TOC PHARMACEUTICALS NIG. LTD.

SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

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1. NAME OF THE MEDICINAL PRODUCT
AL-DOULEURS TABLETS
(Diclofenac Potassium 50mg)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each Tablet Contains:

Diclofenac Potassium 50mg B.P
Excipients: q.s.

For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM:
Tablets.

4. CLINICAL PARTICULARS
4.1. THERAPEUTIC INDICATIONS

Rheumatoid arthritis
Osteoarthrosis
Low back pain
Migraine attacks
Acute musculo-skeletal disorders and trauma such as periarthritis (especially frozen shoulder), tendinitis, tenosynovitis, bursitis, sprains, strains and dislocations; relief of pain in fractures
Ankylosing spondylitis
Acute gout
Control of pain and inflammation in orthopaedic, dental and other minor surgery
Pyrophosphate arthropathy and associated disorders

4.2. POSOLOGY AND METHOD OF ADMINISTRATION

For oral administration.
To be taken preferably with or after food.
The tablets should be swallowed whole with liquid.

Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms.

Adults
The recommended daily dose is 100 – 150 mg in two or three divided doses. For milder cases, 75 – 100 mg daily in two or three divided doses is usually sufficient.
In migraine an initial dose of 50 mg should be taken at the first signs of an impending attack. In cases where relief 2 hours after the first dose is not sufficient, a further dose of 50 mg may be taken. If needed, further doses of 50 mg may be taken at intervals of 4 – 6 hours, not exceeding a total dose of 200 mg per day.

Paediatric population
For children over 14 years of age, the recommended daily dose is 75-100mg in two or three divided doses. Diclofenac Potassium 25mg Tablets are not recommended for children under 14 years of age. The use of Diclofenac Potassium 50 mg tablets in migraine attacks has not been established in children.

Elderly
The elderly 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.

Renal impairment
No adjustment of the starting dose is required for renally impaired patients.

Hepatic impairment
No adjustment of the starting dose is required for hepatically impaired patients.

4.3 CONTRAINDICATIONS

- Hypersensitivity to the active substance or any of the excipients.
- Active, gastric or intestinal ulcer, bleeding or perforation.
- Active, or history of recurrent peptic ulcer / haemorrhage (two or more distinct episodes of proven ulceration or bleeding).
- NSAIDs are contraindicated in patients who have previously shown hypersensitivity reactions (e.g. asthma, rhinitis, angioedema, or urticaria) in response to ibuprofen, aspirin, or other non-steroidal anti-inflammatory drugs.
- Established congestive heart failure (NYHA II-IV), ischemic heart disease, peripheral arterial disease and/or cerebrovascular disease.
- Severe heart failure, hepatic failure and renal failure.
- History of gastro-intestinal bleeding or perforation, relating to previous NSAID therapy.
- During the last trimester of pregnancy.
- This product contains soya. If you are allergic to peanut or soya, do not use this medicinal product.

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.
The use of Diclofenac potassium with concomitant NSAIDs including cyclooxygenase-2 selective inhibitors should be avoided due to the absence of any evidence demonstrating synergistic benefits and the potential for additive undesirable effects.

Elderly
Caution is indicated in the elderly on basic medical grounds. The elderly increased frequency of adverse reactions to NSAIDs especially gastro intestinal bleeding and perforation which may be fatal. In particular, it is recommended that the lowest effective dose be used in frail elderly patients or those with a low body weight.

Gastrointestinal
Close medical surveillance is imperative in patients with symptoms indicative of gastrointestinal disorders, with a history suggestive of gastric or intestinal ulceration, bleeding or perforation, with ulcerative colitis, or with Crohn's disease as these conditions may be exacerbated.

Patients with a history of GI toxicity, particularly when elderly, should report any unusual abdominal symptoms (especially GI bleeding) particularly in the initial stages of treatment.
GI bleeding (haematemesis, melaena), 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. They generally have more serious consequences in the elderly.
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 and in the elderly. These patients should commence and maintain 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.
Caution should be advised in patients receiving concomitant medications which increase the risk of ulceration or bleeding, such as oral corticosteroids, anticoagulants such as warfarin, selective serotonin-reuptake inhibitors or anti-platelet agents such as aspirin.
When GI bleeding or ulceration occurs in patients receiving diclofenac potassium, the treatment should be withdrawn.
NSAIDs

Hypersensitivity reactions

As with other non-steroidal anti-inflammatory drugs, allergic reactions, including anaphylactic/anaphylactoid reactions, can occur without earlier exposure to the drug.

