SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Sulindac 200 mg tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 200 mg of sulindac.

3 PHARMACEUTICAL FORM

Brilliant yellow, hexagonal-shaped tablets, with one side scored and marked '942'.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Sulindac is a non-steroidal, analgesic/anti-inflammatory agent with antipyretic properties.

Indicated in osteoarthritis, rheumatoid arthritis, ankylosing spondylitis, acute gouty arthritis, peri-articular disorders such as bursitis, tendinitis, and tenosynovitis.

4.2 Posology and method of administration

Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms (see section 4.4 'Special warnings and special precautions for use').

For oral use to be taken preferably with or after food.

The dosage should be taken twice a day and adjusted to the severity of the disease.

The usual dosage is 200 mg twice daily. However, the dosage may be lowered depending on the response. Doses above 400 mg per day are not recommended.

In the treatment of acute gouty arthritis, therapy for seven days is usually adequate.

In peri-articular disorders, treatment should be limited to seven to ten days.

Sulindac should be administered preferably with fluids or food.

Children: The use of sulindac in children is contra-indicated.

Use in the elderly: The elderly are at increased risk of the serious consequences of adverse reactions. If an NSAID is considered necessary, the lowest effective dose should be used and for the shortest possible duration. The patient should be monitored regularly for GI bleeding during NSAID therapy.

4.3 Contraindications

Hypersensitivity to any component of this product.

Severe heart failure.

The use of sulindac is contra-indicated in severe renal failure and in patients with hepatic insufficiency. Poor liver function may alter the blood levels of circulating metabolites of sulindac.

Sulindac should not be used in patients in whom acute asthmatic attacks, urticaria, rhinitis, or angioedema have been precipitated by ibuprofen, aspirin or other non-steroidal anti-inflammatory agents.

The drug should not be administered to patients with active gastro-intestinal bleeding or a history of gastro-intestinal bleeding or perforation related to previous NSAID therapy.

The use of sulindac should be avoided in patients with active or previous peptic ulcer or haemorrhage (two or more distinct episodes of proven ulceration or bleeding).

Since paediatric indications and dosage have not yet been established, sulindac should not be given to children.

Use of sulindac is contraindicated during the last trimester of pregnancy (see section 4.6 ‘Pregnancy and lactation’).

4.4 Special warnings and precautions for use

Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms (see section 4.2 ‘Posology and method of administration’ and GI and cardiovascular risks below).

Caution should be advised in patients receiving concomitant medications which could increase the risk of gastrotoxicity or bleeding, such as corticosteroids, or anticoagulants such as warfarin, selective serotonin re-uptake inhibitors, or anti-platelet agents such as aspirin (see section 4.5 'Interaction with other medicinal products and other forms of interaction').

The use of sulindac with concomitant NSAIDs including cyclooxygenase-2-inhibitors should be avoided (see Section 4.5 'Interaction with other medicinal products and other forms of interaction').

Elderly
The elderly have an increased frequency of adverse reactions to NSAIDs especially gastrointestinal bleeding and perforation which may be fatal (see Section 4.2 'Posology and method of administration')

Platelet aggregation
Sulindac has less effect on platelet function and bleeding time than aspirin; however, since sulindac is an inhibitor of platelet function, patients who may be adversely affected should be carefully observed when sulindac is administered.

Gastro-intestinal effects
Sulindac should be used with caution in patients having a history of gastro-intestinal haemorrhage, ulcers, ulcerative colitis or Crohn's disease. Gastro-intestinal bleeding, ulceration or perforation, which can be fatal, has been reported with all NSAIDs at any time during treatment, with or without warning symptoms or a previous history of serious GI events. Patients should report experiencing any of these effects, particularly the elderly and the treatment should be withdrawn. Patients with a history of GI toxicity, particularly when elderly, should report any unusual abdominal symptoms (especially GI bleeding).

In patients with a history of peptic ulcer disease and in the elderly, NSAIDs should be given only after other forms of treatment have been considered.

The risk of GI bleeding, ulceration or perforation is higher with increasing NSAID doses, in patients with a history of ulcer, particularly if complicated with haemorrhage or perforation (see section 4.3 'Contraindications'), and in the elderly. These patients should commence treatment on the lowest dose available. Combination therapy with protective agents (e.g. misoprostol or proton pump inhibitors) should be considered for these patients, and also for patients requiring concomitant low dose aspirin, or other drugs likely to increase gastrointestinal risk (see section 4.5 'Interaction with other medicinal products and other forms of interaction').

