SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

E-Z-HD 98 % w/w powder for oral suspension

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Active Constituent:
Barium sulfate 98.45 % w/w

Excipients include:
Sorbitol (E420), 1.89 g per 340 g dose.
Approximately 266 mg sodium per 340 g dose.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Powder for oral suspension.
White powder.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

This medicinal product is for diagnostic use only.

E-Z-HD is a high density suspension for use as a radiopaque agent during X-ray visualisation of the upper gastro-intestinal tract (oesophagus, stomach and duodenum). It is designed for optimal use in double contrast X-ray examinations.

E-Z-HD is indicated in adults and children

4.2 Posology and method of administration

Posology

E-Z-HD must be administered orally. The powder must be reconstituted prior to administration (see section 6.6).

The administered dose of E-Z-HD will depend on the patient in question and the section of the gastrointestinal tract to be viewed.

Method of administration

Adults: The contents of one prefilled bottle (340 g) are dispersed in 65 mL of water to produce a 250 % w/v suspension which is swallowed by the patient after a suitable gas producing agent has been administered.

Children: The dosage will be dependent on the size, age, health state and anatomical region to be imaged of the child. Individual requirements should be determined, from experience, by the radiologist.

Elderly: There are no special dosage recommendations. The dosage should be determined, from experience, by the radiologist.

4.3 Contraindications

Immune System Disorders
Hypersensitivity to barium sulfate or to any of the excipients listed in section 6.1.

Gastrointestinal Disorders
Patients with any of the following:
- a known or suspected, perforation of the gastrointestinal tract
- known or suspected trachea-esophageal fistula
- gastrointestinal haemorrhage
- gastrointestinal ischemia
- megacolon or toxic megacolon
- necrotising entercolitis
- severe ileus

should not receive E-Z-HD.

E-Z-HD should not be used for infants with swallowing disorders.

Surgical and Medical Procedures
Barium Sulphate should not be administered immediately after gastrointestinal surgery, including snare polypectomy or 'hot' colonic biopsy because of the potential for post-surgical or post-procedural leakage or the potential for gastrointestinal perforation. In case the patient has to undergo gastrointestinal surgery immediately after barium sulfate administration, caution should be exercised.

Injury, Poisoning and Procedural Complications

Barium Sulphate products should not be used during and up to four weeks after radiotherapy to the rectum or prostate; similarly, Barium Sulphate products should not be used in patients with new injuries or chemical burns of the gastrointestinal tract.

4.4 Special warnings and precautions for use

The product should be administered under the supervision of a physician.

Diagnostic procedures which involve the use of radiopaque contrast agents should be carried out under the direction of personnel with the requisite training and with a thorough knowledge of the particular procedure to be performed.

Barium Sulphate should not be administered in its dry form. The powder must be reconstituted, and some of the commercially prepared suspensions require further dilution, prior to administration.

Hypersensitivity
A history of bronchial asthma, atopy, as evidenced by hay fever and eczema, a family history of allergy, or a previous reaction to a contrast agent warrant special attention. These responses are thought to be caused by the flavours and/or preservatives used in the product.

As stated in section 4.8, serious adverse reactions, including death, have been reported with the administration of barium sulfate formulations and are usually associated with the technique of administration, the underlying pathological condition and/or patient hypersensitivities. Anaphylactic and allergic reactions have been reported during double contrast examinations in which glucagon has been used. Rapid recognition, assessment, and diagnosis are crucial to the effective implementation of treatment. Imaging facilities should be staffed with well-trained personnel for the diagnosis and treatment of hypersensitivity reactions.

Barium sulfate preparations used as radiopaque media contain a number of additives to provide diagnostic properties and patient palatability. Allergic responses following the use of barium sulfate suspensions have been reported. Skin irritation, redness, inflammation and hives have been reported for infants and small children following spillage of barium sulfate suspension on their skin.

Perforation
In patients with a serious stenosis at any level of the gastro-intestinal tract, especially if it is distal to the stomach, and in the presence of conditions and ailments that increase the risk of perforation such as known gastrointestinal fistulae and carcinomas, inflammatory intestinal disease, diverticulitis and

diverticulosis and amoebiasis, careful consideration of the risks and benefits of the administration of a barium sulfate suspension is required.

