SCHEDULING STATUS: S4

PROPRIETARY NAME (AND DOSAGE FORM):

ARTHROTEC® 50 (Tablets)

ARTHROTEC® 75 (Tablets)

COMPOSITION:

ARTHROTEC 50: Each tablet consists of an enteric-coated core containing 50 mg diclofenac sodium surrounded by an outer mantle containing 200 mcg misoprostol.

ARTHROTEC 75: Each tablet consists of an enteric-coated core containing 75 mg diclofenac sodium surrounded by an outer mantle containing 200 mcg misoprostol.

PHARMACOLOGICAL CLASSIFICATION:

A 3.1 Antirheumatics

PHARMACOLOGICAL ACTION:

Diclofenac is a non-steroidal anti-inflammatory medicine with anti-inflammatory and analgesic properties.

Misoprostol is a synthetic prostaglandin E_1 analogue that enhances several of the factors that maintain gastroduodenal mucosal integrity.

The pharmacokinetic profiles of diclofenac and misoprostol administered as ARTHROTEC are similar to the profiles when the two drugs are administered as separate tablets. No pharmacokinetic interaction between the two drugs has been observed following multiple doses.

INDICATIONS:

ARTHROTEC is indicated for patients who require a nonsteroidal anti-inflammatory drug (NSAID) together with misoprostol.

The diclofenac component of ARTHROTEC is indicated for the treatment of osteoarthritis and rheumatoid arthritis. The misoprostol component of ARTHROTEC is indicated for the prophylaxis of NSAID-induced gastric and duodenal ulceration.

CONTRA-INDICATIONS:

ARTHROTEC is contra-indicated in patients with a history of gastrointestinal bleeding or perforation (PUBs) related to previous NSAIDs (see also WARNINGS AND SPECIAL PRECAUTIONS) and in patients with active or history of recurrent ulcer/haemorrhage/perforations.

ARTHROTEC is contra-indicated in pregnant women and in women planning a pregnancy as it may increase uterine tone and contractions in pregnancy which could produce miscarriage. Also, it may cause premature closure of the ductus arteriosus.

ARTHROTEC is contra-indicated during lactation.

ARTHROTEC is contra-indicated in patients with a known hypersensitivity to diclofenac, aspirin, other NSAIDs, misoprostol or other prostaglandins.

ARTHROTEC is contra-indicated in patients with heart failure.

WARNINGS AND SPECIAL PRECAUTIONS:

Use in pre-menopausal women (see also Contra-indications): ARTHROTEC should not be used in pre-menopausal women unless they use effective contraception and have been advised of the risks of taking the product if pregnant (see Contra-indications).

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 ARTHROTEC therapy.

Elderly: The elderly have an increased frequency of adverse reactions to NSAIDs, especially gastrointestinal bleeding and perforation (PUBs) which may be fatal.

The risk of gastrointestinal bleeding or perforation is higher with increasing doses of ARTHROTEC in patients with a history of ulcers, and the elderly.

When gastrointestinal bleeding or ulceration occurs in patients receiving ARTHROTEC, treatment should be stopped.

ARTHROTEC 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.

Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis have been reported. ARTHROTEC should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

ARTHROTEC may decrease platelet aggregation and prolong bleeding time. This effect should be considered when bleeding times are determined.

Fluid retention and oedema have been observed in patients taking NSAIDs, including ARTHROTEC. Therefore, ARTHROTEC should be used with caution in patients with compromised cardiac function or conditions predisposing to fluid retention.

In patients with renal, cardiac or hepatic impairment, caution is required since the use of NSAIDs, including ARTHROTEC, may result in deterioration of renal function. The dose should be kept as low as possible and renal function should be monitored.

All patients who are receiving long-term treatment with NSAIDs, including ARTHROTEC, should be monitored as a precautionary measure (eg. renal, hepatic function and blood counts).

DOSAGE AND DIRECTIONS FOR USE:

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

Adults

ARTHROTEC 50: One tablet to be taken with food, two or three times daily.

ARTHROTEC 75: One tablet to be taken with food, twice daily.

Tablets should be swallowed whole and not be chewed.

