SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

SCOPEX CO TABLETS, 10 mg / 250 mg tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

SCOPEX CO TABLETS: Each tablet contains hyoscine-N-butylbromide 10 mg and metamizole sodium 250 mg

Excipient(s) with known effect:

Contains sugar (sucrose): 82,52 mg

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablets

Round and smooth, white sugar-coated tablets. Odourless.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Biliary and renal colic, associated with abdominal pain,

acute spastic pain, spastic functional dysmenorrhoea, and painful spastic conditions of the female genital system.

4.2 Posology and method of administration

Posology

To relieve spastic pain in gastrointestinal, renal and female genital tracts, and for dysmenorrhoea, 1 to 2 tablets may be taken three times a day until pain is relieved.

Special populations

No information available.

Paediatric population

Safety and efficacy in children under the age of 18 years has not been established.

No data is available.

Method of administration

For oral administration.

4.3 Contraindications

- Hypersensitivity to pyrazolone or pyrazolidines (e.g., metamizole sodium, isopropylaminophenazone, propyphenazone, phenazone or phenylbutazone), or to hyoscine-N-butylbromide, or any of the inactive ingredients of SCOPEX CO TABLETS (see section 6.1). This includes patients who developed agranulocytosis, for example, following use of one of these substances.
- Patients with closed angle glaucoma or patients with a narrow angle between the iris and the cornea since its use may lead to increased intra-ocular pressure.
- Patients with prostatic enlargement, patients suffering from paralytic ileus or pyloric stenosis where its use may lead to obstruction.
- In patients, especially children, where the ambient temperature is high.
- Pronounced tachycardia, hypotension, anaphylaxis and cardiac diseases or history of cardiac disease or hypertension (see section 4.4).
- Patients with granulocytopenia.

- Patients with known analgesic-induced asthma syndrome or known analgesic intolerance of the urticaria-angioedema type, i.e. patients who develop bronchospasm or other anaphylactoid reactions in response to salicylates, paracetamol or other non-narcotic analgesics such as diclofenac, ibuprofen, indomethacin or naproxen.
- The potential of cross-sensitivity with aspirin and other non-steroidal anti-inflammatory agents exists. SCOPEX CO TABLETS should not be given to patients in whom aspirin or other nonsteroidal anti-inflammatory drugs induce symptoms of asthma, rhinitis or urticaria.
- Impaired bone marrow function (e.g., after treatment with cytostatic agents) or diseases of the haemopoietic system.
- Genetic glucose-6-phosphate-dehydrogenase deficiency (risk of haemolysis).
- Patients with acute intermittent hepatic porphyria (risk of triggering a porphyria attack).
- Megacolon.
- Myasthenia gravis.
- Asthma.
- In case of rare hereditary conditions that may be incompatible with an excipient of the product (see section 4.4).
- The third trimester of pregnancy (see section 4.6)

4.4 Special warnings and precautions for use

SCOPEX CO TABLETS should be used with caution in patients:

Hyoscine-N-butylbromide as in SCOPEX CO TABLETS is contraindicated in patients who have tachycardia, hypotension, anaphylaxis and cardiac diseases or history of cardiac disease or hypertension (see section 4.3).

Unexplained abdominal pain

- In severe cases, unexplained abdominal pain persists or worsens, or occurs together with symptoms like fever, nausea, vomiting, changes in bowel movements, abdominal tenderness,

decreased blood pressure, fainting or blood in stool, appropriate diagnostic measures are needed to investigate the etiology of the symptoms.

Haematologic reactions

- Metamizole sodium in SCOPEX CO TABLETS is a derivative of amidopyrine, and there is a risk of agranulocytosis, therefore continued administration over lengthy periods is inadvisable.
- In the event of clinical signs of haematologic reactions (such as agranulocytosis, aplastic anaemia, thrombocytopenia or pancytopenia), treatment with SCOPEX CO TABLETS must be discontinued immediately and the blood count (including differential blood count) must be monitored until it has returned to normal (see section 4.8). Discontinuation of treatment must not be delayed until the results of the lab tests are available. All patients should be advised to immediately consult a physician if during treatment with SCOPEX CO TABLETS, signs and symptoms occur which are suggestive of blood dyscrasia (e.g. general malaise, infection, persistent fever, bruising, bleeding or pallor).