Respiratory effects
Caution is required if administered to patients suffering from, or with a previous history of bronchial asthma, since NSAIDs have been reported to precipitate bronchospasm in some patients.

Hypersensitivity syndrome
A potentially life-threatening, apparent hypersensitivity syndrome has been reported. In cases where the syndrome is suspected, therapy should be discontinued immediately, and not recontinued. This syndrome may include constitutional symptoms (fever, chills, diaphoresis, flushing), cutaneous findings (rash or other dermatological reactions - see 4.8 'Undesirable Effects'), conjunctivitis, involvement of major organs (changes in liver-function tests, hepatic failure, jaundice, pancreatitis, pneumonitis with or without pleural effusion, leucopenia, leucocytosis, eosinophilia, disseminated intravascular coagulation, anaemia, renal impairment, including renal failure), and other less specific findings (adenitis, arthralgia, arthritis, myalgia, fatigue, malaise, hypotension, chest pain, tachycardia).

Infections
Non-steroidal anti-inflammatory drugs, including sulindac, may mask the usual signs and symptoms of infection; therefore, the physician must be continually on the alert for this and should use the drug with extra care in the presence of existing infection.

Ocular effects
Because of reports of adverse eye findings with agents of this class it is recommended that patients who develop eye complaints during treatment with sulindac have ophthalmological evaluations.

Cardiovascular and cerebrovascular effects
Peripheral oedema has been observed in some patients taking sulindac; therefore, as with other drugs in this class, sulindac should be used with caution in patients with compromised cardiac function, hypertension, or other conditions predisposed to fluid retention.

Appropriate monitoring and advice are required for patients with a history of hypertension and/or mild to moderate congestive heart failure as fluid retention and oedema have been reported in association with NSAID therapy.

Clinical trial and epidemiological data suggest that use of some NSAIDS (particularly at high doses and in long term treatment) may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke). There are insufficient data to exclude such a risk for sulindac.

Patients with uncontrolled hypertension, congestive heart failure, established ischaemic heart disease, peripheral arterial disease, and/or cerebrovascular disease should only be treated with sulindac after careful consideration. Similar consideration should be made before initiating longer-term treatment of patients with risk factors for cardiovascular disease (e.g. hypertension, hyperlipidaemia, diabetes mellitus, smoking).

Hepatic effects
A patient with signs and/or symptoms suggesting liver dysfunction, or in whom an abnormal liver-function test has occurred, should be evaluated for

evidence of a more severe hepatic reaction while on therapy. Significant elevations of AST (SGOT) and ALT (SGPT) (three times higher than normal) were seen in less than 1% of patients in controlled clinical trials.

Cases of hepatitis, jaundice, or both, with or without fever, may occur within the first three months of therapy. In some patients, the findings are consistent with those of cholestatic hepatitis.

Fever or other evidence of hypersensitivity, including abnormalities in one or more liver-function tests and skin reactions, have occurred during therapy. Some fatalities have occurred.

Whenever a patient develops unexplained fever, rash or other dermatological reactions, or constitutional symptoms, sulindac should be permanently stopped and liver function investigated. Fever and abnormal liver function are reversible.

Renal effects
As with other non-steroidal anti-inflammatory drugs, there have been reports of acute interstitial nephritis with haematuria, proteinuria and, occasionally, nephrotic syndrome in patients receiving sulindac.

In patients with reduced renal blood flow where renal prostaglandins play a major role in maintaining renal perfusion, administration of a non-steroidal anti-inflammatory agent may precipitate overt renal decompensation. Patients at greatest risk of this reaction are those with renal or hepatic dysfunction, diabetes mellitus, advanced age, extracellular volume depletion, congestive heart failure, sepsis, or concomitant use of any nephrotoxic drug. A non-steroidal anti-inflammatory drug should be given with caution and renal function should be monitored in any patient who may have reduced renal reserve. Discontinuation of non-steroidal anti-inflammatory therapy is usually followed by recovery to the pre-treatment state.

