NEW ZEALAND DATA SHEET

ACLIN

1. Product Name

ACLIN, 100 mg, 200 mg tablets.

2. Qualitative and Quantitative Composition

Each tablet contains 100 mg or 200 mg of sulindac.

ACLIN tablets contain lactose. For the full list of excipients, see section 6.1.

3. Pharmaceutical Form

ACLIN 100 mg tablets: 8 mm flat bevelled edge orange-yellow tablet marked with “SD” over breakline “100” on one side and “α” on the other side.

ACLIN 200 mg tablets: 10 mm flat bevelled edge orange-yellow tablet marked with “SD” over breakline “200” on one side and “α” on the other side.

The tablet can be divided into equal doses.

Sulindac is a non-steroidal anti-inflammatory indene-type compound. Sulindac is a yellow crystalline compound. It is a weak organic acid [pKa (25°C) 4.7]. It is soluble in water as the sodium salt or in buffers of pH 6 or higher but is practically insoluble in water below pH 4.5 and sparingly soluble in alcohol.

4. Clinical Particulars

4.1 Therapeutic indications

ACLIN is indicated for acute or long-term use in the treatment of the following:

- Osteoarthritis
- Rheumatoid arthritis
- Ankylosing spondylitis
- Periarticular diseases such as acute painful shoulder (acute subacromial bursitis/supraspinatus tendonitis) and tenosynovitis
- Acute gouty arthritis
- Painful low back syndrome (low back pain, commonly referred to as lumbago).

4.2 Dose and method of administration

After assessing the risk/benefit ratio in each individual patient, the lowest effective dose for the shortest possible duration should be used.

Dose

The usual daily dosage of ACLIN is 400 mg per day. However, the dosage may be lowered depending on the response. Dosages above 400 mg per day are not recommended (see section 4.4).

In acute gouty arthritis, therapy for 7 days is usually adequate.

Patients on long term treatment should be reviewed regularly with regards to efficacy, risk-factors and ongoing need for treatment.

Method of administration

ACLIN should be administered twice a day with fluids or food. Dosage should be adjusted to the severity of the disease. If used once daily, the drug should be taken in the evening.

4.3 Contraindications

Sulindac is contraindicated for patients with known hypersensitivity to sulindac or to any other component of this product.

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

As with other NSAIDs, sulindac may mask the signs and symptoms of peptic ulcer. Sulindac itself may cause peptic ulceraction or irritation of the gastrointestinal tract, therefore it should not be administered to patients with active gastrointestinal bleeding, active peptic ulcer, or a history of recurrent gastrointestinal ulceration or bleeding.

Sulindac should not be used for treatment of peri-operative pain in the setting of coronary artery bypass graft (CABG) surgery.

Sulindac should not be used in patients with severe heart failure (see section 4.4).

Patients with severe hepatic impairment.

4.4 Special warnings and precautions for use

Sulindac should not be used in patients in whom acute asthmatic attacks, rhinitis or urticaria have been precipitated by aspirin or other NSAIDs.

Cardiovascular thrombotic events

Observational studies have indicated that non-selective NSAIDs may be associated with an increased risk of serious cardiovascular events, including myocardial infarction and stroke. Patients with cardiovascular disease, history of atherosclerotic cardiovascular disease or cardiovascular risk factors may also be at greater risk.

Physicians and patients should remain alert for such CV events, even in the absence of previous CV symptoms. Patients should be informed about signs and/or symptoms of serious CV toxicity and the steps to take if they occur.

To minimise the potential risk of an adverse cardiovascular event in patients taking an NSAID, especially in those with cardiovascular risk factors, the lowest effective dose should be used for the shortest possible duration (see section 4.2).

There is no consistent evidence that the concurrent use of aspirin mitigates the possible increased risk of serious cardiovascular thrombotic events associated with NSAID use.

Clinical trial and epidemiological data suggest that the use of coxibs and some NSAIDs (particularly at high doses and with either short or long-term treatment) may be associated with an increased risk of arterial thrombotic events (e.g. myocardial infarction or stroke).

Hypertension

NSAIDs may lead to the onset of new hypertension or worsening of pre-existing hypertension, and patients taking anti-hypertensives with NSAIDs may have an impaired anti-hypertensive response. Caution is advised when prescribing NSAIDs to patients with hypertension. Blood pressure should be monitored closely during initiation of NSAID treatment and at regular intervals thereafter.

Heart failure

Fluid retention and oedema have been observed in some patients taking NSAIDs; therefore, caution is advised in patients with fluid retention or heart failure.

