SCHEDULING STATUS

S3

1. NAME OF THE MEDICINE

PONSTEL 250, 250 mg capsules

PONSTEL FORTE, 500 mg tablets

PONSTEL S, 50 mg/5 mL suspension

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

PONSTEL 250:

Each capsule contains:

Mefenamic acid 250 mg

Excipients with known effect:

Contains sugar (lactose monohydrate): 60 mg

For full list of excipients, see section 6.1.

PONSTEL FORTE:

Each tablet contains:

Mefenamic acid 500 mg

Sugar free

For full list of excipients, see section 6.1.

PONSTEL S:

Each 5 mL suspension contains:

Mefenamic acid 50 mg

Excipients with known effect:

Preservative (sodium benzoate): 0,5 % *m/v*

Contains ethanol 96,5 %: 0,025 mL

Contains sugar (sucrose): 1,0 g

Contains sorbitol 70 % solution: 970 mg

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

PONSTEL 250:
Capsules.
Size '1' hard gelatin capsules with an ivory opaque body and cap containing a white to slightly off-white powder.

PONSTEL FORTE:
Tablets.
Buff-coloured, round, biconvex tablets.

PONSTEL S:
Suspension.
A creamy, light caramel coloured, uniform suspension with a butter toffee and anise mint odour and taste.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

PONSTEL is indicated for the treatment of post traumatic conditions such as pain, swelling and inflammation, for a maximum period of 5 days.
PONSTEL is indicated for the relief of mild to moderate pain in acute and chronic conditions including: pain of traumatic, arthritic or muscular origin; primary dysmenorrhoea; headache and dental pain. It is also indicated as an antipyretic in febrile conditions.

PONSTEL reduces blood loss in menorrhagia where the menorrhagia is due to ovulatory dysfunctional bleeding. Uterine and other pathology should first be excluded before prescribing PONSTEL for this indication.

4.2 Posology and method of administration

Posology

Use the lowest effective dose for the shortest possible duration of treatment. Therapy should not be continued for longer than 7 days.

Adults: 500 mg three times per day
In menorrhagia the dosage is 500 mg three times a day beginning with the onset of menstrual flow and continuing for five days or until cessation of flow, whichever is less.

In primary dysmenorrhoea the dosage is 500 mg three times a day commencing at the onset of period pain and continued for up to three days while the symptoms persist.

The doses may be repeated as necessary, up to three times daily.
Gastric irritation may be reduced by taking medication during meals.

Special populations
No information available.

Paediatric population
Children (6 months and older): 25 mg/kg of body weight daily, in divided doses, or:

- 6 months to 1 year: One medicine measureful (5 mL)
- 2 to 4 years: Two medicine measuresful (10 mL)
- 5 to 8 years: Three medicine measuresful (15 mL)
- 9 to 12 years: Four medicine measuresful (20 mL)

The doses may be repeated as necessary, up to three times daily.
Gastric irritation may be reduced by taking medication during meals.

Method of administration
For oral administration.

4.3 Contraindications

- Hypersensitivity to any of the active ingredients, as listed in section 6.
- Non-selective NSAIDs are contraindicated in heart failure.
- Sensitivity to mefenamic acid and other non-steroidal anti-inflammatory agents with prostaglandin-synthetase inhibiting activity. Because the possibility exists for cross-sensitivity among nonsteroidal anti-inflammatory agents, PONSTEL should not be given to patients in whom these drugs induce symptoms of bronchospasm, allergic rhinitis, or urticaria.
- PONSTEL is contraindicated in patients with chronic inflammation of either the upper or lower gastro-intestinal tract, in patients with a history of peptic and/or intestinal ulceration, patients with impaired renal or hepatic function, and epileptics.

- All non-selective NSAIDs are contraindicated where there is a history of gastrointestinal perforation, ulceration or bleeding (PUBs) related to previous NSAIDs, including PONSTEL.
- Non-selective NSAIDs are also contraindicated where there is active or a history of recurrent ulcer/ haemorrhage/ perforations.
- Avoid use of NSAIDs in women around 30 weeks gestation and later in pregnancy due to the risks of oligohydramnios/foetal renal dysfunction and premature closure of the foetal ductus arteriosus (see section 4.4 and 4.6).

