Proposed Professional Information for AXIM E-Z-PAQUE

SCHEDULING STATUS: S4

1. NAME OF THE MEDICINE

AXIM E-Z-PAQUE 96 % *m/m* powder for oral suspension

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 100 g powder contains

Barium sulphate 96,3096 g

Each bottle of 176 g powder contains 169,5 g barium sulphate.

Excipients with known effects (per 100 g powder):

Contains sugar alcohol (2,2 g sorbitol).

Contains sweetener (0,036 g saccharin sodium).

Contains 44 mg propylene glycol.

Contains 133 mg sodium.

Contains traces of sulphites.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder for oral suspension.

Before reconstitution: A white to lightly coloured powder, with a characteristic odour and no grittiness.

After reconstitution: A white, sweet, unflavoured, non-gritty suspension.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

AXIM E-Z-PAQUE is indicated for single use, as an opaque contrast media for the X-ray examination of the oesophagus, stomach and duodenum.

4.2 Posology and method of administration

Posology

The volume and concentration of AXIM E-Z-PAQUE to be administered will depend on the degree and extent of contrast required in the area(s) under examination and on the equipment and technique employed.

Mixing instructions: Add water to the desired % *m/m* fill line on the bottle. Secure lid, invert the bottle and shake vigorously for 30 seconds. Wait five minutes, then add more water as necessary to achieve the % *m/m* desired. Replace the lid and shake vigorously for 30 seconds. Always re-shake just prior to administration to the patient.

AXIM E-Z-PAQUE is primarily intended for use in the upper gastrointestinal tract.

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

Adults: Single contrast of the oesophagus, stomach and duodenum – give orally 175 to 300 mL of suspension at 100 % *m/v*.

Small bowel – give orally 250 to 300 mL of suspension at 60 % *m/v*.

The actual administered dose should be determined from experience, by the radiologist.

Children: The dosage will be dependent on the size, age, health state and anatomic 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.

Method of administration:

For oral administration.

For instructions on reconstitution of AXIM E-Z-PAQUE before administration, see section 6.6.

4.3 Contraindications

- Known hypersensitivity to barium sulphate or any of the excipients listed in section 6.1.
- Obstruction of the colon, or in the presence of suspected or impending gastrointestinal perforation.
- Patients at risk of perforation as in acute ulcerative colitis or diverticulitis and following rectal or colonic biopsy, sigmoidoscopy or radiotherapy.

4.4 Special warnings and precautions for use

AXIM E-Z-PAQUE should be administered under the supervision of a medical practitioner.

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 procedure to be performed.

AXIM E-Z-PAQUE should not be administered in its dry form. The powder must be reconstituted, 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 (see section 4.8).

Serious adverse reactions, including death, have been reported with the administration of barium sulphate formulations and are usually associated with the technique of administration, the underlying pathological condition and/or patient hypersensitivities (see section 4.8). 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.

AXIM E-Z-PAQUE contain several additives to provide diagnostic properties and patient palatability. Allergic responses following the use of barium sulphate suspensions, such as AXIM E-Z-PAQUE, have been reported. Skin irritation, redness, inflammation and hives have been reported for infants and small children following spillage of barium sulphate suspension on their skin. These responses are thought to be caused by the flavours and/or preservatives used in AXIM E-Z-PAQUE.

Because of reported anaphylactoid reactions to latex, the use of non-latex gloves during the procedure should be considered.

Perforation

In patients with a serious stenosis at any level of the gastrointestinal 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 sulphate 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 AXIM E-Z-PAQUE may lead to aspiration pneumonitis. Oral administration of AXIM E-Z-PAQUE 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 AXIM E-Z-PAQUE is not recommended in patients with a history of food aspiration. If the procedure with AXIM E-Z-PAQUE is required in these patients or in patients in whom integrity of the swallowing mechanism may be compromised, proceed with caution. If AXIM E-Z-PAQUE is aspirated into the larynx, further administration should be immediately discontinued.

Obstruction or fluid overload

AXIM E-Z-PAQUE suspensions, after oral administration, may cause obstruction of the small bowel (impaction) in paediatric patients with cystic fibrosis.
AXIM E-Z-PAQUE suspensions may cause fluid overload due to water absorption.

Children and patients with impaired renal function are the most susceptible to water intoxication.

Constipation or diarrhoea

AXIM E-Z-PAQUE 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 a 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 administration of AXIM E-Z-PAQUE to prevent severe constipation and the risk of impaction.