Since sulindac is eliminated primarily by the kidneys, patients with significantly impaired renal function should be closely monitored; a lower daily dosage should be used to avoid excessive drug accumulation.

Sulindac metabolites have been reported rarely as the major, or a minor, component in renal stones in association with other calculus components. Sulindac should be used with caution in patients with a history of renal lithiasis and they should be kept well hydrated while receiving sulindac. In patients with renal functional impairment, since the major route of excretion of the drug is via the kidney, the dosage may need to be reduced.

Skin reactions
Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis, have been reported very rarely in association with the use of NSAIDs (see section 4.8 ‘Undesirable effects’). Patients appear to be at highest risk for these reactions early in the course of therapy: the onset of the reaction occurring in the

majority of cases within the first month of treatment. Sulindac should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

Female fertility
The use of sulindac may impair female fertility and is not recommended in women attempting to conceive. In women who have difficulties conceiving or who are undergoing investigation of infertility, withdrawal of sulindac should be considered.

SLE and connective tissue disease
In patients with systemic lupus erythematosus (SLE) and mixed connective tissue disorders there may be an increased risk of aseptic meningitis (see Section 4.8 'Undesirable effects')

4.5 Interaction with other medicinal products and other forms of interaction

Dimethyl sulphoxide

Dimethyl sulphoxide should not be used with Sulindac. Concomitant use has been reported to reduce plasma levels of the active metabolite of Sulindac, and also cause peripheral neuropathy.

Methotrexate

Caution should be used if Sulindac is administered concomitantly with methotrexate. Non-steroidal anti-inflammatory drugs have been reported to decrease the tubular secretion of methotrexate and potentiate the toxicity.

Ciclosporin

Administration of non-steroidal anti-inflammatory drugs concomitantly with ciclosporin has been associated with an increase in ciclosporin-induced toxicity, possibly due to the decreased synthesis of renal prostaciclin. NSAIDs should be used with caution in patients taking ciclosporin, and renal function should be monitored carefully.

Oral anticoagulants

NSAIDs may enhance the effects of anticoagulants, such as warfarin (see section 4.4, Special warnings and precautions for use). Although Sulindac and its sulphide metabolite are highly bound to protein, studies (in which Sulindac was given at a dose of 400 mg daily) have shown no clinically significant interaction with oral anticoagulants. However patients should be monitored carefully until it is certain that no change in their anticoagulant dose is required.

Hypoglycaemic agents

Although sulindac and its sulphide metabolite are highly bound to protein, studies (in which Sulindac was given at a dose of 400 mg daily) have shown no clinically

significant interaction with oral hypoglycaemic agents. However, patients should be monitored carefully until it is certain that no change in their hypoglycaemic dose is required.

Lithium

Concomitant use of indomethacin with lithium, produced a clinically relevant elevation of plasma lithium and reduction in renal lithium clearance in psychiatric patients and normal subjects with steady-state plasma lithium concentrations. This effect has been attributed to inhibition of prostaglandin synthesis and the potential exists for a similar effect with other NSAIDs. As a consequence, when an NSAID and lithium are given concomitantly, the patient should be observed carefully for signs of lithium toxicity. In addition the frequency of monitoring serum lithium concentrations should be increased at the outset of such combination therapy.

Aspirin

Concomitant administration with aspirin in normal volunteers significantly depressed plasma levels of the active sulphide metabolite. Clinical study of the combination showed an increase in GI side effects with no improvement in the therapeutic response to Sulindac. The combination is not recommended.

Diflunisal

Concomitant administration with diflunisal in normal volunteers reduced the plasma level of active sulphide metabolite by approximately one-third.

Other NSAIDS

The concomitant use of Sulindac with other NSAIDs including cyclooxygenase-2-selective inhibitors is not recommended due to the increased possibility of gastro-intestinal toxicity, with little or no increase in efficacy.

Probenecid

Probenecid given concomitantly with sulindac had only a slight effect on plasma sulphide levels, while plasma levels of sulindac and sulphone were increased. Sulindac was shown to produce a modest reduction in the uricosuric action of probenecid which probably is not usually significant.