Aspiration
For patients who are prone to aspiration (the newborn, elderly and stroke patients), it is recommended that the procedure starts with a small ingested volume.

Vomiting following oral administration of barium sulfate may lead to aspiration pneumonitis. Oral administration of barium sulfate suspension by an infant sucking a bottle and administration of large quantities by catheter are reported to be likely to result in aspiration into the tracheobronchial tree. Cardiopulmonary arrest leading to fatality has been reported in infants following aspiration. Aspiration of smaller amounts may cause respiratory tract inflammation and pneumonia.

Ingestion of barium is not recommended in patients with a history of food aspiration. If barium procedures are required in these patients or in patients in whom integrity of the swallowing mechanism may be compromised, proceed with caution. If this product is aspirated into the larynx, further administration should be immediately discontinued.

Obstruction/Fluid Overload
Barium Sulphate suspensions, after oral administration, have been reported to cause obstruction of the small bowel (impaction) in paediatric patients with cystic fibrosis.
Barium sulfate suspensions have been reported to cause fluid overload due to water absorption.

Children and patients with impaired renal function are the most susceptible to water intoxication, as are children with Hirschsprung’s Disease.

Intravasation
Barium sulfate may also intravasate into the venous drainage of the large bowel and enter the circulation as a "barium embolus". This complication occurs rarely during a barium enema and is exceedingly uncommon in oral administration. It can lead to potentially fatal complications, including systemic and pulmonary embolism, disseminated intravascular coagulation, septicaemia and prolonged severe hypotension. It is more likely to occur in elderly patients, due to thinning of the rectal wall and vaginal thinning with age, and in those with colorectal disease, when intraluminal pressure overcomes the resistance of the colonic wall affected by colitis, diverticulitis or intestinal obstruction. The diagnosis should be considered in any patient who collapses during or shortly after a barium procedure, and in those who become suddenly unwell in the hours following the procedure.

Constipation or Diarrhoea
E-Z-HD should be used with care if the patient is dehydrated, suffers from any condition or is on any other treatment that can cause constipation, or if the patient has history of constipation. In this situation a mild bulk laxative

should be administered following completion of the X-ray examination. Increased intake of liquids is recommended after oral or rectal administration of barium sulfate to prevent severe constipation and the risk of impaction.

Conversely, since E-Z-HD contains sorbitol, administration may have a mild laxative effect. The calorific value of sorbitol is 2.6 kcal/g.

Other Possible Complications
Apprehensive patients may develop weakness, pallor, tinnitus, diaphoresis and bradycardia following the administration of any diagnostic agent. Such reactions are usually unpredictable and are best treated by having the patient lie flat for an additional 10 - 30 minutes under observation.

Patient preparation for diagnostic gastrointestinal examinations frequently requires cathartics and a liquid diet. The various preparations can result in water loss for the patient. Patients should be rehydrated quickly following a barium sulfate suspension examination of the gastrointestinal tract. Saline cathartics are recommended on a routine basis in patients with a history of constipation unless clinically contraindicated.

Baroliths
Baroliths consist of inspissated barium associated with faeces. They are often asymptomatic, but may be associated with abdominal pain, appendicitis, bowel obstruction, or perforation. Patients who are elderly, with impaired gastrointestinal motility, colon obstruction, electrolyte imbalance, dehydration or on a low residue diet may be at risk of developing baroliths. To reduce this risk, adequate hydration should be maintained during and in the days following barium sulfate procedure. The use of laxatives (especially in case of constipation) should be considered.

E-Z-HD contains 1.89g of sorbitol per 340g dose
- The additive effect of concomitantly administered products containing sorbitol (or fructose) and dietary intake of sorbitol (or fructose) should be taken into account.
- The content of sorbitol in medicinal products for oral use may affect the bioavailability of other medicinal products for oral use administered concomitantly.
- Patients with hereditary fructose intolerance (HFI) should not be given this medicinal product.
- Sorbitol can cause gastrointestinal discomfort and mild laxative effect.

Patients on a Controlled Sodium Diet
This medicinal product contains 266 mg sodium per 340 g dose, equivalent to 13% of the WHO recommended maximum daily intake of 2 g of sodium for an adult.