Infection

Like other NSAIDs, Diclofenac Potassium tablets may mask the signs and symptoms of infection due to their pharmacodynamic properties.

SLE and mixed connective tissue disease:

In patients with systemic lupus erythematosus (SLE) and mixed connective tissue disorders there may be an increased risk of aseptic meningitis.
Cardiovascular, Renal and Hepatic Impairment:
The administration of an NSAID may cause a dose dependent reduction in prostaglandin formation and precipitate renal failure.
As fluid retention and oedema have been reported in association with NSAIDs therapy, including diclofenac, particular caution is called for in patients with impaired cardiac or renal function, history of hypertension, the elderly, patients receiving concomitant treatment with diuretics or medicinal products that can significantly impact renal function, and those patients with substantial extracellular volume depletion from any cause, e.g. before or after major surgery. Monitoring of renal function is recommended as a precautionary measure when using diclofenac in such cases. Discontinuation therapy is usually followed by recovery to the pre-treatment state.

Hepatic

Close medical surveillance is required when prescribing diclofenac to patients with impairment of hepatic function as their condition may be exacerbated.
As with other NSAIDs, including diclofenac, values of one or more liver enzymes may increase. During prolonged treatment with Diclofenac, regular monitoring of hepatic function is indicated as a precautionary measure. If abnormal liver function tests persist or worsen, clinical signs or symptoms consistent with liver disease develop or if other manifestations occur (eosinophilia, rash), Diclofenac Potassium tablets should be discontinued.
Hepatitis may occur without prodromal symptoms.
Use of Diclofenac Potassium tablets in patients with hepatic porphyria may trigger an attack.

Haematological

Diclofenac Potassium tablets may reversibly inhibit platelet aggregation. Patients with defects of haemostasis, bleeding diathesis or haematological abnormalities should be carefully monitored.

Long term treatment
All patients who are receiving long term treatment with non-steroidal, anti-inflammatory agents should be monitored as a precautionary measure eg renal function, hepatic function (elevation of liver enzymes may occur) and blood counts. This is particularly important in the elderly.

Respiratory disorders
In patients with asthma, seasonal allergic rhinitis, swelling of the nasal mucosa (i.e. nasal polyps), chronic obstructive pulmonary diseases or chronic infections of the respiratory tract (especially if linked to allergic rhinitis-like symptoms), reactions on NSAIDs like asthma exacerbations (so called intolerance to analgesics/analgesics asthma), Quincke's oedema or urticaria are more frequent than in other patients. Therefore, special precaution is recommended in such patients (readiness for emergency). This is applicable as well for patients who are allergic to other substances, e.g. with skin reactions, pruritus or urticaria.
Like other drugs that inhibit prostaglandin synthetase activity, diclofenac sodium and other NSAIDs can precipitate bronchospasm if administered to patients suffering from, or with a previous history of bronchial asthma.

Cardiovascular and cerebrovascular effects
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 including diclofenac.
Clinical trial and epidemiological data suggest that use of diclofenac, particularly at high dose (150mg daily) and in long term treatment may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke).
Patients with uncontrolled hypertension, congestive heart failure, established ischaemic heart disease, peripheral arterial disease, and/or cerebrovascular disease and with significant risk factors for cardiovascular events (e.g.,, hyperlipidaemia, diabetes mellitus, smoking) should only be treated with diclofenac after careful consideration.
As the cardiovascular risks of diclofenac may increase with dose and duration of exposure, the shortest duration possible and the lowest effective daily dose should be used. The patient's need for symptomatic relief and response to therapy should be re-evaluated periodically.

Dermatological
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. 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. Diclofenac potassium should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