Conversely, since AXIM E-Z-PAQUE 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 (ringing in the ears), sweating and bradycardia following the administration of any diagnostic agent. Such reactions are usually unpredictable and are best treated by having the patient lie down for an additional 10 to 30 minutes and observed with appropriate reassurance.

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 an AXIM E-Z-PAQUE suspension examination of the gastrointestinal tract.

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 AXIM E-Z-PAQUE procedure. The use of laxatives (especially in case of constipation) should be considered.

Propylene glycol

AXIM E-Z-PAQUE contains 43,4 mg propylene glycol per 100 g dose. Co-administration with any substrate for alcohol dehydrogenase such as ethanol may induce serious adverse effects in neonates.

Sulphites

The flavourants of AXIM E-Z-PAQUE contain traces of sulphites, which may rarely cause severe hypersensitivity reactions and bronchospasm.

Patients on a sodium-controlled diet

AXIM E-Z-PAQUE contains 117,3 mg sodium per 100 g dose, equivalent to 5,9 % of the WHO recommended maximum daily intake for sodium of 2 g sodium for an adult.

Children, elderly and debilitated patients

Care should be taken when administering AXIM E-Z-PAQUE to children, elderly or debilitated patients. It should be used cautiously in patients with pre-existing heart disease.

AXIM E-Z-PAQUE contains 2 g sorbitol per 100 g powder

- The additive effect of concomitantly administered products containing sorbitol and dietary intake of sorbitol should be taken into account.
- The content of sorbitol in medicine for oral use may affect the bioavailability of other medicine for oral use administered concomitantly.
- Patients with hereditary fructose intolerance (HFI) must not be given AXIM E-Z-PAQUE.
- Sorbitol may cause gastrointestinal discomfort and mild laxative effect.

4.5 Interaction with other medicines and other forms of interaction

No interaction studies have been performed.

Barium sulphate, as in AXIM E-Z-PAQUE, is biologically inert and there are no known interactions with other medicines. However, the presence of barium sulphate formulations in the gastrointestinal tract may alter the absorption of therapeutic medicines taken concomitantly. In order to minimise any potential change in absorption, the separate administration of AXIM E-Z-

PAQUE 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 sulphate (residue) in the gastrointestinal tract up to several days following the examination with barium contrast media.

4.6 Fertility, pregnancy and lactation

Pregnancy

Radiographic procedures may damage the fetus, particularly during the first trimester of pregnancy. Any examination should only be carried out after careful consideration.

Breastfeeding

The use of AXIM E-Z-PAQUE is not contraindicated during breastfeeding since the absorption of barium sulphate is negligible.

Fertility

No data on fertility are available.

4.7 Effects on ability to drive and use machines

AXIM E-Z-PAQUE is unlikely to affect the ability to drive and use machines. AXIM E-Z-PAQUE has no effect on the ability to drive a vehicle and use machines.

4.8 Undesirable effects

Adverse reactions have been reported with the administration of AXIM E-Z-PAQUE formulation and are usually associated with faulty technique of administration or with underlying pathological conditions.

Undesirable effects may occur during or after a procedure with AXIM E-Z-PAQUE.

MedDRA system organ class	Frequency	Adverse event
Infections and infestations	Less frequent	peritonitis, perforation
	Unknown	pneumonitis
Blood and the lymphatic system disorders	Less frequent	adhesions, granulomas
Immune system disorders	Frequent	serious allergic reactions (rhinitis, laryngeal oedema or bronchospasm)
Vascular disorders	Less frequent	venous intravasation has led to the formation of emboli (including the hepatic portal vein, vena cava and pulmonary embolism that may be fatal in approximately 50 % of cases), deaths have occurred
Gastrointestinal disorders	Frequent	constipation, diarrhoea, nausea, abdominal pain/distention
	Unknown	impaction, obstruction, appendicitis, cramping,
Skin and subcutaneous tissue disorders	Frequent	erythema, urticaria, rash

Respiratory, thoracic and mediastinal disorders	Less frequent	accidental aspiration
Investigations	Unknown	ECG change

Post-marketing adverse events

MedDRA system organ class	**Frequency**	**Adverse event**
Infections and infestations	Unknown	bacteraemia
	Less frequent	abscess intestinal, liver abscess, peritoneal infection, pneumonia
Blood and the lymphatic system disorders	Unknown	lymphadenopathy
Immune system disorders	Unknown	hypersensitivity (including pruritus and facial swelling), potential hypersensitivity
	Less frequent	anaphylactic reaction and anaphylactic shock
Metabolism and nutrition disorders	Unknown	hyperglycaemia (in diabetic patients)
Psychiatric disorders	Unknown	agitation, confusional state, nervousness and related symptoms during administration