Gastrointestinal events

All NSAIDs can cause gastrointestinal discomfort and serious, potentially fatal gastrointestinal effects such as ulcers, bleeding and perforation, which may increase with dose or duration of use, but can occur at any time without warning. Upper gastrointestinal ulcers, gross bleeding, or perforation caused by NSAIDs occur in approximately 1% of patients treated for 3-6 months and in about 2-4% of patients treated for one year. These trends continue with longer duration of use, increasing the likelihood of developing a serious gastrointestinal event at some time during the course of therapy. However, even short-term therapy is not without risk.

Caution is advised in patients with risk factors for gastrointestinal events who may be at greater risk of developing serious gastrointestinal events, e.g. the elderly, those with a history of serious gastrointestinal events, smoking and alcoholism. When gastrointestinal bleeding or ulcerations occur in patients receiving NSAIDs, the medicine should be withdrawn immediately. Doctors should warn patients about the signs and symptoms of serious gastrointestinal toxicity.

The concurrent use of aspirin and NSAIDs also increase the risk of serious gastrointestinal adverse events.

Sulindac should not be administered to patients with active gastrointestinal bleeding and should be used with caution in patients with a history of gastrointestinal haemorrhage or ulcers. In patients with an active peptic ulcer, an appropriate therapeutic regimen should be instituted and the physician must weigh the benefits of ACLIN against possible hazards (see section 4.8) and carefully monitor the patient's progress. In a drug interaction study, an antacid (magnesium and aluminium hydroxides, in suspension, 30 mL) was administered with sulindac with no significant difference in absorption.

Severe skin reactions

NSAIDs may very rarely cause serious cutaneous adverse events such as exfoliative dermatitis, toxic epidermal necrolysis (TEN) and Stevens-Johnson syndrome (SJS), which can be fatal and occur without warning. These serious adverse events are idiosyncratic and are independent of dose or duration of use. Patients should be advised of the signs and symptoms of serious skin reactions and to consult their doctor at the first appearance of a skin rash or any other sign of hypersensitivity.

Hypersensitivity syndrome

A potentially life-threatening, apparent hypersensitivity syndrome has been reported. In cases where this syndrome is suspected, therapy should be discontinued immediately, and not reinstituted.

This syndrome may include constitutional symptoms (fever, chills, diaphoresis, flushing), cutaneous findings (rash or other dermatologic reactions – see section 4.8), 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).

Platelet aggregation

Sulindac is a moderate to weak inhibitor of platelet function and, therefore, patients who may be adversely affected by this (e.g. those undergoing surgery) should be observed closely.

Oral anticoagulants

Concurrent use of NSAIDs and warfarin has been associated with severe, sometimes fatal, haemorrhage, especially in the elderly. The exact mechanism is unknown, but may involve enhanced bleeding from NSAID-induced gastrointestinal ulceration, or an additive effect of anticoagulation by warfarin and inhibition of platelet function by NSAIDs. Sulindac should be used in combination with warfarin only if absolutely necessary, and patients taking this combination should be closely monitored. Adjustment of dosage for oral anticoagulants may be required.

Oral hypoglycaemic agents

Data available from limited animal studies have shown no evidence of interaction of sulindac with oral hypoglycaemic agents. However, ACLIN should be used with caution in patients receiving such agents.

Infections

Non-steroidal anti-inflammatory medicines, 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 medicine with extra care in the presence of existing infection.

Corticosteroids

As is the case during therapy with other anti-inflammatory-analgesic-antipyretic medicines, if corticosteroids are reduced or discontinued during therapy with sulindac, the dose of the corticosteroid should be reduced slowly and the patient observed closely for adverse effects, particularly adrenal insufficiency and exacerbation of rheumatoid arthritis.

Ocular effects

Adverse ophthalmological effects have been observed with non-steroidal anti-inflammatory agents; accordingly, patients who develop visual disturbances during treatment with sulindac should have an ophthalmological examination.

Hepatic effects

As with other NSAIDs elevations of one or more liver function tests may occur in up to 15% of patients. These abnormalities may progress, may remain essentially unchanged, or may resolve with continued therapy. Significant (3 times the upper limit of normal) elevations of ALT (SGPT) or AST (SGOT) occurred in controlled clinical trials in less than 1% of patients receiving this therapy.

Physicians and patients should remain alert for hepatotoxicity. It is recommended that, in those patients with a history of liver dysfunction, periodic liver function tests be carried out. A patient should be informed about the symptoms and/or signs suggesting liver dysfunction (e.g. nausea, fatigue, lethargy, pruritis, jaundice, abdominal tenderness in the right upper quadrant and “flu-like” symptoms). If symptoms/signs or abnormal liver tests were to occur the patient should be evaluated for evidence of the development of more severe hepatic reactions while on therapy.