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

4.5 INTERACTION WITH OTHER MEDICINAL PRODUCTS AND PHARMACEUTICAL FORM

Other NSAIDs including cyclooxygenase-2 selective inhibitors and corticosteroids: Co-administration of diclofenac with other systemic NSAIDs or corticosteroids may increase the risk of gastrointestinal bleeding or ulceration. Avoid concomitant use of two or more NSAIDs.
Diuretics and antihypertensive agents: Like other NSAIDs, concomitant use of diclofenac with diuretics and antihypertensive agents (e.g. beta-blockers, angiotensin converting enzyme (ACE) inhibitors may cause a decrease in their antihypertensive effect via inhibition of vasodilatory prostaglandin synthesis. Therefore, the combination should be administered with caution and patients, especially the elderly, should have their blood pressure periodically monitored. Patients should be adequately hydrated and consideration should be given to monitoring of renal function after initiation of concomitant therapy periodically thereafter, particularly for diuretics and ACE inhibitors due to the increased risk of nephrotoxicity.
Cardiac glycosides: NSAIDs may exacerbate cardiac failure, reduce GFR and increase plasma glycoside levels.
Lithium: If used concomitantly, diclofenac may increase plasma concentrations of lithium Monitoring of the serum lithium level is recommended.
Methotrexate: Diclofenac can inhibit the tubular renal clearance of methotrexate hereby increasing methotrexate levels. Caution is recommended when NSAIDs, including diclofenac, are administered less than 24 hours before treatment with methotrexate, since blood concentrations of methotrexate may rise and the toxicity of this substance be increase. Cases of serious toxicity have been reported when methotrexate and NSAIDs including diclofenac are given within 24 hours of each other. This interaction is mediated through accumulation of methotrexate resulting from impairment of renal excretion in the presence of the NSAID.
Ciclosporin: Diclofenac, like other NSAIDs, may increase the nephrotoxicity of ciclosporin due to the effect on renal prostaglandins. Therefore, it should be given at doses lower than those that would be used in patients not receiving ciclosporin.
Mifepristone: NSAIDs should not be used for 8-12 days after mifepristone administration as NSAIDs can reduce the effect of mifepristone.
Anti-coagulants and anti-platelet agents: Caution is recommended since concomitant administration could increase the risk of bleeding. Although clinical investigations do not appear to indicate that diclofenac has an influence on the effect of anticoagulants, there are reports of an increased risk of haemorrhage in patients receiving diclofenac and anticoagulant concomitantly (see section 4.4). Therefore, to be certain that no change in anticoagulant dosage is required, close monitoring of such patients is required. As with other nonsteroidal anti-inflammatory agents, diclofenac in a high dose can reversibly inhibit platelet aggregation NSAID.
Digoxin: If used concomitantly, diclofenac may raise plasma concentrations of digoxin. Monitoring of the serum digoxin level is recommended.
Selective serotonin reuptake inhibitors (SSRls): lncreased risk of gastrointestinal bleeding.
Tacrolimus: Possible increased risk of nephrotoxicity when NSAIDs are given with tacrolimus. This might be mediated through renal antiprostagladin effects of both NSAID and calcineurin inhibitor.
Quinolone antibacterials: Convulsions may occur due to an interaction between quinolones and NSAIDs. This may occur in patients with or without a previous history of epilepsy or convulsions. Therefore, caution should be exercised when considering the use of a quinolone in patients who are already receiving an NSAID.
Phenytoin: When using phenytoin concomitantly with diclofenac, monitoring of phenytoin plasma concentrations is recommended due to an expected increase in exposure to phenytoin.
Colestipol and cholestyramine: These agents can induce a delay or decrease in absorption of diclofenac. Therefore, it is recommended to administer diclofenac at least one hour before or 4 to 6 hours after administration of colestipol/ cholestyramine.
Zidovudine: lncreased risk of haematological toxicity when NSAIDs are given with zidovudine. There is evidence of an increased risk of haemarthroses and haematoma in HIV (+) haemophiliacs receiving concurrent treatment with zidovudine and ibuprofen.

Antidiabetic agents: Clinical studies have shown that Diclofenac Potassium tablets can be given together with oral antidiabetic agents without influencing their clinical effect. However there have been isolated reports of hypoglycaemic and hyperglycaemic effects which have required adjustment to the dosage of hypoglycaemic agents. For this reason, monitoring of the blood glucose level is recommended as a precautionary measure during concomitant therapy.
Drugs known to cause hyperkalemia: Concomitant treatment with potassium-sparing diuretics, ciclosporin, tacrolimus or trimethoprim may be associated with increased serum potassium levels, which should therefore be monitored frequently.
Potent CYP2C9 inhibitors: Caution is recommended when co-prescribing diclofenac with potent CYP2C9 inhibitors (such as voriconazole), which could result in a significant increase in peak plasma concentrations and exposure to diclofenac due to inhibition of diclofenac metabolism.