Children, Elderly and Debilitated Patients
As with any barium sulfate preparation, care should be taken when administering E-Z-HD to children, the elderly or the debilitated. It should be used cautiously in patients with pre-existing heart disease.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.

Barium sulfate is biologically inert and there are no known interactions with other medicinal products. However, the presence of barium sulfate formulations in the gastrointestinal tract may alter the absorption of therapeutic agents taken concomitantly. In order to minimise any potential change in absorption, the separate administration of barium sulfate from that of other medicines should be considered.

Other examinations of the same area of the gastrointestinal tract with another contrast agent may be complicated by the presence of barium sulfate (residue) in the gastrointestinal tract up to several days following the examination with barium contrast media.

4.6 Fertility, pregnancy and lactation

Fertility
Following oral or rectal administration, barium sulfate is absorbed systemically in negligible amounts. Though barium sulfate is pharmacologically inert, no studies of its mutagenic or teratogenic potential are available.

Pregnancy
Although this product is not contraindicated in pregnancy, we would like to point out that radiographic procedures may damage the foetus, particularly during the first trimester of pregnancy. Any examination should only be carried out after careful consideration of the benefit/risk of the procedure.

Breastfeeding
Since the absorption of barium sulfate is negligible, its use is not contraindicated during breastfeeding.

4.7 Effects on ability to drive and use machines

E-Z-HD has negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Undesirable effects may occur during or after a procedure with barium sulfate.

Skin and subcutaneous disorders together with immune system disorders, reflecting allergic reactions either to barium sulfate or the product excipients, are among the most commonly reported effects; for example urticaria, erythema and rash.

Gastrointestinal disorders are also one of the most frequently reported class of undesirable effects; for example diarrhoea, nausea, abdominal pain/distention, constipation.

Within the table below, clinically significant adverse reactions are listed if they have been reported during post approval use of all barium sulfate formulations. Their frequency is not known, therefore relative reporting rate (for example, less commonly) compared to overall reporting for barium sulfate is used.

MedDRA System Organ Class	**Adverse events**	
	Clinical Trials	**Post-marketing Surveillance**
	Rare (≥1/10,000 to <1/1,000)	
Infections and infestations		Appendicitis, Bacteraemia. Less commonly other infections have been reported including rare cases of Abscess intestinal, Liver abscess, Peritoneal infection and Pneumonia
Blood and the lymphatic system disorders		Lymphadenopathy
Immune system disorders		Hypersensitivity presenting with a wide range of signs and symptoms including skin and subcutaneous reactions such as urticaria, pruritus, rash, erythema and facial swelling. Potential hypersensitivity associated respiratory signs and symptoms including dyspnoea, pharyngeal oedema and throat tightness have been reported. Anaphylactic reaction and anaphylactic shock have been reported less commonly.
Metabolism and nutrition disorders		Infrequent cases of Hyperglycaemia have been reported in diabetic patients
Psychiatric disorders		Agitation, Confusional state, Nervousness and related symptoms

		have been reported during the administration of barium sulfate
Nervous system disorders		Loss of consciousness, Syncope, Syncope vasovagal, Dizziness, Burning sensation, Headache, Dysarthria, Hypotonia
Eye disorders		Eye disorders, including Eye swelling, usually associated with allergic reactions have been reported
Ear and labyrinth disorders		Tinnitus
Cardiac disorders		Bradycardia, Cyanosis, Tachycardia
Vascular disorders		Hypotension, Pallor, Vasodilatation
Respiratory, thoracic and mediastinal disorders		Bronchospasm, Dyspnoea, Laryngeal oedema, Pharyngeal oedema and pain, Throat irritation or tightness, Cough. When administered orally, Aspiration, Pneumonia aspiration.
Gastrointestinal disorders	Abdominal pain Nausea; Vomiting	Gastrointestinal signs and symptoms are widely reported, it is not always possible to differentiate between pre-existing medical conditions and procedural complications. Events reported include: Intestinal ischemia, constipation and in severe cases gastrointestinal blockage; Gastrointestinal inflammation, ulceration or perforation; Abdominal discomfortabdominal distension; Diarrhoea; Colitis ulcerative may be aggravated and Retching; Flatulence; Swollen tongue
Skin and subcutaneous tissue disorders		Skin reactions are varied and most likely to be associated with allergic reactions. Reports include: Erythema, Dermatitis Contact, Excessive granulation tissue, Hyperhidrosis, Periorbital oedema, Pruritus, Rash, Swelling face, Urticaria