Elderly/Renal Impairment/Hepatic Impairment

No adjustment of dosage is necessary in the elderly or in patients with hepatic impairment or mild to moderate renal impairment as pharmacokinetics are not altered to any clinically relevant extent. Nevertheless, patients with severe renal or hepatic impairment should be closely monitored (see also WARNINGS AND SPECIAL PRECAUTIONS).

Children

The safety and efficacy of ARTHROTEC in children has not been established.

SIDE-EFFECTS:

Gastrointestinal: The most commonly 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.

Magnesium containing antacids may aggravate the diarrhoea caused by ARTHROTEC.

Cardiovascular: Oedema, hypertension and cardiac failure.

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

Liver: Clinically significant elevations of SGPT, SGOT, alkaline phosphatase or bilirubin have been observed in association with ARTHROTEC without symptomatic evidence of hepatic disease.

Kidney: As a class, NSAIDs have been associated with renal pathology such as papillary necrosis and interstitial nephritis.

Female reproductive system: Menorrhagia, intermenstrual bleeding and vaginal bleeding have been reported in pre-menopausal women and vaginal bleeding in post-menopausal women.

Other adverse effects: Headache, dizziness, skin rashes and allergic reactions including anaphylaxis may occur.

Interactions with other medicaments and other forms of interaction

NSAIDs: use of two or more NSAIDs concomitantly could result in an increase in side-effects.

ARTHROTEC may attenuate the natriuretic efficacy of diuretics due to inhibition of intrarenal synthesis of prostaglandins. Concomitant treatment with potassium-sparing diuretics may be associated with increased serum potassium levels. Hence serum potassium should be monitored.

Steady state plasma lithium and digoxin levels may be increased.

Pharmacodynamic studies with diclofenac have shown no potentiation of oral hypoglycaemic and anticoagulant drugs. However, as interactions have been reported with other NSAIDs, caution and adequate monitoring are nevertheless advised.

Corticosteroids: increased risk of gastrointestinal ulceration or bleeding (PUBs).

Anti-coagulants: ARTHROTEC may enhance the effects of anti-coagulants such as warfarin.

Anti-platelet agents and selective serotonin reuptake inhibitors (SSRIs): increased risk of gastrointestinal bleeding.

Caution is advised when methotrexate is administered concurrently with ARTHROTEC because of possible enhancement of its toxicity as a result of an increase of methotrexate plasma levels.

Pregnancy and lactation

ARTHROTEC is contra-indicated in pregnancy (see Contra-indications). ARTHROTEC should not be administered during breast feeding (see Contra-indications).

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

The toxic dose of ARTHROTEC has not been determined and there is no experience of overdosage. Intensification of the pharmacological effects may occur with overdosage. Management of acute poisoning with ARTHROTEC essentially consists of supportive and symptomatic measures. It is reasonable to take measures to reduce absorption of any recently consumed drug by forced emesis, gastric lavage or activated charcoal.

IDENTIFICATION:

ARTHROTEC 50: White, round, biconvex tablets marked  on one side and SEARLE 1411 on the other side.

ARTHROTEC 75: White, round, biconvex tablets marked 

on one side and SEARLE 1421 on the other side.

PRESENTATION:

ARTHROTEC 50 is available in blister packs of 20 and 60 tablets.

ARTHROTEC 75 is available in blister packs of 30 tablets.

STORAGE INSTRUCTIONS:

Store in a cool dry place (below 25 °C).

Keep out of reach of children.

REGISTRATION NUMBERS:

ARTHROTEC 50: 28/3.1/0440

ARTHROTEC 75: 32/3.1/0353

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION:

Pfizer Laboratories (Pty) Ltd
85 Bute Lane
Sandton 2196
South Africa

DATE OF PUBLICATION OF THIS PACKAGE INSERT:

1. Last Council Approval : 23 September 2006
2. Compliance with regulation 9 & 10 : 15 February 2017

Arthrotec 50:

BOTSWANA: Reg No.:

NAMIBIA:S2 Reg No.: 04/3.1/0719

Arthrotec 75:

NAMIBIA:S2 Reg No.: 04/3.1/0719