In patients with poor liver function, delayed, elevated and prolonged circulating levels of the sulfide and sulfone metabolites may occur. Such patients should be monitored closely and a reduction of daily dosage may be required. 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 and other evidence of hypersensitivity, including abnormalities in one or more liver function tests and skin reactions, have occurred during therapy with sulindac. Fatalities have occurred in some of these patients.

Determinations of liver function should be considered whenever a patient on therapy with sulindac develops unexplained fever, rash or other dermatologic reactions or constitutional symptoms. If unexplained fever or other evidence of hypersensitivity occurs, therapy with sulindac should be discontinued. Administration of sulindac should not be reinstituted in such patients.

The elevated temperature and abnormalities in liver function tests observed with sulindac characteristically have reverted to normal after discontinuation of therapy.

Renal effects

As sulindac is mainly excreted in urine, it should be used with caution in patients with impaired renal function. In severe renal failure the dosage may need to be reduced.

As with other non-steroidal anti-inflammatory agents, long-term administration of sulindac in animals has resulted in renal papillary necrosis and other abnormal renal pathology. In humans, there have been reports of acute interstitial nephritis with haematuria, proteinuria, and occasionally nephrotic syndrome.

A second form of renal toxicity has been observed in patients with pre-renal and renal conditions leading to a reduction in renal blood flow or blood volume, where the renal prostaglandins have a supportive role in the maintenance of renal perfusion. In these patients, administration of a NSAID may cause a dose dependent reduction in prostaglandin formation and precipitate overt renal decompensation. Sulindac may affect renal function less than other NSAIDs in patients with glomerular renal disease. Until these observations are better understood and clarified, however, and because renal adverse experiences have been reported with sulindac (see section 4.8), caution should be exercised when administering this medication to patients with those conditions associated with increased risk of the effects of non-steroidal anti-inflammatory drugs on renal function, such as those with renal or hepatic dysfunction, diabetes mellitus, complications associated with advanced age, extracellular volume depletion from any cause, congestive heart failure, sepsis, or concomitant use of any nephrotoxic medicine. A non-steroidal anti-inflammatory medicine 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 typically followed by recovery to the pre-treatment state.

As sulindac is eliminated primarily by the kidneys, those patients with significantly impaired renal functions should be closely monitored and a lower daily dosage anticipated to avoid excessive medicine 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.

Paediatric use

Sulindac should not be given to children.

4.5 Interaction with other medicines and other forms of interaction

Dimethyl sulfoxide

DMSO (dimethyl sulfoxide) should not be used with sulindac. Concomitant administration has been reported to reduce the plasma levels of the active sulfide metabolite and may potentially reduce efficacy. In addition, this combination has been reported to cause peripheral neuropathy.

Methotrexate

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

Ciclosporin

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

Aspirin (acetylsalicylic acid)

The concomitant administration of aspirin with sulindac in normal volunteers significantly depressed the plasma levels of the active sulfide metabolite. In a clinical study, the combination showed an increase in the incidence of gastrointestinal adverse effects. Since the addition of aspirin did not have a favourable effect on the therapeutic response to sulindac, the combination is not recommended.

Other NSAIDs

The concomitant use of sulindac with other NSAIDs is not recommended due to the increased possibility of gastrointestinal toxicity, with little or no increase in efficacy.

Oral hypoglycaemic

Although sulindac and its sulfide metabolite are highly bound to protein, studies in which sulindac was given at a dose of 400 mg daily, have shown no proven interaction with oral hypoglycaemic agents. However, patients should be monitored carefully until it is certain that no change in their hypoglycaemic dosage is required.

Dextroproxyphene hydrochloride / paracetamol

Neither dextropropoxyphene hydrochloride nor paracetamol had any effect on the plasma levels of sulindac or its sulfide metabolite.

Diflunisal

The concomitant administration of sulindac and diflunisal in normal volunteers resulted in lowering of the plasma levels of the active sulindac sulfide metabolite by approximately one third.

Antacids

A single dose crossover study compared 100 mg sulindac with 100 mg of sulindac administered with an antacid (magnesium and aluminium hydroxides, in suspension, 30 mL). There was no significant difference in absorption as measured by the urinary recovery of sulindac.