Renal and urinary disorders		Dysuria
General disorders and administration site conditions		Malaise, Pain, Swelling, Asthenia, Pyrexia, Face oedema
Investigations		Electrocardiogram abnormal
Injury and poisoning		Intravasation by barium sulfate, associated with pre-existing bowel disease or diverticulitis, has been reported rarely. Barium impaction

More rarely and depending on the route of administration, i.e. oral or rectal, the following procedural complications have been reported:
Infections (e.g. peritonitis) subsequent to existing or new gastrointestinal perforation. Complications include adhesions and granuloma.
Subsequent to existing or procedural gastrointestinal trauma, intravasation of barium sulfate with rare subsequent venous emboli formation, including the hepatic portal vein, vena cava and pulmonary embolism that may be fatal in approx 50% of cases.
Following oral administration, aspiration, with pulmonary complications, may occur and may be fatal in rare cases.

Please see section 4.4 for measures to be taken to avoid these adverse reactions, and actions to take if such adverse reactions occur.

Very rare cases of death associated with barium sulfate administration have been reported in the literature. The majority of the deaths relate to procedural complications usually caused by failure to follow generally accepted radiological practice. Some cases had a history indicating that barium sulfate administration was highly unlikely to be a primary or even secondary causative factor in patient fatality.

Paediatric patients
The type of adverse reactions is similar in children and adults.

4.9 Overdose

Barium sulfate is non-toxic and absorbed systemically in negligible amounts.

Repeated use within a very short period of time has led to abdominal cramps, nausea, vomiting, diarrhoea, and constipation. These symptoms are transitory in nature and may be allowed to resolve without medical intervention or may be treated according to currently accepted standards of care.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: X-ray contrast media, barium sulfate with suspending agents, ATC code: V08BA01

The active constituent of E-Z-HD, barium sulfate, is inert and has no pharmacological action. It serves only as a radiopaque substance to opacify the gastro-intestinal tract during X-ray examinations.

5.2 Pharmacokinetic properties

Under physiological conditions, barium sulfate passes through the gastrointestinal tract in an unchanged form and is absorbed only in small, pharmacologically insignificant amounts.

5.3 Preclinical safety data

There are no preclinical data of relevance to the prescriber which are additional to that already included elsewhere in the SPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sorbitol (E420)
Acacia gum (E414)
Sodium citrate (E331)
Simeticone
Citric acid anhydrous (E330)
Polysorbate 80 (E433)
Carrageenan (E407)
Ethyl Maltol (E637)
Saccharin sodium (E954)
Strawberry Flavour
Cherry flavour

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Two years.

This pack is for single-dose use only. E-Z-HD should be administered immediately following reconstitution and must not be stored.

6.4 Special precautions for storage

Store below 25°C.

6.5 Nature and contents of container

Unit dose bottle (containing 340 g of E-Z-HD) composed of high density polyethylene (HDPE) with a polypropylene screw-on lid having a liner of three-ply co-extruded liner (foamed polyolefin blend between two layers of solid polypropylene co-polymer) and an aluminium seal (polyethylene terephthalate (PET) film, polymer adhesive, PET tab, polyolefin foam, aluminium foil, PET layer and heat seal).

6.6 Special precautions for disposal and other handling

Reconstitution information for use of E-Z-HD is provided below.

Do not use if inner seal is broken or missing.

1. Add 65 mL of water to bottle.
2. Secure lid and invert bottle, tapping base to loosen powder.
3. Shake well for 10-20 secs. Leave until required.
4. Immediately before giving to patient to drink shake again for 10-20 secs.

Any unused, opened product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Bracco U.K. Limited,
Magdalen Centre,
The Oxford Science Park,
Oxford, OX4 4GA.
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 18920/0029

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30th March 1993 / 30th March 1998

10 DATE OF REVISION OF THE TEXT

18/01/2022