Antihypertensive agents

NSAIDs reduce antihypertensive effect. There is some evidence that Sulindac reduces the antihypertensive effect of thiazides and a variety of other agents used to treat mild to moderate hypertension to a lesser extent than other NSAIDs. However, the blood pressure of patients taking Sulindac with antihypertensive agents should be closely monitored.

Cardiac glycosides/digoxin

An increase in serum-digoxin concentration has been reported with concomitant use of aspirin, indomethacin and other NSAIDs. Therefore when concomitant digoxin and

NSAID therapy is initiated or discontinued, serum-digoxin levels should be closely monitored. NSAIDs may exacerbate cardiac failure, reduce GFR and increase plasma glycoside levels.

Diuretics

NSAIDs may reduce the effect of diuretics. Diuretics can increase the risk of nephrotoxicity of NSAIDs.

Corticosteroids

The risk of gastro-intestinal bleeding and ulceration associated with NSAIDs is increased when used with corticosteroids.

Mifepristone

NSAIDs and aspirin should be avoided until at least 8 to 12 days after administration of mifepristone.

Quinolone antibiotics

Animal data indicate that NSAIDs can increase the risk of convulsions associated with quinolone antibotics. Patients taking NSAIDs and quinolones may have increased risk of developing convulsions.

Antiplatelet agents and serotonin re-uptake inhibitors (SSRIs)

Increased risk of gastrointestinal bleeding (see section 4.4 'Special warnings and precautions for use')

Tacrolimus

Possible increased risk of nephrotoxicity when NSAIDs are given with tacrolimus.

Zidovudine

There is evidence of an increased risk of haemarthroses and haematoma in HIV (+) haemophiliacs receiving concurrent treatment with zidovudine and ibuprofen. This increased risk of haematological toxicity may apply to other NSAIDs when given with zidovudine.

4.6 Fertility, pregnancy and lactation

Pregnancy

Sulindac should not be used during the first two trimesters of pregnancy unless clearly necessary.

Congenital abnormalities have been reported in association with NSAID administration in man; however, these are low in frequency and do not appear to follow any discernible pattern.

The known effects of drugs of this class on the human foetus during the third trimester of pregnancy include: constriction of the ductus arteriosus prenatally, tricuspid incompetence, and pulmonary hypertension; non-closure of the ductus arteriosus postnatally which may be resistant to medical management; myocardial degenerative changes, platelet dysfunction with resultant bleeding, intracranial bleeding, renal dysfunction or failure, renal injury/dysgenesis which may result in prolonged or permanent renal failure, oligohydramnios, gastro-intestinal bleeding or perforation and increased risk of necrotising enterocolitis.

Among above, oligohydramnios resulted from foetal renal dysfunction may be caused by sulindac use from the 20th week of pregnancy onward. This may occur shortly after treatment initiation and is usually reversible upon discontinuation. In addition, there have been reports of ductus arteriosus constriction following treatment in the second trimester, most of which resolved after treatment cessation. **Therefore, during the first and second trimester of pregnancy, sulindac should not be given unless clearly necessary.** If sulindac is used by a woman attempting to conceive, or during the first and second trimester of pregnancy, the dose should be kept as low and duration of treatment as short as possible. Antenatal monitoring for oligohydramnios and ductus arteriosus constriction should be considered after exposure to sulindac for several days from gestational week 20 onward. Sulindac should be discontinued if oligohydramnios or ductus arteriosus constriction are found.

Use of sulindac during the third trimester of pregnancy is contraindicated (see below and section 4.3).

During the third trimester of pregnancy, all prostaglandin synthesis inhibitors may expose the foetus to:
- Cardiopulmonary toxicity (premature constriction/closure of the ductus arteriosus and pulmonary hypertension);
- Renal dysfunction (see above);

the mother and the neonate, at the end of pregnancy to:
- Possible prolongation of bleeding time, an anti-aggregating effect which may occur even at very low doses;
- Inhibition of uterine contractions resulting in the delayed onset of labour or prolonged labour.

Lactation
It is not known whether sulindac is excreted in human milk. Because other drugs of this class are excreted in human milk, a decision should be made whether to discontinue breast-feeding or discontinue the drug, taking into account the importance of the drug to the mother.

Fertility

See Section 4.4 ‘Special warnings and precautions for use’ regarding female fertility.

