Bracco Diagnostics

# E-Z-PAQUE® (BARIUM SULFATE) FOR ORAL SUSPENSION, 96% w/w

**HIGHLIGHTS OF PRESCRIBING INFORMATION**
**These highlights do not include all of the information needed to use E-Z-PAQUE safely and effectively. See full prescribing information for E-Z-PAQUE.**

**E-Z-PAQUE (barium sulfate) for oral suspension**
**Initial U.S. Approval: 2016**

**----------INDICATIONS AND USAGE----------**
E-Z-PAQUE is a radiographic contrast agent indicated for use in single contrast radiographic examinations of the esophagus, stomach, duodenum and small bowel small bowel to visualize the gastrointestinal (GI) tract in adult and pediatric patients (1)

**----------DOSAGE AND ADMINISTRATION-------**
- Adults: Recommended reconstituted oral dose is between 150 – 750 mL (2.1)
- Pediatric patients: adjust reconstituted dose based on relative GI volume (2.1)
- Must reconstitute supplied powder with water prior to use. See Full Prescribing Information for reconstitution instructions (2.2)

**-------DOSAGE FORMS AND STRENGTHS-------**
- For oral suspension: 169 grams of barium sulfate (96% w/w) in a single-dose bottle for reconstitution (3)

**----------CONTRAINDICATIONS----------**
- Known or suspected perforation of the GI tract (4)
- Known obstruction of the GI tract (4)
- Conditions associated to high risk of GI aspiration (4)
- Conditions associated to high risk of GI perforation (4)
- Known hypersensitivity to barium sulfate or any of the excipients of E-Z-PAQUE (4)

**----------WARNINGS AND PRECAUTIONS-------**
- Hypersensitivity reactions: Emergency equipment and trained personnel should be immediately available (5.1)
- Intra-abdominal barium leakage: May occur in conditions such as GI fistula, ulcer, inflammatory bowel disease, appendicitis or diverticulitis, severe stenosis or obstructing lesions of the GI tract (5.2)
- Delayed GI transit and obstruction: Patients should maintain adequate hydration in days following a barium sulfate procedure to avoid obstruction or impaction caused by baroliths (5.3)
- Aspiration pneumonitis: Patients with history of food aspiration or with swallowing disorders are at increased risk (5.4)

**----------ADVERSE REACTIONS----------**
Common adverse reactions include nausea, vomiting, diarrhea and abdominal cramping (6)

**To report SUSPECTED ADVERSE REACTIONS, contact Bracco Diagnostics Inc at 1-800-257-5181 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch**

**See 17 for PATIENT COUNSELING INFORMATION**

Revised 4/2017

**FULL PRESCRIBING INFORMATION: CONTENTS***



*Sections or subsections omitted from the full prescribing information are not listed

## FULL PRESCRIBING INFORMATION

### 1 INDICATIONS AND USAGE
E-Z-PAQUE is indicated for use in single contrast radiographic examinations of the esophagus, stomach, duodenum and small bowel to visualize the gastrointestinal tract (GI) in adult and pediatric patients.

### 2 DOSAGE AND ADMINISTRATION
#### 2.1 Recommended Dosage
The optimal oral dose of E-Z-PAQUE will vary depending on the size and anatomy of the patient and the procedure being performed. The recommended oral dose of reconstituted E-Z-PAQUE:
- Adults: 150 to 750 mL, 169 to 450 g barium sulfate, depending on the reconstituted concentration *[see Dosage and Administration (2.2)]*.
  - Volumes closer to 150 mL are recommended for examination of the esophagus and stomach.
  - Volumes up to 750 mL are recommended for examination of the small bowel.
- Pediatric Patients: Adjust dose of reconstituted E-Z-PAQUE based on GI volume.
  - For examinations of the upper GI tract, administer a volume sufficient to fully distend the esophagus or stomach.
  - For small bowel examinations:
    - Age birth to less than 2 years: 30 mL to 75 mL.
    - Age 2 years to less than 17 years: 75 mL to 480 mL.

#### 2.2 Instructions for Reconstitution
The reconstituted concentration will vary, depending on the procedure being performed.
- A barium suspension up to 115% w/v is recommended for examinations of the esophagus and upper GI
- A barium suspension of 60% w/v is recommended for examinations of the small bowel.

Reconstitute the E-Z-PAQUE prior to administration according to the following instructions:
- Tap bottle on a hard surface (right side up) several times to compact the product in the bottle.
- Add water to the blue line marked 'Initial Fill Line' on the bottle.
- Replace cap securely on the bottle.
- Invert bottle and tap with fingers to mix contrast into the water.
- Shake vigorously for 30 seconds; wait 5 minutes.
- Add more water as needed to achieve the desired % w/v concentration using the fill lines marked on the bottle. Then, re-shake vigorously for 30 seconds.
- To use with straw, remove adhesive label on top of cap.
- Remove cap and use straw to push out cap liner; replace cap.