4.4 Special warnings and precautions for use

- If diarrhoea or skin rash appear, PONSTEL should be discontinued immediately. Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolyis have been reported. PONSTEL should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.
- Caution is required in patients with a history of hypertension and/or heart failure as fluid retention and oedema have been reported in association with PONSTEL therapy. In view of the product's inherent potential to cause fluid retention, heart failure may be precipitated in some compromised patients.
- Elderly: The elderly have an increased frequency of adverse reactions to NSAIDs including PONSTEL, especially gastrointestinal perforation, ulceration and bleeding (PUBs) which may be fatal.
- The risk of gastrointestinal perforation, ulceration or bleeding (PUBs) is higher with increasing doses of PONSTEL, in patients with a history of ulcers, and the elderly.
- When gastrointestinal bleeding or ulceration occurs in patients receiving PONSTEL, treatment with PONSTEL should be stopped.
- PONSTEL should be given with caution to patients with a history of gastrointestinal disease (e.g. ulcerative colitis, Crohn's disease, hiatus hernia, gastro-oesophageal reflux disease, angiodysplasia) as the condition may be exacerbated.
- Caution should be exercised in the administration of PONSTEL to patients suffering from dehydration and/or renal disease, particularly the elderly.
- Bronchoconstriction may occur with mefenamic acid in asthmatic patients with aspirin sensitivity.
- Mefenamic acid and its metabolites may give a false positive reaction to certain urine tests for the presence of bile.

- Toxicity has also been seen in patients with prerenal condition leading to a reduction in renal blood flow or blood volume. Patients at greatest risk are those with impaired renal function, heart failure, liver dysfunction, those taking diuretics, and the elderly.
- Caution is required in patients with significant risk factors for cardiovascular events (e.g. hypertension, hyperlipidaemia, diabetes mellitus, smoking) and should only be treated with mefenamic acid after careful consideration.
- Regular use of NSAIDs such as PONSTEL during the third trimester of pregnancy, may result in premature closure of the foetal ductus arteriosus *in utero*, and possibly, in persistent pulmonary hypertension of the new-born. The onset of labour may be delayed and its duration increased (see section 4.6).
- Foetal Toxicity: Limit use of NSAIDs, including PONSTEL, between 20 and 30 weeks of pregnancy due to the risk of oligohydramnios/foetal renal dysfunction. Avoid use of NSAIDs in women around 30 weeks gestation and later in pregnancy due to the risks of oligohydramnios/foetal renal dysfunction and premature closure of the foetal ductus arteriosus.
- If NSAID treatment is necessary between 20 weeks and 30 weeks gestation, limit PONSTEL use to the lowest effective dose and shortest duration possible. Consider ultrasound monitoring of amniotic fluid if PONSTEL treatment extends beyond 48 hours. Discontinue PONSTEL if oligohydramnios occurs and follow up according to clinical practice (see section 4.3 and 4.6).
- Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) has been reported in patients taking NSAIDs such as PONSTEL. Some of these events have been fatal or life-threatening. DRESS typically, although not exclusively, presents with fever, rash, lymphadenopathy, and/or facial swelling. Other clinical manifestations may include hepatitis, nephritis, haematological abnormalities, myocarditis, or myositis. Sometimes symptoms of DRESS may resemble an acute viral infection. Eosinophilia is often present. Because this disorder is variable in its presentation, other organ systems not noted here may be involved. It is important to note that early manifestations of hypersensitivity, such as fever or lymphadenopathy, may be present even though rash is not evident. If such signs or symptoms are present, discontinue PONSTEL and evaluate the patient immediately.

PONSTEL 250 contains lactose monohydrate

Patients with rare hereditary disorders such as galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

PONSTEL S contains sodium benzoate

This medicine contains 5 mg sodium benzoate in each 10 mL which is equivalent 0,5 % *m/v*. Sodium benzoate may increase jaundice (yellowing of the skin and eyes) in new-born babies (up to 4 weeks old) (see section 4.3).