Anaphylactic/anaphylactoid reactions

The risk of potentially severe anaphylactoid reactions to SCOPEX CO TABLETS is markedly higher for patients with:

- Analgesic-induced asthma syndrome or analgesic intolerance of the urticaria-angioedema type (see section 4.3).
- Bronchial asthma, in particular in the presence of rhinosinusitis and nasal polyps
- Chronic urticaria.
- Alcohol intolerance. These patients react to even minute amounts of alcoholic drinks with symptoms such as sneezing, watering eyes and severe facial flushing. Alcohol intolerance of this kind may be an indication of as yet undiagnosed analgesic-induced asthma syndrome (see section 4.3). Patients should abstain from alcohol.
- Metamizole may cause the rare, but life-threatening risk of shock (see section 4.8).
- The likelihood of anaphylactic shock is greater in susceptible patients. Particular caution is

therefore required when using SCOPEX CO TABLETS in patients with asthma or atopy.

- Patients who show an anaphylactic or other immunological reaction to SCOPEX CO TABLETS are also at high risk of responding similarly to other pyrazolones, pyrazolidines and other non-narcotic analgesics.

Severe skin reaction

- Life-threatening skin reactions, such as Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) were reported under treatment of metamizole. If signs or symptoms of SJS or TEN develop (such as skin rash often progressive with blisters or mucosal injury), treatment with SCOPEX CO TABLETS must be discontinued immediately and never be reintroduced.
- Patients should be advised of the signs and symptoms of these severe skin reactions, so that in case they develop, medical advice is sought, and these reactions can be monitored closely, particularly in the first weeks of treatment.

Gastrointestinal bleeding

- Gastrointestinal bleeding has been reported in patients treated with metamizole. Many patients had concomitantly received other treatment (e.g., NSAIDs) associated with gastrointestinal bleeding, or used an overdose of metamizole.

Intraocular pressure

- Elevation of intraocular pressure may be produced by the administration of anticholinergic agents such as hyoscine butylbromide in patients with undiagnosed and therefore untreated narrow angle glaucoma. Therefore, patients should be advised to seek urgent ophthalmological advice in case they should develop a painful, red eye with loss of vision.

Drug-induced liver injury

- Cases of acute hepatitis of predominantly hepatocellular pattern have been reported in patients treated with metamizole with an onset of few days to few months following treatment

initiation. Signs and symptoms include elevated serum hepatic enzymes with or without jaundice, frequently in context of other drug hypersensitivity reactions (e.g. skin rash, blood dyscrasias, fever and eosinophilia) or accompanied by features of autoimmune hepatitis. Most patients recovered on discontinuation of metamizole treatment; nevertheless, in isolated cases, progression to acute liver failure requiring liver transplantation was reported.

- The mechanism of metamizole-induced liver injury is not clearly elucidated, but data indicate an immuno-allergic mechanism.
- Patients should be instructed to contact their physician in case symptoms suggestive of liver injury occur. In such patients metamizole should be discontinued and liver function should be assessed.
- Metamizole should not be re-introduced in patients with an episode of hepatic injury during treatment with metamizole for which no other cause of liver injury has been determined.

Risk in specific populations

- Use with caution in elderly men and in patients with fever.
- SCOPEX CO TABLETS should only be used after consideration of the benefit-risk ratio and appropriate precautions must be taken for elderly or patients with impaired renal or hepatic function (see section 4.2).
- In diabetic patients the pyrazolone derivative can affect the enzymatic blood sugar assay by the glucose-oxidase method (GOD).

Contains sucrose

SCOPEX CO TABLETS contains sucrose which may have an effect on the glycaemic control of patients with diabetes mellitus. Patients with rare hereditary conditions such as fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take SCOPEX CO TABLETS (see sections 2 and 6.1).

4.5 Interactions with other medicines and other forms of interaction

Methotrexate

Concomitant administration of SCOPEX CO TABLETS with methotrexate may increase blood toxicity of methotrexate particularly in elderly patients. Therefore, this combination should be avoided.

Chlorpromazine

Concomitant use of metamizole and chlorpromazine can cause severe hypothermia.