#### 2.3 Administration Instructions
- Use immediately after reconstitution.
- Ensure patients have nothing by mouth for the following time period prior to the examination:
  - Neonates and infants < 3 months — 2 hours
  - Infants 3-12 months — 3 hours
  - > 12 months of age — 4 hours
- Discard any unused suspension.
- Encourage patients to maintain hydration following the barium sulfate procedure.

### 3 DOSAGE FORMS AND STRENGTHS
For oral suspension: 169 g of barium sulfate supplied as a fine, white to lightly colored powder (96 % w/w) in a single-dose HDPE plastic bottle for reconstitution. The suspension can be reconstituted to a desired strength of 60, 70, 85, 100, or 115% w/v when prepared according to the corresponding fill line on the bottle. The reconstituted solution should be opaque, white to lightly-colored and free from particles.

### 4 CONTRAINDICATIONS
E-Z-PAQUE is contraindicated in patients with the following conditions:
- Known or suspected perforation of the GI tract
- Known obstruction of the GI tract
- High risk of GI perforation such as those with a recent prior GI perforation, acute GI hemorrhage or ischemia, toxic megacolon, severe ileus, post GI surgery or biopsy, acute GI injury or burn, or recent radiotherapy to the pelvis
- High risk of aspiration such as those with prior aspiration, tracheo-esophageal fistula, or obtundation
- With known severe hypersensitivity to barium sulfate or any of the excipients of E-Z-PAQUE

### 5 WARNINGS AND PRECAUTIONS
#### 5.1 Hypersensitivity Reactions
Barium sulfate preparations contain a number of excipients, including natural and artificial flavors and may induce serious hypersensitivity reactions. The manifestations include hypotension, bronchospasm and other respiratory impairments, dermal reactions including rashes, urticaria, and itching. A history of bronchial asthma, atopy, or a previous reaction to a contrast agent may increase the risk for hypersensitivity reactions. Emergency equipment and trained personnel should be immediately available for treatment of a hypersensitivity reaction.

#### 5.2 Intra-abdominal Barium Leakage
The use of E-Z-PAQUE is contraindicated in patients at high risk of perforation of the GI tract *[see Contraindications (4)]*. Administration of E-Z-PAQUE may result in leakage of barium from the GI tract in the presence of conditions such as carcinomas, GI fistula, inflammatory bowel disease, gastric or duodenal ulcer, appendicitis, diverticulitis, and in patients with a severe stenosis at any level of the GI tract, especially distal to the stomach. Barium leakage has been associated with peritonitis and granuloma formation.

#### 5.3 Delayed Gastrointestinal Transit and Obstruction
Orally administered barium sulfate may accumulate proximal to a constricting lesion of the colon, causing obstruction or impaction with development of baroliths (inspissated barium associated with feces) and may cause abdominal pain, appendicitis, bowel obstruction, or rarely perforation. Patients with the following conditions are at higher risk for developing obstruction or baroliths: severe stenosis at any level of the GI tract, impaired GI motility, electrolyte imbalance, dehydration, on a low residue diet, on medications that delay GI motility, constipation, cystic fibrosis, Hirschsprung disease, and the elderly *[see Use in Specific Populations (8.4, 8.5)]*. To reduce the risk of delayed GI transit and obstruction, patients should maintain adequate hydration during and in the days following a barium sulfate procedure. Consider the administration of laxatives.

#### 5.4 Aspiration Pneumonitis
The use of E-Z-PAQUE is contraindicated in patients at high risk of aspiration [see Contraindications (4)]. Oral administration of barium is associated with aspiration pneumonitis, especially in patients with a history of food aspiration or with compromised swallowing mechanism. Vomiting following oral administration of barium sulfate may lead to aspiration pneumonitis. In patients at risk for aspiration, begin the procedure with a small ingested volume of E-Z-PAQUE. Discontinue administration of E-Z-PAQUE immediately if aspiration is suspected.

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**5.5 Systemic Embolization**
Barium sulfate products may occasionally intravasate into the venous drainage of the large bowel and enter the circulation as a "barium embolus" leading to potentially fatal complications which include systemic and pulmonary embolism, disseminated intravascular coagulation, septicemia and prolonged severe hypotension. Although this complication is exceedingly uncommon after oral administration of a barium sulfate suspension, monitor patients for potential intravasation when administering barium sulfate.