4.7 Effects on ability to drive and use machines

Sulindac may cause dizziness, drowsiness, fatigue or visual disturbances in some people. Patients taking the product should not drive or operate machinery unless it has been shown not to interfere with their physical or mental ability.

4.8 Undesirable effects

Sulindac is generally well tolerated. Those side effects experienced are usually mild and may often respond to a reduction in dosage.

Side effects reported frequently

Gastro intestinal: the most frequent types of side effects occurring with sulindac are gastro intestinal; these include gastro intestinal pain, dyspepsia, nausea with or without vomiting, diarrhoea, constipation, flatulence, anorexia, and gastro intestinal cramps.

Dermatological: rash, pruritus.

Central nervous system: dizziness, headache, nervousness.

Special senses: tinnitus.

Miscellaneous: oedema.

Side effects reported less frequently

The following side effects were reported less frequently. The probability exists of a causal relationship between sulindac and these side effects:

Gastro intestinal: stomatitis, gastritis or gastro enteritis. Peptic ulcer, exacerbation of colitis and Crohn’s disease (see Section 4.4‘Special warnings and precautions for use’) have been reported, as well as gastro intestinal bleeding and gastro-intestinal perforations, sometimes fatal, particularly in the elderly. Pancreatitis, ageusia, glossitis, intestinal strictures (diaphragms), haematemisis, melaena, nausea.

It has also been reported that a probable sulindac metabolite has been found in biliary sludge in patients with symptoms of cholecystitis who underwent a cholecystectomy.

Hepatic: Liver-function-test abnormalities, jaundice sometimes with fever, cholestasis, hepatitis, hepatic failure.

Dermatological: purpura, sore or dry mucous membranes, alopecia, photosensitivity, erythema multiforme, toxic epidermal necrolysis, Stevens Johnson syndrome, exfoliative dermatitis.

Cardiovascular: congestive heart failure, especially in patients with marginal cardiac function; palpitation, hypertension.

Oedema, hypertension and cardiac failure have been reported in association with NSAID treatment.

Clinical trial and epidemiological data suggest that use of some NSAIDS (particularly at high doses and in long term treatment) may be associated with an increased risk of arterial thrombotic events (for example myocardial infarction or stroke) (see section 4.4 'Special warnings and precautions for use').

Haematological: thrombocytopenia; ecchymosis; purpura; leucopenia; agranulocytosis; neutropenia; bone-marrow depression, including aplastic anaemia; haemolytic anaemia, increased prothrombin time in patients on oral anticoagulants.

Renal/Genito urinary: urine discoloration, dysuria, vaginal bleeding, haematuria, proteinuria, crystalluria, renal impairment including renal failure, interstitial nephritis, nephrotic syndrome.

Nervous system: hallucinations, malaise, fatigue, drowsiness, vertigo, somnolence, insomnia, sweating, asthenia, paraesthesia, convulsions, syncope, depression, confusion, psychic disturbances including acute psychosis, aseptic meningitis (especially in patients with systemic lupus erythematosus (SLE) and, mixed connective tissue disease), with symptoms such as stiff neck, headache, nausea, vomiting, fever, or disorientation (see Section 4.4 'Special warnings and precautions for use').

Metabolic: Hyperkalaemia.

Musculoskeletal: Muscle weakness.

Special senses: visual disturbances including blurred vision, optic neuritis, decreased hearing, metallic or bitter taste.

Respiratory: epistaxis.

Hypersensitivity: Hypersensitivity reactions have been reported following treatment with NSAIDs. These may consist of (a) non-specific allergic reactions and anaphylaxis (b) respiratory tract reactivity comprising asthma, aggravated asthma,

bronchospasm or dyspnoea, or (c) assorted skin disorders, including rashes of various types, pruritus, urticaria, purpura, angioedema and, more rarely exfoliative and bullous dermatoses (including epidermal necrolysis and erythema multiforme),hypersensitivity vasculitis, hypersensitivity syndrome (see section 4.4 'Special warnings and precautions for use').

Causal relationship unknown: other reactions have been reported in clinical trials or since the drug was marketed, but occurred under circumstances where a causal relationship could not be established. However, in these rarely reported events, that possibility cannot be excluded. Therefore, these observations are listed to serve as alerting information to physicians.

Cardiovascular: arrhythmia.

