SCHEDULING STATUS

S3

1. NAME OF THE MEDICINE

ASACOL SUPPOSITORIES, (500 mg) Suppositories

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Per suppository: Mesalazine (5-aminosalicylic acid) 500 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Suppositories

An opaque, pale beige, torpedo-shaped suppository with a faint fatty odour.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

ASACOL SUPPOSITORIES is used for the treatment and maintenance of remission in ulcerative colitis. The suppositories are used for the treatment of mild to moderate proctitis and proctosigmoiditis.

4.2 Posology and method of administration

Adult dose: In proctitis and proctosigmoiditis one suppository to be inserted rectally up to three times daily, after defaecation. The dosage is dependent upon the severity of the disease and it may be possible to reduce the dosage as the condition improves.

4.3 Contraindications

Hypersensitivity to mesalazine or to any other excipients, see section 6.1.

History of allergy to salicylates.

Severe liver impairment.

Patients with impaired renal function (GFR less than 30 ml per minute).

Safety in pregnancy and lactation has not been established.

Safety and efficacy have not been established in children.

Bleeding tendencies.

History of mesalazine-induced cardiac hypersensitivity.

Salicylate sensitive asthma.

4.4 Special warnings and precautions for use

Blood tests (differential blood count, liver function parameters such as ALT or AST; serum creatinine) and urinary status (dip sticks) should be determined prior to and during treatment, at the discretion of the treating medical practitioner. As a guideline, follow-up tests are recommended 14 days after commencement of treatment and then every 4 weeks for the following 12 weeks. If the findings are normal, follow-up tests should be carried out every three months. If additional signs appear, these tests should be performed immediately.

Renal impairment

ASACOL SUPPOSITORIES should not be used in patients with renal impairment. Caution should be exercised in patients with raised serum creatinine or proteinuria.

The possibility of ASACOL SUPPOSITORIES-induced nephrotoxicity should be suspected in patients developing impairment of renal function during treatment.

Treatment with ASACOL SUPPOSITORIES should be stopped **immediately** if there is evidence of renal impairment and patients should seek immediate medical advice.

Nephrolithiasis

Cases of nephrolithiasis have been reported with the use of mesalazine including stones with a 100 % mesalazine content. It is recommended to ensure adequate fluid intake during treatment.

Concurrent use of non-steroidal anti-inflammatory drugs (NSAIDs) or azathioprine may increase the risk of renal reactions (see section 4.5).

Mesalazine as contained in ASACOL SUPPOSITORIES may produce red-brown urine discoloration after contact with sodium hypochlorite bleach (e.g., in toilets cleaned with sodium hypochlorite contained in certain bleaches).

Severe cutaneous adverse reactions

Severe cutaneous adverse reactions (SCARs), including drug reaction with eosinophilia and systemic symptoms (DRESS), Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), have been reported in association with ASACOL SUPPOSITORIES treatment.

ASACOL SUPPOSITORIES should be discontinued, at the first appearance of signs and symptoms of severe skin reactions, such as skin rash, mucosal lesions, or any other sign of hypersensitivity.

Hepatic impairment

There have been reports of increased liver enzyme levels in patients taking preparations containing mesalazine. Caution is recommended if ASACOL SUPPOSITORIES is administered to patients with liver impairment. Blood tests (liver function parameters such as ALT or AST) should be performed prior to and during treatment, at the discretion of the treating medical practitioner. As a guideline, follow-up tests are recommended 14 days after commencement of treatment, then a further two to three tests at intervals of 4 weeks. If the findings are normal, follow-up tests should be carried out every 3 months. If additional symptoms occur, these tests should be performed immediately.

Blood dyscrasia

Very rarely serious blood dyscrasia has been reported. To avoid blood dyscrasia resulting from developing bone marrow depression patients should be monitored with care.

Haematological investigations including a complete blood count should be performed prior to initiation and whilst on therapy. Such tests are generally recommended within 14 days of initiation of therapy with 2 to 3 repeat tests each after another 4 weeks. If the results are normal, tests are recommended quarterly. In case additional signs of illness appear, further control tests are necessary. This procedure is to be followed especially, if a patient develops signs and symptoms suggestive of blood dyscrasia during treatment, such as unexplained bleeding, haematoma, purpura, anaemia, persistent fever or sore throat.