Acetylsalicylic acid

SCOPEX CO TABLETS can reduce the antiplatelet effect of acetylsalicylic acid if administered concomitantly. SCOPEX CO TABLETS should therefore be used with caution in patients who are taking low-dose acetylsalicylic acid for cardio protection.

Bupropion

Blood levels of bupropion can be reduced by metamizole. Caution is therefore required if metamizole and bupropion are used concomitantly.

Cyclosporin

If SCOPEX CO TABLETS is taken concomitantly with cyclosporin, cyclosporin blood levels may be reduced and should therefore be monitored.

Medicines with anticholinergic effects

The effects of SCOPEX CO TABLETS may be enhanced by the concomitant administration of other medicines with anticholinergic properties such as amantadine, some antihistamines, butyrophenones, phenothiazines and tricyclic antidepressants, quinidine, disopyramide and other anticholinergics (e.g. tiotropium, ipratropium, atropine-like compounds) may be intensified.

Dopamine antagonists

Concomitant treatment with dopamine antagonists such as metoclopramide may result in diminution of the effects of both medicines on the gastrointestinal tract.

Beta-adrenergic agents

The tachycardic effects of beta-adrenergic agents may be enhanced by SCOPEX CO TABLETS.

Alcohol

The effect of alcohol and SCOPEX CO TABLETS can be potentiated when taken concurrently.

Additional interactions of pyrazolones

Pyrazolones may also cause interactions with oral anticoagulants, captopril, lithium and triamterene. The efficacy of antihypertensives and diuretics may be affected by pyrazolones. It is not known to what extent metamizole causes these interactions. SCOPEX CO TABLETS may also alter the effect of other active substances such as digoxin.

4.6 Fertility, pregnancy and lactation

- Safety during pregnancy and lactation has not been established. SCOPEX CO TABLETS is not recommended for use during pregnancy and lactation.

Metamizole sodium monohydrate:

- Metamizole sodium monohydrate passes the placental barrier and is excreted in breast milk and should therefore only be used during pregnancy and lactation after careful consideration of the indications.
- The breakdown products of metamizole are excreted into breast milk in considerable amounts and a risk to the breastfed infant cannot be excluded. Especially the repeated use of metamizole during breastfeeding must therefore be avoided. In case of a single administration of metamizole mothers are advised to collect and discard the breastmilk for 48 hours from its administration.

Fertility

No data on male and female fertility is available.

4.7 Effects on ability to drive and use machines

SCOPEX CO TABLETS has a moderate influence on the ability to drive and use machines (see section 4.8).

The use of SCOPEX CO TABLETS may cause drowsiness, accommodation disturbances and dulling of mental alertness. Patients should not take charge of vehicles, other means of transport, or machinery where loss of attention may lead to accidents.

If taken in the recommended dose, metamizole is not expected to affect concentration or reactions. As a precaution, at least if higher doses are taken, the possibility of impaired reactions should be borne in mind, and patients should be advised not to drive, operate machinery or conduct hazardous activities. This applies in particular in combination with alcohol.

It is not always possible to predict to what extent SCOPEX CO TABLETS may interfere with the daily activities of a patient. Patients should ensure that they do not engage in the above activities until they are aware of the measure to which SCOPEX CO TABLETS affects them.

4.8 Undesirable effects

a. Summary of the safety profile

Occasionally vomiting, giddiness and staggering may occur. Retrosternal pain may occur due to increased gastric reflux.

Hyoscine-N-butylbromide:

Side-effects of antimuscarinic agents include dryness of the mouth with difficulty of swallowing and talking, thirst, dilation of the pupils (mydriasis) with loss of accommodation (cycloplegia) and photophobia, flushing and dryness of the skin, transient bradycardia followed by tachycardia, with

palpitation and arrhythmias, and urinary urgency, difficulty and retention, as well as reduction in the tone and mobility of the gastro-intestinal tract leading to constipation. Occasionally vomiting, giddiness and staggering may occur. Retrosternal pain may occur due to increased gastric reflux.

Tricyclic anti-depressants, quinidine and amantadine can potentiate the anticholinergic effect of hyoscine-N-butylbromide. Hyoscine-N-butylbromide does not readily cross the blood-brain barrier, so central effects are rare.

Hyoscine-N-butylbromide may cause drowsiness; patients so affected should not drive or operate machinery. Patients should abstain from alcohol.