Metabolic: hyperglycaemia.

Nervous system: neuritis.

Special senses: disturbances of the retina and its vasculature.

Miscellaneous: gynaecomastia.

Rarely, occurrences of fulminant necrotising fasciitis, particularly in association with Group A β-haemolytic streptococcus, has been described in persons treated with non-steroidal anti-inflammatory agents, sometimes with fatal outcome (see 4.4 'Special warnings and precautions for use').

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard.

4.9 Overdose

Cases of overdosage have been reported and, rarely, fatalities have occurred. The following signs and symptoms may be observed following overdosage: headache, nausea, vomiting, epigastric pain, gastrointestinal pain and bleeding, rarely, diarrhoea, disorientation, excitation, stupor, coma, drowsiness, dizziness, tinnitus, fainting, occasionally convulsions, diminished urine output and hypotension. In isolated cases patients have received up to 600 mg a day without adverse consequences being reported. In cases of significant poisoning acute renal failure and liver damage are possible.

Within one hour of ingestion of a potentially toxic amount, activated charcoal should be considered. Alternatively, in adults, gastric lavage may be considered within one hour of ingestion of a potentially life-threatening overdose. Good urine output should be ensured. Renal and liver function should be closely monitored. Patients should be observed for at least eight hours after ingestion of doses exceeding 600 mg. Frequent or prolonged convulsions should be treated with intravenous diazepam, Other measures may be indicated by the patient's clinical condition.

Animal studies show that absorption is decreased by the prompt administration of activated charcoal, and excretion is enhanced by alkalinisation of the urine.

The readiness of sulindac and its metabolites to dialyse is unknown at present. But because they are highly bound to plasma proteins, dialysis is not likely to be effective.

The mean half-life of sulindac is 7.8 hours while the mean half-life of the active sulphide metabolite is 16.4 hours.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Sulindac is a non-steroidal, antirheumatic agent with anti-inflammatory analgesic and antipyretic properties. It is not a salicylate, propionic acid, pyrazolone or corticosteroid.

Prostaglandin synthetase inhibition has been hypothesised to be the mechanism of action of non-steroidal anti-inflammatory agents. Following absorption, sulindac undergoes two major biotransformations: reversible reduction to the sulphide metabolite, and irreversible oxidation to the inactive sulphone metabolite. The sulphide metabolite is a potent inhibitor of prostaglandin synthesis, and available evidence indicates that the biological activity of sulindac resides with the sulphide metabolite, thus the sulphoxide form (sulindac) is a prodrug.

5.2 Pharmacokinetic properties

Sulindac is approximately 90% absorbed in man after oral administration. The peak plasma concentrations of the biologically active sulphide metabolite are achieved in about two hours when sulindac is administered in the fasting state; and in about three to four hours when sulindac is administered with food. The mean half-life of sulindac is 7.8 hours, while the mean half-life of the sulphide

metabolite is 16.4 hours. Sustained plasma levels of the sulphide metabolite are consistent with a prolonged anti-inflammatory action.

Sulindac and its sulphone metabolite undergo extensive enterohepatic circulation relative to the sulphide metabolite. The enterohepatic circulation together with the reversible metabolism are probably major contributors to sustained plasma levels of the active drug.

The primary route of excretion in man is via the urine as both sulindac and its sulphone metabolite and glucoronide conjugates. Approximately 50% of an oral dose is excreted in the urine, with the conjugated sulphone metabolite accounting for the major portion. Approximately 25% of an oral dose is found in the faeces, primarily as the sulphone and sulphide metabolites.

The bioavailability of sulindac and the active sulphide metabolite from the oral liquid is greater than 90% of that of the tablet.

5.3 Preclinical safety data

No relevant information.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Cellulose microcrystalline, pregelatinised maize starch, magnesium stearate, and purified water. (An alternative method of manufacture uses maize starch instead of pregelatinised maize starch.)

6.2 Incompatibilities

None known.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Do not store above 25°C. Store in the original package. Keep in outer carton.

6.5 Nature and contents of container

Bottles containing 100 tablets or blister packs containing 56 or 60 tablets

6.6 Special precautions for disposal

None.

7 MARKETING AUTHORISATION HOLDER

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8 MARKETING AUTHORISATION NUMBER(S)

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