**5.6 Risk with Hereditary Fructose Intolerance**
E-Z-PAQUE contains sorbitol which may cause severe symptoms if ingested by patients with hereditary fructose intolerance. Severe symptoms may include the following: vomiting, hypoglycemia, jaundice, hemorrhage, hepatomegaly, hyperuricemia, and kidney failure. Before administration of E-Z-PAQUE assess patients for a history of hereditary fructose intolerance and avoid use in these patients.

## 6 ADVERSE REACTIONS
The following adverse reactions have been identified from spontaneous reporting or clinical studies of barium sulfate administered orally. Because the reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or to establish a causal relationship to drug exposure

- Nausea, vomiting, diarrhea and abdominal cramping
- Serious adverse reactions and fatalities include aspiration pneumonitis, barium sulfate impaction, intestinal perforation with consequent peritonitis and granuloma formation, vasovagal and syncopal episodes

## 8 USE IN SPECIFIC POPULATIONS
**8.1 Pregnancy**
Risk Summary
E-Z-PAQUE is not absorbed systemically following oral administration, and maternal use is not expected to result in fetal exposure to the drug *[see Clinical Pharmacology (12.3)]*.

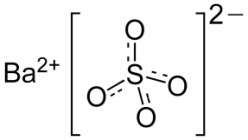
**8.2 Lactation**
Risk Summary
Liquid E-Z-PAQUE is not absorbed systemically by the mother following oral administration, and breastfeeding is not expected to result in exposure of the infant to Liquid E-Z-PAQUE *[see Clinical Pharmacology (12.3)]*.

**8.4 Pediatric Use**
The efficacy of E-Z-PAQUE in pediatric patients from birth to less than 17 years of age is based on successful opacification of the esophagus, stomach, duodenum and small bowel during radiologic examinations *[see Clinical Pharmacology (12.1)]*. Safety and dosing recommendations in pediatric patients are based on clinical experience *[see Dosage and Administration (2.1)]*.

E-Z-PAQUE is contraindicated in pediatric patients with tracheo-esophageal fistula *[see Contraindications (4)]*. Pediatric patients with a history of asthma or food allergies may be at increased risk for development of hypersensitivity reactions *[see Warnings and Precautions (5.1)]*. Pediatric patients with cystic fibrosis or Hirschsprung disease should be monitored for bowel obstruction after use *[see Warnings and Precautions (5.3)]*. Pediatric patients with hereditary fructose intolerance may develop severe symptoms with administration of E-Z-Paque; assess for this risk and avoid use in patients with hereditary fructose intolerance *[see Warnings and Precautions (5.6)]*.

**8.5 Geriatric Use**
Clinical studies of E-Z-PAQUE did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

## 11 DESCRIPTION
E-Z-PAQUE (barium sulfate) is a radiographic contrast agent that is supplied as a fine, white to lightly colored powder for suspension (96 % w/w) for oral administration. The active ingredient barium sulfate is designated chemically as $BaSO_4$ with a molecular weight of 233.4 g/mol, a density of 4.5 g/cm$^3$, and the following chemical structure:




E-Z-PAQUE contains excipients including: carrageenan, citric acid, natural and artificial strawberry flavor, natural and artificial vanilla flavor, pectin, polysorbate 80, propylene glycol, saccharin sodium, simethicone, sodium citrate, sorbitol, tragacanth and xanthan gum.

## 12 CLINICAL PHARMACOLOGY
**12.1 Mechanism of Action**
Due to its high atomic number, barium (the active ingredient in E-Z-PAQUE) is opaque to x-rays and therefore acts as a positive contrast agent for radiographic studies.

**12.3 Pharmacokinetics**
Under physiological conditions, barium sulfate passes through the GI tract in an unchanged form and is absorbed only in pharmacologically insignificant amounts.

## 13 NONCLINICAL TOXICOLOGY
**13.1 Carcinogenesis,Mutagenesis, Impairment of Fertility**
No animal studies have been performed to evaluate the carcinogenic potential of barium sulfate or potential effects on fertility.

## 16 HOW SUPPLIED/STORAGE AND HANDLING
How Supplied
E-Z-PAQUE (barium sulfate) is supplied as a fine white to lightly colored powder (96 % w/w) in a single dose HDPE plastic bottle containing 169 g of barium sulfate.

Provided as: 24 bottles per pack (NDC 32909-750-03)

Storage and Handling
Store at USP controlled room temperature 20 to 25°C (68 to 77° F).

## 17 PATIENT COUNSELING INFORMATION
After administration advise patients to:

- Maintain adequate hydration
- Seek medical attention for worsening of constipation or slow gastrointestinal passage
- Seek medical attention for any delayed onset of hypersensitivity: rash, urticaria, or respiratory difficulty

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