PONSTEL S contains sodium

This medicine contains less than 1 mmol sodium (23 mg) per 5 mL, that is to say essentially 'sodium-free'.

PONSTEL S contains ethanol

This medicine contains 0,025 mL of alcohol (ethanol) in each unit volume which is equivalent to 5 % *v/v*. The small amount of alcohol in this medicine will not have any noticeable effects.

PONSTEL S contains sucrose

Patients with rare hereditary problems of fructose intolerance, glucose-galactose mal-absorption or sucrase-isomaltase insufficiency should not take this medicine.

PONSTEL S contains sorbitol

This medicine contains 970 mg sorbitol in each 5 mL which is equivalent to 19,4 % *m/v*.
Patients with the rare hereditary condition of sorbitol / maltitol / lactitol intolerance should not take PONSTEL S.
Sorbitol may cause gastrointestinal discomfort and mild laxative effect.

4.5 Interactions with other medicines and other forms of interaction

- Patients receiving an anticoagulant drug concurrently with PONSTEL have had a prolongation of prothrombin time. PONSTEL is contraindicated for patients taking an anticoagulant drug if careful and continuous monitoring of the levels of prothrombin and Factors VII, IX and X is not available.
- Anti-coagulants: PONSTEL may enhance the effects of anti-coagulants such as warfarin.
- Anti-platelet medicines and selective serotonin reuptake inhibitors (SSRIs): increased risk of gastrointestinal bleeding.
- Patients receiving lithium concurrently with NSAIDs, including PONSTEL, have produced an elevation of plasma lithium levels and a reduction in renal lithium clearance. Thus, when

PONSTEL and lithium are administered concurrently, patients should be observed carefully for signs of lithium toxicity.

- NSAIDs: use of two or more NSAIDs concomitantly could result in an increase in side effects.
- Corticosteroids: increased risk of gastrointestinal perforation, ulceration or bleeding (PUBs).

4.6 Fertility, pregnancy and lactation

Pregnancy

- Safety in pregnancy has not yet been established.
- Regular use of non-steroidal anti-inflammatory drugs during the third trimester of pregnancy, may result in premature closure of the foetal ductus arteriosus *in utero*, and possibly, in persistent pulmonary hypertension of the new-born. The onset of labour may be delayed and its duration increased (see section 4.3).
- Use of NSAIDs, including PONSTEL, can cause premature closure of the foetal ductus arteriosus and foetal renal dysfunction leading to oligohydramnios and, in some cases, neonatal renal impairment. Because of these risks, the use of PONSTEL dose and duration between 20 and 30 weeks of gestation should be limited and avoided at around 30 weeks of gestation and later in pregnancy (see section 4.3 and 4.4).

Breastfeeding

Safety in lactation has not yet been established.

Fertility

No data on male and female fertility is available.

4.7 Effects on ability to drive and use machines

No information available.

4.8 Undesirable effects

a. Summary of the safety profile

The most frequently reported side effects were gastrointestinal disturbances, and include: diarrhoea, nausea with or without vomiting and abdominal pain. Diarrhoea may occur within 24 hours following usual analgesic dosage. When diarrhoea occurs, the medication should be discontinued immediately. Serious gastro-intestinal toxicity such as bleeding, ulceration, and

perforation can occur at any time with or without warning symptoms, sometimes fatal, in patients treated chronically with nonsteroidal anti-inflammatory agents. Elderly or debilitated patients seem unable to tolerate ulceration or bleeding as well as some other individuals; most spontaneous reports of gastro-intestinal events are in this population.

