SCHEDULING STATUS

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1 NAME OF THE MEDICINE

Dr Du Toit's Pain Expeller Tablets (300 mg)

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains Aspirin 300 mg

Excipients with known effect: Dr Du Toit's Pain Expeller contains sugar (sucrose 3,30 mg) per tablet.

For full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Tablets

Dr du Toit's Pain Expeller tablets are white, normal concave round, scored on one side and plain on the other side, having a faint acidic odour.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Effective for the relief of pain of moderate intensity.

4.2 Posology and method of administration

Use the lowest effective dose for the shortest possible duration of treatment.

Posology

ADULTS: One or two tablets three times a day with water.

Method of administration

Dr Du Toit's Pain Expeller tablets can be dissolved in water, or if preferred, on the tongue.

4.3 Contraindications

- Hypersensitivity to aspirin, or to any of the excipients in Dr Du Toit's Pain Expeller
- Heart failure
- History of gastrointestinal perforation, ulceration or bleeding (PUBs) related to previous NSAIDs, including Dr Du Toit's Pain Expeller
- Active or history of recurrent ulcer, haemorrhage or perforations
- Severe renal impairment
- Concomitant oral anti-coagulant therapy

- Haemophilia
- Pregnancy and lactation (see section 4.6)
- Not to be used in children under the age of 12 years (see section 4.4).

4.4 Special warnings and precautions for use

Do not use continuously for longer than ten days without consulting your doctor.

Not for children under 12 years of age (see section 4.3).

Heart conditions:

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 Dr Du Toit's Pain Expeller therapy. In view of the Dr Du Toit's Pain Expeller'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 Dr Du Toit's Pain Expeller, especially gastrointestinal perforation, ulceration and bleeding (PUBs) which may be fatal.

Gastrointestinal perforation, ulceration or bleeding (PUBs):

The risk of gastrointestinal perforation, ulceration or bleeding (PUBs) is higher with increasing doses of Dr Du Toit's Pain Expeller, in patients with a history of ulcers, and the elderly.

When gastrointestinal bleeding or ulceration occurs in patients receiving Dr Du Toit's Pain Expeller, treatment with Dr Du Toit's Pain Expeller should be stopped.

Dr Du Toit's Pain Expeller should be given with caution to patients with a history of gastrointestinal disease (e.g. ulcerative colitis, Crohn's disease, hiatus hernia, gastroesophageal reflux disease, angiodysplasia) as the condition may be exacerbated.

Dr Du Toit's Pain Expeller should be stopped several days before scheduled surgical procedures because of the possibility of increased bleeding times.

Hypersensitivity reactions:

Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis have been reported. Dr Du Toit's Pain Expeller should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity including paroxysmal bronchospasm and dyspnoea.

Dr Du Toit's Pain Expeller should not be used in patients with asthma or allergic disorders. It should not be given to patients with a history of sensitivity reactions to aspirin or to other NSAID's, including those in whom attacks of asthma, angioedema, urticaria, or rhinitis have been precipitated by such medicines (see section 4.3).

Pregnancy:

Regular use of NSAIDs such as Dr Du Toit's Pain Expeller 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.

The use of Dr Du Toit's Pain Expeller around 20 weeks of gestation or later in pregnancy may cause foetal renal dysfunction, which may progress to renal failure with oligohydramnios, and in some cases neonatal renal impairment.

Complications of prolonged oligohydramnios may include limb contractures and delayed lung maturation.

Reye's Syndrome:

Aspirin as contained in Dr Du Toit's Pain Expeller has been implicated in Reye's syndrome, a rare but serious illness in children and teenagers with chickenpox and influenza. A doctor should be consulted before Dr Du Toit's Pain Expeller is used in such patients.

General:

High doses of Dr Du Toit's Pain Expeller may precipitate acute haemolytic anaemia in patients with G6PD deficiency.

Aspirin such as Dr Du Toit's Pain Expeller should be administered with caution to patients with impaired renal function, dyspepsia, anaemia and when the patient is dehydrated.