Probenecid

Probenecid given concomitantly with sulindac had only a slight effect on plasma sulfide levels. While plasma levels of sulindac and sulfone were increased. Sulindac was shown to produce a modest reduction in the uricosuric action of probenecid, which probably is not significant under most circumstances.

Combination use of ACE inhibitors or angiotensin receptor antagonists, anti-inflammatory medicines and thiazide diuretics

The use of an ACE-inhibitor or angiotensin receptor antagonist, an anti-inflammatory medicine (NSAID or COX-2 inhibitor) and a thiazide diuretic at the same time increases the risk of renal impairment. This includes use in fixed-combination products containing more than one class of medicine. Combined use of these medications should be accompanied by increased monitoring of

serum creatinine, particularly at the institution of the combination. The combination of medicines from these classes should be used with caution, particularly in elderly patients or those with pre-existing renal impairment.

4.6 Fertility, pregnancy and lactation

Pregnancy

Category C

Australian Pregnancy Categorisation Definition of Category C: Drugs which, owing to their pharmacological effects, have caused or may be suspected of causing, harmful effects on the human fetus or neonate without causing malformations. These effects may be reversible. Accompanying texts should be consulted for further details.

Sulindac should not be given to pregnant women since safety for its use has not been established.

Non-steroidal anti-inflammatory agents have an inhibitory effect on prostaglandin synthesis which may adversely affect pregnancy and/or embryo/fetal development. Some data from epidemiological studies suggest an increased risk of miscarriage after use of a prostaglandin synthesis inhibitor (such as NSAIDs) in early pregnancy. In animals, administration of prostaglandin synthesis inhibitors has been shown to result in increased pre- and post-implantation loss. 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 as possible and the duration of treatment as short as possible.

When given during the third trimester of pregnancy, prostaglandin synthesis inhibitors may cause closure of the foetal ductus arteriosus, 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, gastrointestinal bleeding or perforation, increased risk of necrotizing enterocolitis, and delayed labour and birth.

Breast-feeding

Sulindac should not be given to nursing mothers since safety for its use in breastfeeding has not been established.

Fertility

No data available.

4.7 Effects on ability to drive and use machines

Sulindac has the potential to cause nervous system and visual effects. Patients should be advised not to drive or operate machinery until their individual susceptibility is known.

4.8 Undesirable effects

Sulindac is generally well-tolerated. If adverse effects are experienced, they are usually mild and may often respond to a reduction in dosage.

The following adverse effects were reported in clinical trials or have been reported since the medicine was marketed.

Adverse effects reported frequently

Gastrointestinal

The most frequent types of adverse effects occurring with sulindac are gastrointestinal; these include gastrointestinal pain, dyspepsia, nausea with or without vomiting, diarrhoea, constipation, flatulence, anorexia and gastrointestinal cramps.

Dermatological

Rash, pruritus.

Central nervous system

Dizziness, headache, nervousness.

Special senses

Tinnitus.

Miscellaneous

Oedema.

Adverse effects reported less frequently

The probability exists of a causal relationship between sulindac and these adverse effects:

Gastrointestinal

Stomatitis, gastritis or gastroenteritis. Peptic ulcer, colitis, gastrointestinal bleeding and GI perforations have been reported rarely. Fatalities have occurred. Liver function test abnormalities, jaundice (sometimes with fever), cholestasis, hepatitis, hepatic failure, pancreatitis, ageusia, glossitis and intestinal strictures (diaphragms).

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

Dermatological

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.

Haematological

Thrombocytopenia, ecchymosis, purpura, leucopenia, agranulocytosis, neutropenia, bone marrow depression (including aplastic anaemia), haemolytic anaemia, increased prothrombin time in patients on oral anticoagulants.

Genitourinary

Urine discolouration, dysuria, vaginal bleeding, haematuria, proteinuria, crystalluria, renal impairment (including renal failure), interstitial nephritis, nephrotic syndrome.

Nervous system

Vertigo, somnolence, insomnia, sweating, asthenia, paraesthesiae, convulsions, syncope, depression, psychic disturbances including acute psychosis, aseptic meningitis.

Metabolic

Hyperkalaemia.

Musculoskeletal

Muscle weakness.

Special senses

Visual disturbances including blurred vision, decreased hearing, metallic or bitter taste.

Respiratory

Epistaxis.

Hypersensitivity reactions

Anaphylaxis and angioneurotic oedema. Bronchial spasm, dyspnoea, hypersensitivity vasculitis, hypersensitivity syndrome (see section 4.4).

Adverse effects – causal relationship unknown

Other reactions have been reported in clinical trials or since the medicine 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. Rare occurrences of fulminant necrotizing 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 section 4.4).

