PACKAGE INSERT

SCHEDULING STATUS:

S3

PROPRIETARY NAME AND DOSAGE FORM:

ROXIFEN (CAPSULES)

COMPOSITION:

Each capsule contains: Piroxicam 20 mg

PHARMACOLOGICAL CLASSIFICATION:

A 3.1 ANTIRHEUMATICS (Anti-inflammatory Agents)

PHARMACOLOGICAL ACTION:

Piroxicam has analgesic, anti-inflammatory and antipyretic properties. Piroxicam acts as an inhibitor of prostaglandin biosynthesis.

Piroxicam is completely absorbed after oral administration: peak concentrations in plasma occur within two to four hours. Neither food nor-antacids alter the rate or extent of absorption.

After absorption, piroxicam is extensively (99 %) bound to plasma proteins, and has a long plasma half-life of approximately forty eight hours. At steady state (eg. After seven to ten days) concentrations of piroxicam in plasma and synovial fluid are approximately equal.

Piroxicam is metabolised in the liver by hydroxylation of the pyridyl ring of the piroxicam side chain followed by conjugation with glucuronic acid and urinary elimination. Less than 5 % of the medicine is excreted in the urine unchanged.

INDICATIONS:

Roxifen is indicated for conditions requiring anti-inflammatory and/or analgesic activity, such as rheumatoid arthritis: osteo-arthritis (arthrosis, degenerative joint disease): ankylosing spondylitis: acute musculoskeletal disorders and acute gout.

CONTRA-INDICATIONS:

Roxifen should not be used in those patients who have previously shown a sensitivity to piroxicam.
The potential exists for cross sensitivity to aspirin and other non-steroidal anti-inflammatory agents. Do not administer to patients sensitive to aspirin or other non-steroidal anti-inflammatory agents; patients who have hepatic dysfunction; patients with a history of gastrointestinal haemorrhage or ulcers.
Roxifen should not be used in patients on coumarin-type anticoagulants, established ischaemic heart disease and/or cerebrovascular disease (stroke) and peripheral arterial disease, perioperative analgesia in the setting of coronary artery bypass surgery (CABS).

Roxifen should not be used in those patients with a known sulphonamide hypersensitivity.

Use during Pregnancy: The safety of Roxifen use during pregnancy or during lactation has not yet been established. Use in Children: Roxifen is not recommended for children.

WARNINGS:

Roxifen may predispose to cardiovascular events, gastrointestinal events, or cutaneous reactions which may be fatal.

Care should be exercised in patients with impairment of renal function. **Roxifen** decreases platelet aggregation and prolongs bleeding time. Use with caution in patients with cardiovascular disorders, where oedema may worsen the condition. Serious skin reactions, which can be fatal, may occur. There appears

to be a higher risk for cardiovascular events with higher doses and longer duration of treatment. Caution is advised when **Roxifen** is prescribed to patients with cardiovascular risk factors e.g. hypertension, diabetes, smoking and hypercholesterolaemia. Because of its lack of platelet effects, **Roxifen** is not a substitute for aspirin for cardiovascular prophylaxis.

INTERACTIONS:

Because of its lack of platelet effects, **Roxifen** is not a substitute for aspirin for cardiovascular prophylaxis. There is no consistent evidence that concurrent use of aspirin mitigates the increased risk of serious cardiovascular thrombotic events associated with **Roxifen**. **Roxifen** increases plasma lithium levels.

PREGNANCY AND LACTATION:

The safety of Roxifen use during pregnancy or during lactation has not yet been established.

Regular use of non steroidal anti-inflammatory drugs during the thrid 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.

DOSAGE AND DIRECTIONS FOR USE:

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

Rheumatoid arthritis; osteo-arthritis (arthrosis, degenerative joint disease); ankylosing spondylitis:

The usual daily dose for the relief of signs and symptoms of rheumatoid arthritis or ostea-arthritis is 20 mg given in single or divided doses. Since steady state concentrations in plasma are not reached for seven to ten days, maximal therapeutic responses should not be expected for two weeks. Longterm administration of doses higher than 30 mg carries an increased risk of gastrointestinal side-effects.

Acute musculoskeletal disorders:

Therapy should be initiated with 40 mg daily for the first two days given in single or divided doses. For the remainder of the seven to fourteen day treatment period, the dose should be reduced to 20 mg daily.

Acute gout:

Therapy should be initiated by a single oral dose of 40 mg followed on the next four to six days by 40 mg given in a single or divided dosage. Roxifen is not indicated for the long-term management of gout.

SIDE-EFFECTS AND SPECIAL PRECAUTIONS:

Gastrointestinal symptoms are the most commonly encountered side-effects. Long-term administration of doses higher than 30 mg daily carries an increased risk of gastrointestinal side effects.

Peptic ulceration and gastrointestinal bleeding have been reported with Roxifen.

Other than the gastrointestinal symptoms, cardiac symptoms include peripheral oedema, aggravated hypertension, arrhythmia, hypertension, palpitations, tachycardia, congestive cardiac failure, myocardial infarction and cardiovascular thrombotic events. Neurological events include cerebrovascular events (stroke).

Changes in different liver function parameters have been observed. Some patients may develop increased serum transaminase levels during treatment with **Roxifen**. Blood-urea-nitrogen elevation has been observed in some patients. These elevations are not progressive over the course of treatment with **Roxifen**, a plateau being reached which returns to or towards baseline levels if treatment is stopped. The rise in blood-urea-nitrogen is not associated with elevations in serum creatinine.

Dermal sensitivity reactions, usually in the form of skin rash, have been reported. Stevens-Johnson syndrome may develop.

Decreases in haemoglobin and haematocrit, independent of gastrointestinal bleeding, have occurred. Thrombocytopenia and non-thrombocytopenic purpura (Henoch-Schonlein), aplastic anaemia, leucopenia and eosinnophilia have been reported and constitute indications for immediate withdrawal of **Roxifen**.

It should be assumed that **Roxifen** will precipitate bronchoconstriction in those patients who are hypersensitive to aspirin. Central nervous system effects such as dizziness, headache, somnolence and vertigo have been reported.

In view of the product's inherent potential to cause fluid retention, heart failure may be precipitated in some compromised patients.

Special precautions:

Due to inhibition of prostaglandin synthesis, fluid retention and oedema have been observed in patients taking **Roxifen**, therefore **Roxifen** should be used with caution in patients with compromised cardiac function and other conditions predisposing to, or worsened be, fluid retention. Patients wit pre-existing congestive heart failure or hypertension should be closely monitored.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

See Side-Effects and Special Precautions

In the event of overdosage with **Roxifen** supportive and symptomatic therapy is indicated.

IDENTIFICATION:

Capsule with opaque white body/opaque maroon cap.

PRESENTATION:

Glass bottles of 30 capsules

White Polypropylene containers of 30 capsules

STORAGE INSTRUCTIONS:

Store below 25°C. Protect from light.

KEEP OUT OF REACH FROM CHILDREN.

REGISTRATION:

27/3.1/0059

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

Gulf Drug Company (Pty)

Ltd 22 Burnside Drive

Old Mill Industrial Park

Mount Edgecombe, 4300

www.gulfdrug.co.za

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