b. Tabulated summary of adverse reactions

SYSTEM ORGAN CLASS	ADVERSE REACTIONS
Blood and lymphatic system disorders	Temporary lowering of the white blood cell count has occurred but does not appear to be dose-related. Blood counts should be performed at regular intervals during long term administration. Haemolytic anaemia may develop in patients taking PONSTEL continuously for extended periods. While this condition is generally reversible, death due to PONSTEL-associated haemolytic anaemia has been reported. Liver function tests must be carried out regularly to monitor elevation of enzymes and bilirubin. Other reported haematological effects include agranulocytosis, decreased hematocrit, leukopenia, eosinophilia, aplastic anaemia, pancytopenia, thrombocytopenia or thrombocytotopenic purpura and bone marrow aplasia.
Immune system disorders	Acute hypersensitivity reactions (urticaria, bronchospasm, anaphylaxis) have occurred. Because of the possibility of cross-sensitivity due to structural relationships which exist among nonsteroidal anti-inflammatory medicines, acute allergic reactions may be more likely to occur in patients who have exhibited allergic reactions to these compounds. Angioedema, oedema of the larynx, Stevens-Johnson syndrome, Lyell's syndrome (toxic epidermal necrolysis), erythema multiforme, perspiration, urticaria, rash and facial oedema may occur. Occurrence of rash is a definite reason for stopping medication because exfoliative dermatitis has been reported on continued use after development of a rash.
Metabolism and nutrition	Glucose intolerance in diabetic patients.

disorders	
Nervous system disorders	Headache, drowsiness, dizziness, nervousness, convulsions, insomnia, visual disturbances and ear pain have been reported.
Cardiac disorders	Hypotension, palpitations, oedema, hypertension and cardiac failure.
Respiratory, thoracic and mediastinal disorders	Asthma, dyspnoea.
Gastrointestinal disorders	The most frequently reported side effects were gastrointestinal disturbances, and include: diarrhoea, nausea with or without vomiting and abdominal pain. Diarrhoea may occur within 24 hours following usual analgesic dosage. When diarrhoea occurs, the medication should be discontinued immediately. Serious gastro-intestinal toxicity such as bleeding, ulceration, and perforation can occur at any time with or without warning symptoms, sometimes fatal, in patients treated chronically with nonsteroidal anti-inflammatory agents. Elderly or debilitated patients seem unable to tolerate ulceration or bleeding as well as some other individuals; most spontaneous reports of gastro-intestinal events are in this population. Less frequently reported gastrointestinal side effects include: anorexia, pyrosis, flatulence, enterocolitis, colitis, steatorrhoea, cholestatic jaundice, hepatitis, pancreatitis, hepatorenal syndrome, mild hepatic toxicity, constipation and peptic ulceration with and without gastro-intestinal haemorrhage. Other gastrointestinal effects include: dyspepsia, melaena, haematemesis, ulcerative stomatitis, exacerbation of colitis and Crohn's disease, gastritis.
Skin and subcutaneous tissue disorders	Bullous reactions, including Stevens-Johnson syndrome and toxic epidermal necrolysis. Less frequently reported side effects include: Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) (see section 4.4).

Renal and urinary disorders	Renal failure, allergic glomerulonephritis, papillary haematuria, dysuria and hyponatremia have occurred. There have been reports of acute interstitial nephritis with haematuria, proteinuria and occasionally, nephrotic syndrome.

c. Description of selected adverse reactions

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

Mefenamic acid has a marked tendency to induce tonic-clonic (grand mal) convulsions in overdosage. Dyskinesia, acute renal failure and coma have been reported. Overdose has led to fatalities.

Treatment is symptomatic and supportive. Following accidental overdosage, the stomach should be emptied by inducing emesis or gastric lavage followed by administration of activated charcoal. Vital functions should be monitored and supported. Haemodialysis is of little value since mefenamic acid and its metabolites are firmly bound to plasma proteins.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and class: A 2.7 Antipyretic or antipyretic and anti-inflammatory analgesics.

PONSTEL is an analgesic preparation with anti-inflammatory properties. PONSTEL is known to have a peripheral anti-inflammatory effect and has also shown antipyretic action.

The pharmacological activity of PONSTEL may be due in part to its ability to inhibit the synthesis of prostaglandins. PONSTEL also inhibits the action of exogenous prostaglandins on uterine muscle, uterine tube contraction and ovarian cyclic AMP and progesterone formation in animal models.

5.2 Pharmacokinetic properties

Mefenamic acid is well absorbed from the gastro-intestinal tract. Peak plasma concentrations occur in about 2 to 4 hours, with a half-life of 2 to 4 hours. Plasma levels are proportional to dose, following multiple doses, with no drug accumulation.