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 diclofenac after careful consideration.

Dr Du Toit's Pain Expeller contains sucrose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

Drug Reaction with Eosinophillia and Systemic Symptoms (DRESS)

Drug Reaction with Eosinophillia and Systemic Symptoms (DRESS) has been reported in patients taking NSAIDs such as Dr Du Toit's Pain Expeller Tablets. 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. Eosinophillia 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 Dr Du Toit's Pain Expeller Tablets and evaluate the patient immediately.

4.5 Interaction with other medicines and other forms of interaction

NSAIDs:

The use of two or more NSAIDs concomitantly could result in an increase in side effects. The plasma concentrations of some other NSAID's, for example fenbufen, indomethacin and piroxicam, may be decreased when given concomitantly with Dr Du Toit's Pain Expeller.

Corticosteroids:

Concomitant treatment with corticosteroids may increase the risk of gastrointestinal perforation, ulceration or bleeding (PUBs).

Corticosteroids may reduce plasma-salicylate concentrations. Conversely, salicylate toxicity may occur if corticosteroids are withdrawn.

Anti-coagulants:

Dr Du Toit's Pain Expeller may enhance the effects of anti-coagulants such as warfarin.

Anti-platelet medicines and selective serotonin reuptake inhibitors (SSRIs):

Increased risk of gastrointestinal bleeding.

Others

Antacids may increase the excretion of aspirin, as in Dr Du Toit's Pain Expeller, in alkaline urine.

Dr Du Toit's Pain Expeller inhibits the effect of uricosurics such as probenecid and sulfinpyrasone and may alter the efficacy of mifepristone.

Dr Du Toit's Pain Expeller may increase the activity of sulfonylurea hypoglycaemic medicines, zafirlukast, methotrexate, phenytoin and valproate.

Use of Dr Du Toit's Pain Expeller with medicines such as dipyridamole, metoclopramide, metoprolol and carbonic anhydrase inhibitors may result in increased plasma-salicylate concentrations.

Barbiturates and other sedatives may mask the respiratory symptoms of Dr Du Toit's Pain Expeller overdosage and have been reported to enhance its toxicity.

Alcohol may exacerbate the gastrointestinal effects of Dr Du Toit's Pain Expeller.

Interference with laboratory tests:

Dr Du Toit's Pain Expeller may produce falsely increased results for blood creatinine, urate (low dose aspirin) and urea. Falsely decreased results may be obtained for blood thyroxine and urate (> 4 g/day aspirin) and for urinary 5-HIAA (with nitrosonaphthol method).

Urinary VMA (HMMA) levels may be falsely increased or decreased depending on the method of analysis.

Urinary glucose oxidase: Dr Du Toit's Pain Expeller may cause a false negative test in the presence of glycosuria.

4.6 Fertility, pregnancy and lactation

Dr Du Toit's Pain Expeller is contraindicated during pregnancy and lactation.

Regular use of non-steroidal anti-inflammatory drugs (NSAIDs) 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.

The administration of Dr Du Toit's Pain Expeller around 20 weeks or later in pregnant patients may cause foetal renal dysfunction, which may progress to renal failure with oligohydramnios, and in some cases neonatal renal impairment (see 4.3 & 4.4).

4.7 Effects on ability to drive and use machines

None known.

4.8 Undesirable effects

Side effects of Dr Du Toit's Pain Expeller treatment are listed below. The frequencies of these reported side effects are unknown.

Blood and lymphatic system disorders

Increased bleeding time decreased platelet adhesiveness. Prolonged use in high doses may lead to hypoprothrombinaemia and other blood disorders including thrombocytopenia.

Immune system disorders

Hypersensitivity reactions, including skin eruptions, urticaria, angioedema, rhinitis, paroxysmal bronchospasm and dyspnoea.

Nervous system disorders

Dizziness

Cardiac disorders

Oedema, hypertension and cardiac failure

Gastrointestinal disorders

The most frequently observed adverse events are gastrointestinal in nature.