Nervous system disorders	Unknown	loss of consciousness, syncope, syncope vasovagal, dizziness, burning sensation, headache, dysarthria, hypotonia
Eye disorders	Unknown	eye disorders, eye swelling (usually associated with allergic reactions)
Ear and labyrinth disorders	Unknown	tinnitus
Cardiac disorders	Unknown	bradycardia, cyanosis, tachycardia
Vascular disorders	Unknown	hypotension, pallor, vasodilatation
Respiratory, thoracic and mediastinal disorders	Unknown	dyspnoea, pharyngeal oedema and pain, throat irritation or tightness, cough (when administered orally), pneumonia aspiration.
Gastrointestinal disorders	Unknown	intestinal ischemia, gastrointestinal inflammation, ulceration or perforation, abdominal discomfort, ulcerative colitis may be

		aggravated, retching; flatulence, swollen tongue
	Less frequent	vomiting
Skin and subcutaneous tissue disorders		contact dermatitis, excessive tissue granulation, hyperhidrosis
Renal and urinary disorders	Unknown	dysuria
General disorders and administration site conditions	Unknown	malaise, pain, swelling, asthenia, pyrexia
Injury and poisoning	Less frequent	diverticulitis

Description of selected adverse reactions

Allergic reactions would most likely be diffuse erythema or urticaria. This generally will respond to an antihistaminic.

More serious allergic reactions, rhinitis, laryngeal oedema or bronchospasm could develop. This should be treated immediately with 0,3 to 0,5 mL or 1:1 000 adrenaline subcutaneously. If bronchospasm predominates, 0,25 to 0,5 g of aminophylline should be given slowly intravenously. Adrenocorticosteroids may also be given.

After any barium study of the gastrointestinal tract, it is important to rehydrate the patient as quickly as possible to prevent impactions in the colon. Prevention of barium impaction in the colon also requires the use of cathartics, following completion of the examination. Saline cathartics are recommended on a routine basis and especially in patients with a history of constipation unless clinically contra-indicated. On occasions following repeated administration, severe stomach

cramps and diarrhoea occur.

Paediatric population

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

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are requested to report any suspected adverse drug reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

4.9 Overdose

Barium sulphate, as in AXIM E-Z-PAQUE, is non-toxic and absorbed systemically in negligible amounts.

Treatment is symptomatic and supportive (see sections 4.4 and 4.8).

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

Category and class: A 28 Contrast media

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

ATC code: V08BA01

Mechanism of action

Barium sulphate, as in AXIM E-Z-PAQUE, an insoluble radiopaque material which provides a positive contrast for X-ray examination. Barium sulphate is inert not absorbed or metabolised by the body and is eliminated unchanged rectally from the body.

5.2 Pharmacokinetic properties

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

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sorbitol (E420)

Sodium citrate dihydrate (E331)

Pectin (E440)

Carrageenan (E407)

Tragacanth (E413)

Citric acid anhydrous (E330)

Simeticone

Polysorbate 80

Xanthan gum (E415)

Propylene glycol

Saccharin sodium (E954)

Vanilla flavour (natural and artificial)

Strawberry flavour (natural and artificial).

6.2 Incompatibilities

Reconstitute with water only.

6.3 Shelf life

36 months.

After reconstitution, AXIM E-Z-PAQUE should be used immediately following dilution and must not be stored.

6.4 Special precautions for storage

Store at or below 25 °C in well-closed containers.

Shake well before use.

For storage conditions after reconstitution of AXIM E-Z-PAQUE, see section 6.3.

6.5 Nature and contents of container

Unit dose bottle (containing 176 g AXIM E-Z-PAQUE powder) composed of high-density polyethylene (HDPE) closed with a polypropylene screw lid.

Pack size: 425 mL bottle containing 176 g powder.

6.6 Special precautions for disposal and other handling

Adults: AXIM E-Z-PAQUE should be suspended over the density range 60 to 100 % *m/v*.

Do not use if inner seal is broken or missing.

Add water to approximately 2,5 cm above barium level. Secure lid, invert bottle and shake vigorously. Add more water to desired % *m/v* line on bottle.

Replace lid and shake for 30 seconds.

Important: Always re-shake just prior to administration to the patient.

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

7. HOLDER OF CERTIFICATE OF REGISTRATION

Axim Pharmaceuticals (Pty) Ltd

63 Old Pretoria Main Road

Halfway House 1685

Midrand, South Africa

8. REGISTRATION NUMBER

35/28/0125

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

6 December 2001

10. DATE OF REVISION OF THE TEXT

Will be allocated by SAHPRA upon registration.