Treatment with ASACOL SUPPOSITORIES should be stopped **immediately** if there is a suspicion or evidence of blood dyscrasia (signs of unexplained bleeding, bruising, purpura, anaemia, persistent fever or sore throat) and patients should seek immediate medical advice (see section 4.8).

Co-administration of immunosuppressive medicines such as azathioprine or 6-MP can precipitate leukopenia (see section 4.5).

Pulmonary disease

Patients with pulmonary disease, in particular asthma, should be very carefully monitored during a course of treatment with ASACOL SUPPOSITORIES.

Cardiac hypersensitivity reactions

Mesalazine-induced cardiac hypersensitivity reactions (myo- and pericarditis) have been reported rarely with ASACOL SUPPOSITORIES. In case of previous mesalazine-induced cardiac hypersensitivity ASACOL SUPPOSITORIES must not be reintroduced. Caution should be used in patients with previous myo- or pericarditis of allergic background regardless of its origin.

Hypersensitivity to sulphasalazine

In patients with a history of hypersensitivity to sulphasalazine, therapy should be initiated only under close medical supervision. Treatment must be stopped **immediately** if acute symptoms of intolerance occur such as abdominal cramps, acute abdominal pain, fever, severe headache and rash.

Gastric and duodenal ulcers

In case of existing gastric or duodenal ulcers treatment should begin with caution based on theoretical grounds.

Geriatric patients

Use in the elderly should be handled with caution and ASACOL SUPPOSITORIES should only be prescribed to patients having a normal or non-severely impaired liver and renal function (see section 4.3).

Paediatric population

There is little experience and only limited documentation for an effect in children.

4.5 Interaction with other medicines and other forms of interaction

No interaction studies have been performed.

There is weak evidence that ASACOL SUPPOSITORIES might decrease the anticoagulant effect of warfarin.

ASACOL SUPPOSITORIES can increase the myelosuppressive effects of azathioprine, 6-mercaptopurine or thioguanine. As a result, life-threatening infection can occur. Patients should be closely observed for signs of infection and myelosuppression.

At initiation of such combination therapy haematological parameters, especially the leukocyte, thrombocyte and lymphocyte cell counts should be monitored regularly (weekly) (see section 4.4). If white blood cells are stable after 1 month, testing every 4 weeks for the following 12 weeks followed by 3 monthly monitoring intervals appears to be justified.

The concurrent use of known nephrotoxic medicines, such as non-steroidal anti-inflammatory drugs (NSAIDs) or azathioprine, may increase the risk of renal reactions (see section 4.4).

4.6 Fertility, pregnancy and lactation

Pregnancy

Safety in pregnancy has not been established.

Breastfeeding

Low concentrations of mesalazine and its N-acetyl metabolite have been detected in human breast milk. Safety in lactation has not been established.

Fertility

No effects on fertility have been observed.

4.7 Effects on ability to drive and use machines

ASACOL SUPPOSITORIES suppositories have no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

a) Summary of the safety profile

Side effects are presented by system organ class.

The only common side effect is abdominal pain (1,2 %). Organ specific allergic reactions affecting the heart, lungs, liver, kidneys, pancreas, skin and subcutaneous tissue have been reported.

In patients with a history of hypersensitivity to sulphasalazine, treatment must be stopped immediately if acute symptoms of intolerance occur such as abdominal cramps, acute abdominal pain, fever, severe headache and rash (see section 4.4).

Severe cutaneous adverse reactions (SCARs), including drug reaction with eosinophilia and systemic symptoms (DRESS), Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), have been reported in association with ASACOL SUPPOSITORIES treatment (see section 4.4).

b) Tabulated summary of adverse reactions

MedDRA System Organ Class	**Rare (≥ 1/10 000 to < 1/1 000)**	**Very rare (< 1/10 000)**	**Frequency not known**
Blood and lymphatic system disorders		Altered blood counts (aplastic anaemia, agranulocytosis, pancytopenia, neutropenia, leukopenia, thrombocytopenia), and eosinophilia (as part of an allergic reaction), bone marrow depression.	
Immune system disorders		Hypersensitivity reactions such as allergic exanthema,	Hypersensitivity Reaction including anaphylactic reaction.