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 https://nzphvc.otago.ac.nz/reporting/.

4.9 Overdose

Symptoms

Cases of overdosage have been reported and, rarely, fatalities have occurred. The following signs and symptoms may be observed following overdosage: stupor, coma, diminished urine output and hypotension. In isolated cases, patients have received up to 900 mg a day without adverse consequences being reported.

Treatment

In the event of acute overdosage, the patient should be carefully observed and given symptomatic and supportive treatment.

Animal studies show that absorption is decreased by the prompt administration of activated charcoal, which should be given within 1 to 2 hours after ingestion.

For further advice on management of overdose please contact the National Poisons Information Centre (0800 POISON or 0800 764 766).

5. Pharmacological Properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Anti-inflammatory and anti-rheumatic products, non-steroids, ATC code: M01AB02

Mechanism of action

Prostaglandin synthetase inhibition has been hypothesised to be the basis of the mechanism of action of NSAIDs. Following absorption, sulindac undergoes two major biotransformations: reversible reduction to the sulfide metabolite, and irreversible oxidation to the inactive sulfone metabolite. The sulfide metabolite is a potent inhibitor of prostaglandin synthesis, and available evidence indicates that the biological activity of sulindac resides with the sulfide metabolite. Thus, the sulfoxide form (sulindac) is a prodrug.

Pharmacodynamic effects

Sulindac usually provides prompt symptomatic relief of inflammation, pain and tenderness, and promotes early restoration of joint mobility. The drug has a prolonged duration of activity which permits a once or twice a day dosage schedule, and can be used for long-term treatment. Sulindac has been shown to be an effective, well tolerated compound.

5.2 Pharmacokinetic properties

Absorption

Sulindac is approximately 90% absorbed in humans after oral administration. The peak plasma concentrations of the biologically active sulfide 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. Sustained plasma levels of the sulfide metabolite are consistent with a prolonged anti-inflammatory action which is the rationale for a twice per day dosage schedule.

Distribution

Sulindac and its metabolites are extensively (90 to 98%) bound to protein in plasma.

Multiple dose pharmacokinetic studies comparing sulindac 400 mg once a day with 200 mg twice a day, found that at steady state the maximum and minimum serum concentrations of the sulfide were not significantly different between the two dosage regimens. Moreover, when sulindac was administered once daily in the evening, plasma levels of active medicine in the early morning were significantly higher than when administered twice daily.

The bioavailability of sulindac, as assessed by urinary excretion, was not changed by concomitant administration of an antacid containing magnesium and aluminium hydroxides.

Biotransformation

Sulindac and the sulfone metabolite undergo extensive enterohepatic circulation relative to the sulfide metabolite. The enterohepatic circulation, together with the reversible metabolism are probably major contributors to sustained plasma levels of the active medicine.

Elimination

The mean half-life of sulindac is 7.8 hours, while the mean half-life of the sulfide metabolite is 16.4 hours.

The primary route of excretion in humans is via the urine as both sulindac and the sulfone metabolite (free, as well as glucuronides), with the sulfone metabolite accounting for the major portion. Less than 1% of the administered dose of sulindac appears in the urine as the sulfide metabolite. Approximately 25% is found in the faeces, primarily as the sulfone and sulfide metabolites. Sulindac, sulfone and the active sulfide metabolite are excreted in the bile and subject to extensive enterohepatic recycling in animals. Further biotransformation of sulindac may take place in the gastrointestinal tract. Similar enterohepatic circulation, together with reversible metabolism are probably major contributors to sustained plasma levels of the active drug in man.

5.3 Preclinical safety data

No data available.

6. Pharmaceutical Particulars

6.1 List of excipients

Lactose, microcrystalline cellulose, povidone, sodium starch glycollate, quinoline yellow CI47005, purified talc, magnesium stearate.

ACLIN tablets are gluten-free.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Store at or below 30°C.

6.5 Nature and contents of container

HDPE bottle with a child-resistant closure. Pack-size of 50 tablets.

6.6 Special precautions for disposal

Not applicable.

7. Medicines Schedule

Prescription Medicine

8. Sponsor Details

Mylan New Zealand Ltd
PO Box 11183
Ellerslie
AUCKLAND
Telephone 09-579-2792

9. Date of First Approval

24 September 1987

10. Date of Revision of the Text

14 June 2019

Section Changed	Summary of New Information
4.4	Under Cardiovascular thrombotic events, added that increased risk associated with short- or long-term treatment in line with other NSAID data sheets.