Mefenamic acid is extensively bound to plasma proteins. Over 50 % of the dose may be recovered in the urine as unchanged drug or conjugated metabolites.

5.3 Preclinical safety data

No information available.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

PONSTEL 250:

D & C yellow No. 10 (CI 47005)

FD & C red No. 3 (CI 45430)

Gelatin

Lactose monohydrate

Titanium dioxide (CI 77891)

PONSTEL FORTE:

Calcium stearate

Colloidal anhydrous silica (silicon dioxide)

Hydroxypropyl cellulose

Microcrystalline cellulose

Starch corn (maize starch)

Sodium lauryl sulphate

Spectracol quinoline (PLK0013) (Colour D & C yellow No. 10 lake (CI 47005)

Spectracol erythrosine lake (805005) FD &C red No.3 lake (CI 45430)

PONSTEL S:

Caramel 48000 (clarkes)
Carboxymethylcellulose sodium 7MF
Ethanol 96,5 %
Flavor anise mint LR3072A
Flavor butter toffee 78185-33
Glucono delta lactone
Hydrochloric acid AR 37 %
Povidone K29-32
Purified water
Sodium benzoate
Sodium hydroxide B.P
Sorbitol 70 % solution (non-crystallising)
Sugar granulated (sucrose)
Veegum HV

6.2 Incompatibilities

No data available.

6.3 Shelf life

PONSTEL 250: 36 months.
PONSTEL FORTE: 24 months.
PONSTEL S: 24 months.

6.4 Special precautions for storage

Store in a cool (at or below 25 ºC), dry place.
Keep the blisters in outer carton until required for use.
Keep bottle tightly closed.
PONSTEL FORTE to be protected from direct sunlight.

6.5 Nature and contents of container

PONSTEL 250:
250 mg capsules in containers of 100's and 250's, and blister packs of 20's.

- **100's pack:** White cylindrically shaped polypropylene securitainer (49 x 75 mm) with a round white LDPE closure.

- **250's pack:** White cylindrically shaped polypropylene securitainer (62 x 152 mm) with a round white LDPE Closure.
- **250's pack:** White cylindrical shaped high-density polyethylene (HDPE) container (475 mL, 53 x 450 cc) with screw cap with an inside wad seal.
- **20's pack:** Clear, transparent, non-toxic well thermo formable, food grade PVC film on printed aluminium foil with VMCH coating (dull side printing).

PONSTEL FORTE:
500 mg tablets in containers of 50's.

- **50's Blister pack**: Clear, transparent, non-toxic, well thermo formable, food grade PVC film on aluminium foil with VMCH coating on bright side (dull side printing).
- **50's Securitainer pack:** White or grey polypropylene securitainer (0205), 49 mm LDPE closure and cotton wool balls as wadding.
- **50's HDPE container:** 160mL (35 x 150) white colour cylindrical screw type high density polyethylene (HDPE) container with a white colour HDPE screw cap with induction seal Wad.

PONSTEL S:
Suspension in bottles of 100 ml, 200 ml and 2,5 L.
PONSTEL S, is packed using the following packaging materials:

- 100 mL or 200 mL amber glass bottles with a 28 mm white polypropylene cap with liner.
- 2,5 L rectangular amber HDPE bottle with a utility thread finish with a 3,15 mm white polypropylene cap with liner.

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
1 New Road,
Erand Gardens,
Midrand,

1685

Customer Care: 0860 ADCOCK / 232625

8. REGISTRATION NUMBER(S)

PONSTEL 250: 28/2.7/0703

PONSTEL FORTE: 28/2.7/0548

PONSTEL S: 28/2.7/0704

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

PONSTEL 250: 28 October 1994

PONSTEL FORTE: 30 March 1994

PONSTEL S: 15 August 1994

10. DATE OF REVISION OF THE TEXT

14 October 2022

Namibia:

PONSTEL 250:	NS2 05/2.7/0266
PONSTEL FORTE:	NS2 05/2.7/0267
PONSTEL S:	NS2 05/2.7/0268

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