		drug fever, lupus erythematosus syndrome, with pericarditis and pleuro-pericarditis as prominent symptoms as well as rash, pancolitis.	
Nervous system disorders	Headache, dizziness.	Peripheral neuropathy.	
Cardiac disorders	Myocarditis, pericarditis.		
Respiratory, thoracic and mediastinal disorders		Allergic and fibrotic lung reactions (including dyspnoea, cough, bronchospasm, alveolitis, pulmonary eosinophilia, lung infiltration, pneumonitis).	Pleurisy, interstitial pneumonia.
Gastrointestinal disorders	Abdominal pain, diarrhoea, flatulence, nausea, vomiting.	Acute pancreatitis.	Exacerbation of the symptoms of colitis.
Hepato-biliary disorders		Changes in liver function parameters (increase in transaminases and cholestasis	

		parameters), hepatitis, cholestatic hepatitis.	
Skin and subcutaneous tissue disorders	Photosensitivity* * See section c).	Alopecia.	Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS), Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN).
Musculo-skeletal, connective tissue and bone disorders		Myalgia, arthralgia.	
Renal and urinary disorders		Impairment of renal function including acute and chronic interstitial nephritis and renal insufficiency.	Nephrotic syndrome, renal failure which may be reversible on withdrawal, nephrolithiasis** ** see section 4.4 for further information.
Reproductive system and breast disorders		Oligospermia (reversible).	
General disorders and administration site conditions			Intolerance to mesalazine with C-reactive protein increased and/or exacerbation of

			symptoms of underlying disease, local reaction.

c) Description of selected adverse reactions

An unknown number of the above undesirable effects are probably associated to the underlying IBD rather than ASACOL SUPPOSITORIES/mesalazine medication. This holds true especially for gastrointestinal undesirable effects.

To avoid blood dyscrasia resulting from developing bone marrow depression patients should be monitored with care, see section 4.4.

Under co-administration of immunosuppressive medicines such as azathioprine, or 6-MP or thioguanine life-threatening infection can occur, see section 4.5.

Photosensitivity

More severe reactions are reported in patients with pre-existing skin conditions such as atopic dermatitis and atopic eczema.

d) Paediatric population

There is only limited safety experience with the use of ASACOL SUPPOSITORIES in the paediatric population. It is expected that the target organs of possible adverse reactions in the paediatric population are the same as for adults (heart, lungs, liver, kidneys, pancreas, skin and subcutaneous tissue).

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

In case of accidental oral ingestion symptoms of overdosage include that of salicylism, e.g.: dizziness, tinnitus, deafness, sweating, nausea and vomiting, headache, mental confusion, hyperventilation, fever, restlessness, ketosis, respiratory alkalosis and metabolic acidosis. Depression of the central nervous system may lead to coma, cardiovascular collapse and respiratory failure.

There is no specific treatment for overdosage of ASACOL SUPPOSITORIES, but early lavage is recommended, if accidentally taken by mouth.

Treatment is symptomatic and supportive.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: ATC code: A07EC02, Intestinal anti-inflammatory agents.

Mesalazine in suppositories act locally, probably involving the inhibition of prostaglandin and leucotriene synthesis.

5.2 Pharmacokinetic properties

Mesalazine is mostly excreted in the faeces either as 5-aminosalicylic acid (5-ASA) or N-acetyl-5-ASA. About 20 percent of the 5-ASA released in the colon, is absorbed and rapidly acetylated to N-acetyl-5-ASA, which is excreted in the urine.

The acetylated metabolite (active ingredient) has a half-life of approximately ten hours and that of the parent compound approximately one hour.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Hard fat.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

6.4 Special precautions for storage

Store at or below 25 °C in a cool place, protected from light.

6.5 Nature and contents of container

Cartons of 20 suppositories, in white opaque cavity-formed PVC strips, printed on one side.

6.6 Special precautions for disposal and other handling

Not applicable

7. HOLDER OF CERTIFICATE OF REGISTRATION

Equity Pharmaceuticals (Pty) Ltd

100 Sovereign Drive

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Nellmapius Drive, Irene

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0157

8. REGISTRATION NUMBER(S)

Z/11.10/206

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of Registration: 27 June 1996

10. DATE OF REVISION OF THE TEXT

22 March 2024

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