Metamizole:

Severe anaphylactic reaction may occur. Other signs of allergy which can affect the skin, mucosa, the granulopoetic system (leucopoenia, agranulocytosis) or the circulation (shock) may also occur. Very serious or even life-threatening bullous skin reactions, generally with mucous membrane involvement (Stevens-Johnson Syndrome, Lyell Syndrome), have been reported with medications containing metamizole. Should such a reaction occur, SCOPEX CO TABLETS should be discontinued at once and a physician immediately consulted.

Patients suffering from existing disturbances of blood cell formation (e.g. under cytostatic treatment) should only use SCOPEX COMPOSITUM under medical supervision.
Particular care is required in patients with systolic blood pressure values below 100 mm Hg in patients with unstable circulation (myocardial infarction, multiple injuries, initial shock).

Should symptoms of agranulocytosis, such as high fever, chills, sore throat, difficulty in swallowing, inflammation in the mouth, nose and throat as well as in the genital or anal region, occur during treatment, it should be discontinued immediately and the doctor concerned informed at once.

Shock may occur immediately or up to 1 hour after administration. If anaphylactic shock should occur intensive treatment for shock should be commenced without delay.

Counter-measures: administration of adrenaline, monitoring of pulse rate and blood pressure (e.g. dysrhythmia), anti-histamine agents, glucocorticoids (e.g. prednisolone up to 1 g i.v.), administration of plasma volume expanders, artificial respiration.

b. Tabulated summary of adverse reactions

SYSTEM ORGAN CLASS	FREQUENCY	ADVERSE REACTIONS
Immune system disorders	Less frequent	Anaphylactic reaction.
	Unknown	Anaphylactic shock including fatal outcome, dyspnoea; hypersensitivity; sweating abnormal, severe angioedema including the laryngeal region, severe bronchospasm, arrhythmia, decreased blood pressure with sometimes initially increased blood pressure.
Eye disorders	Less frequent	Accommodation disorders.

	Unknown	Dilatation of the pupils with loss of accommodation and photophobia, increased intra-ocular pressures.
Cardiac disorders	Unknown	Transient bradycardia followed by tachycardia, with palpitations and dysrhythmia, Kounis Syndrome.
Vascular disorders	Frequent	Hypotension, dizziness.
	Less frequent	Shock, flushing.
Gastrointestinal disorders	Less frequent	Dry mouth.
	Unknown	Thirst, dryness of the mouth difficulty in swallowing, as well as reduction in the tone and motility of the gastrointestinal tract leading to constipation, gastrointestinal haemorrhage.
Hepato-biliary disorders	Unknown	Drug-induced liver injury including acute hepatitis, jaundice, increased liver enzymes (see section 4.4).
Skin and subcutaneous tissue disorders	Less frequent	Skin reactions, rash maculo-papular, toxic epidermal necrolysis, Stevens-Johnson syndrome.

	Unknown	Flushing and dryness of the skin, milder reactions (e.g. skin and mucosal reactions, such as pruritus, burning sensation, erythema, swelling), may lead on to more severe reactions (e.g. generalised urticaria).
Renal and urinary disorders	Less frequent	Acute renal failure, anuria, interstitial nephritis, oliguria, proteinuria, renal impairment.
	Unknown	A desire to urinate with the inability to do so (urinary retention), chromaturia, excretion of rubazonic acid, a harmless metabolite of metamizole, may cause a red colouration of the urine, which disappears on discontinuation of treatment.

c. Description of selected adverse reactions

No information available.

d. Paediatric population

No information available.

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. Healthcare professionals are asked to report any suspected adverse reactions to SAHPRA via the “6.04 Adverse Drug

Reaction Reporting Form", found online under SAHPRA's publications:

https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose

Symptoms of overdosage:

Overdoses of hyoscine-N-butylbromide produce toxic effects similar to those of atropine, but central stimulation rarely precedes depression. The main central systems are drowsiness leading to coma.

Toxic doses may, like atropine, cause tachycardia, rapid respiration, hyperpyrexia and produce restlessness, confusion, rarely excitement with hallucinations, paranoid and psychotic reactions, hallucinations and even delirium, rapid pulse, stertorous breathing, rash on face and upper trunk. These doses may lead to increased drowsiness, stupor, occasionally seizures or convulsions, and general central depression, the latter generally leading to death. After very high doses, elimination of the metabolic rubazonic acid can cause reddish discolouration of the urine.

