	Test	Value

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Pharmacy Prior Authorization Request Form

6. Is there any additional information the prescribing provider feels is important to this review? Please specify below.
For example, explain the negative impact on medical condition, safety issue, reason formulary agent is not suitable to a specific medical condition, expected adverse clinical outcome from use of formulary agent, or reason different dosage form or dose is needed.

Signature affirms that information given on this form is true and accurate and reflects office notes

Prescribing Provider's Signature: Date:

Please note: Some medications may require completion of a drug-specific request form.

Incomplete forms or forms without the chart notes will be returned.

Office notes, labs, and medical testing relevant to the request that show medical justification are required.