Peptic ulcers, perforation or gastrointestinal bleeding, sometimes fatal. Nausea, vomiting, diarrhoea, flatulence, constipation, dyspepsia, abdominal pain, melaena, haematemesis, ulcerative stomatitis, exacerbation of colitis and Crohn's disease, gastritis.

Hepato-biliary disorders

Hepatotoxicity, especially in patients with juvenile idiopathic arthritis or other connective tissue disorders.

Skin and subcutaneous tissue disorders

Bullous reactions, including Stevens-Johnson syndrome and toxic epidermal necrolysis.

Drug Reaction with Eosinophillia and Systemic Symptoms (DRESS) (see section 4.4).

Respiratory, thoracic and mediastinal disorders

Bronchospasm, asthma attacks.

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 providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8.wp-content/uploads/2020/01/6.04_ARF1_v5.1_27Jan2020.pdf

4.9 Overdose

Symptoms include dizziness, tinnitus, deafness, sweating, nausea, headache, vomiting and mental confusion.

Symptoms of more acute or severe intoxication following overdose include hyperventilation, fever, ketosis, respiratory alkalosis and metabolic acidosis.

Depression of the central nervous system may lead to coma, cardiovascular collapse or respiratory failure. In children drowsiness and metabolic acidosis commonly occur, hypoglycaemia may be severe. In cases of overdosage consult a doctor immediately.

Gastric lavage, fluid and electrolyte management is the mainstay of treatment with the immediate aim being correction of acidosis, hyperpyrexia, hypokalaemia and dehydration. Salicylate remaining in the stomach may

be adsorbed by activated charcoal. Alkaline diuresis, haemodialysis or haemoperfusion are effective methods of removing salicylate from the plasma.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Analgesic and antipyretic: ATC code: N02BA01

Aspirin have analgesic, anti-inflammatory and anti-pyretic actions. Aspirin inhibits the cyclo-oxygenase enzyme involved in conversion of phospholipids to prostaglandins. Aspirin also inhibits platelet aggregation.

5.2 Pharmacokinetic properties

Absorption:

Aspirin is rapidly absorbed from the stomach and the upper small intestine when taken orally. Peak values are reached in 1 hour and then declines gradually.

Distribution:

Plasma protein binding is 80 to 90 %.

Biotransformation:

Once absorbed, aspirin is rapidly converted to salicylic acid and then by further conversion to other metabolites.

Elimination:

The plasma half-life of aspirin is approximately 15-20 minutes and that of salicylic acid is 2-3 hours. Metabolites are excreted by the kidneys in both free and conjugated form.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Maize starch, Talc, *Sugar and starch granules* - Benzoic acid (preservative), Gelatine powder, Maize starch, Sucrose

6.2 Incompatibilities

None Known

6.3 Shelf life

3 years

6.4 Special precautions for storage

Store in a well-closed container at or below 25 °C in a dry place.

6.5 Nature and contents of container

DR DU TOIT'S PAIN EXPELLER is packaged in aluminium-aluminium strips or aluminium/OPA-aluminium-PVC blisters.

Strips and blisters contain 7 or 10 tablets per strip. Two or three strips are inserted together with the package insert per outer carton. Pack sizes: 14 or 30 tablets per outer carton.

DR DU TOIT'S PAIN EXPELLER is also packaged in white opaque HDPE bottle and white polypropylene screw cap with induction seal. 10 cm of absorbent cotton and a 2 g silica gel bag are included with 1 000 tablets per bottle.

6.6 Special precautions for disposal and other handling

Oral administration after dissolution in water.

7 HOLDER OF CERTIFICATE OF REGISTRATION

iPharma (Pty) Ltd

124 Elevation Avenue, Randjesfontein

MIDRAND, 1683, SOUTH AFRICA

8 REGISTRATION NUMBER

B/2.8/977

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date on the registration certificate of the medicine: 08/11/1984

10 DATE OF REVISION OF THE TEXT

07/01/2022