Metamizole:

Acute overdosage or chronic use in excessive dosage lead to dizziness, nausea, emesis, gastrointestinal pains, state of agitation, convulsion, clonic cramp, shock, coma, respiratory paralysis, liver and renal damage, sodium and fluid retention with pulmonary oedema in cardiac patients, risk of allergy and anaphylactic reactions, leucopoenia, thrombocytopenia, agranulocytosis and
aplastic anaemia.

Treatment of overdosage

Treatment is symptomatic and supportive as there is no known antidote. If required, parasympathomimetic medicines should be administered.

Hyoscine butylbromide:

- Symptoms of SCOPEX CO TABLETS overdosage respond to parasympathomimetics.
- In patients with glaucoma, pilocarpine should be used locally. Opthalmological advice should be sought urgently in cases of glaucoma.
- Cardiovascular complications should be treated according to usual therapeutic principles.
- In case of respiratory paralysis: intubation or artificial respiration should be considered.
- Catheterisation may be required for urinary retention. In addition, appropriate supportive measures should be used as required.

Metamizole:

There is no known specific antidote for metamizole.

- If metamizole was administered only recently, absorption-reducing measures (e.g. activated charcoal) can be administered in an effort to limit absorption by the body. The major metabolite (4-N-methyl-amino-antipyrine) can be eliminated by means of haemodialysis, haemofiltration, haemoperfusion or plasma filtration.
- Treatment of intoxication and prevention of severe complications may require general and specific intensive medical monitoring and treatment.

Acute measures in the event of severe medicine intolerance (shock):

At the first signs (e.g. skin reactions such as urticaria and flushing, restlessness, headache, profuse sweating, nausea) stop the administration immediately.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and class: A 5.4 Medicines affecting autonomic functions. Cholinolytics (anticholinergics)

SCOPEX CO TABLETS is a combination of hyoscine-N-butylbromide with metamizole sodium. They are used to relieve spasm of the smooth muscle in the gastrointestinal tract, the biliary tract and the urogenital tract, where an analgesic as well as an antispasmodic effect is required.

5.2 Pharmacokinetic properties

After oral administration, hyoscine-N-butylbromide may be incompletely absorbed.

5.3 Preclinical safety data

No information available.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core

Crospovidone

Dibasic Calcium Phosphate (Anhydrous)

Magnesium Stearate

Polvvinylpyrrolidone K25

Purified Talc

Composition of Coating

Purified talc

Syrup BP

Subcoat suspension

Tablet sealing solution

Titanium syrup

Wax solution

Tablet sealing solution

Acid stearic

Diethyl pthalate

Hydroxypropylmethylcellulose (Methocel E5 premium)

Polyvinlyl acetate phthalate

Chloroform spirit

Purified water

Subcoat suspension

Acacia gum powder (low bioburden)

Calcium carbonate B.P.

Polyethylene glycol 6000

Purified talc

Titanium dioxide (CI 77891)

Syrup BP

Chloroform spirit

Nipastat

Titanium syrup

Titanium dioxide (CI 77891)

Syrup B.P.

Syrup BP

Sucrose (Refined sugar)

Purified water

Chloroform spirit

Nipastat

Wax solution

Carnauba wax

Yellow beeswax

Isopropyl alcohol

Chloroform spirit

Chloroform

Ethanol 96,5 %

Purified water

6.2 Incompatibilities

No data available.

6.3 Shelf life

24 months.

6.4 Special precautions for storage

Store at or below 30 °C. Protect from light.

Keep the glass bottle tightly closed.

6.5 Nature and contents of container

SCOPEX CO TABLETS are packed in amber round glass bottles, with an extruded closed cell foam produced from low density polyethylene within a white polypropylene cap, containing either 100, 300 or 350 tablets and one or two silica gel(s) sachet(s).

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements

7. HOLDER OF CERTIFICATE OF REGISTRATION

Adcock Ingram Limited

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8. REGISTRATION NUMBER(S)

SOUTH AFRICA: B1255 (Act 101 of 1965)

NAMIBIA (NS2): 14/11.2/0410

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

December 1969

10. DATE OF REVISION OF THE TEXT

07 April 2021