4.6 PREGNANCY AND LACTATION

Pregnancy

Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or the embryo/foetal development. Data from epidemiological studies suggest an increased risk of miscarriage and or cardiac malformation and gastroschisis after use of a prostaglandin synthesis inhibitor in early pregnancy. The absolute risk for cardiovascular malformation was increased from less than 1% up to approximately 1.5%. The risk is believed to increase with dose and duration of therapy. In animals, administration of a prostaglandin synthesis inhibitor has shown to result in increased pre-and post-implantation loss and embryo-foetal lethality.
In addition, increased incidences of various malformations, including cardiovascular, have been reported in animals given a prostaglandin synthesis inhibitor during organogenetic period. NSAIDs should not be used during the first two trimesters of pregnancy or labour unless the potential benefit to the patient outweighs the potential risk to the foetus. If diclofenac is used by a woman attempting to conceive, or during the 1st or 2nd trimesters of pregnancy, the dose should be kept as low and duration of treatment as short as possible.
During the third trimester of pregnancy, all prostaglandin synthesis inhibitors may expose the foetus to:
- cardiopulmonary toxicity (with premature closure of the ductus arteriosus and pulmonary hypertension)
- renal dysfunction, which may progress to renal failure with oligo-hydroamniosis
The mother and the neonate, at the end of the 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 delayed or prolonged labour
Consequently, diclofenac is contra-indicated during the third trimester of pregnancy.

Lactation

Like other NSAIDs, diclofenac passes into breast milk in small amounts. Hence Diclofenac should not be administered during breast feeding in order to avoid undesirable effects in the infant.

Female fertility

As with other NSAIDs, the use of diclofenac may impair female fertility and is not recommended in women attempting to conceive. In women who may have difficulties conceiving or who are undergoing investigation of infertility, withdrawal of diclofenac should be considered.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Undesirable effects such as dizziness, drowsiness, fatigue and visual disturbances are possible after taking NSAIDs. If affected, patients should not drive or operate machinery.

4.8 UNDESIRABLE EFFECTS

Adverse reactions are ranked under the heading of frequency, the most frequent first, using the following convention:

very common: (>1/10); common (≥ 1/100, <1/10); uncommon (≥ 1/1,000, <1/100); rare (≥1/10,000, <1/1000); very rare (<1/10,000); Unknown: cannot be estimated from available data.

The following undesirable effects include those reported with other short-term or long-term use:

Blood and lymphatic system disorders	
Very rare	Thrombocytopenia, leucopoenia, anaemia (including haemolytic and aplastic anaemia), agranulocytosis.
Unknown	Neutropenia
Immune system disorders	
Rare	Hypersensitivity, anaphylactic and anaphylactoid reactions (including hypotension and shock).
Very rare	Angioneurotic oedema (including face oedema).
Psychiatric disorders	
Very rare	Disorientation, depression, insomnia, nightmare, irritability, psychotic disorder.
Nervous system disorders	
Common	Headache, dizziness.
Rare	Somnolence, tiredness.
Very rare	Paraesthesia, memory impairment, convulsion, anxiety, tremor, aseptic meningitis*, taste disturbances, cerebrovascular accident.
Unknown	Confusion, hallucinations, disturbances of sensation malaise
Eye disorders	
Very rare	Visual disturbance, vision blurred, diplopia.
Unknown	Optic neuritis.
Ear and labyrinth disorders	
Common	Vertigo.
Very rare	Tinnitus, hearing impaired.
Cardiac disorders	
Very rare	Palpitations, chest pain, cardiac failure, myocardial infarction.
Vascular disorders	
Very rare	Hypertension, hypotension, vasculitis.
Respiratory, thoracic and mediastinal disorders	
Rare	Asthma (including dyspnoea).
Very rare	Pneumonitis.
Gastrointestinal disorders	
Common	Nausea, vomiting, diarrhoea, dyspepsia, abdominal pain, flatulence, anorexia.
Rare	Gastritis, gastrointestinal haemorrhage, haematemesis, diarrhoea haemorrhagic, melaena, gastrointestinal ulcer with or without bleeding or perforation (sometimes fatal particularly in the elderly).
Very rare	Colitis (including haemorrhagic colitis and exacerbation of ulcerative colitis or Crohn's disease), constipation, stomatitis (including ulcerative stomatitis), glossitis, oesophageal disorder, diaphragm-like intestinal strictures, pancreatitis.
Unknown	Ischaemic colitis
Hepatobiliary disorders	
Common	Transaminases increased.
Rare	Hepatitis, jaundice, liver disorder.

Very rare	Fulminant hepatitis, hepatic necrosis, hepatic failure.
Skin and subcutaneous tissue disorders	
Common	Rash.
Rare	Urticaria.
Very rare	Bullous eruptions, eczema, erythema, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis (Lyell's syndrome), dermatitis exfoliative, loss of hair, photosensitivity reaction, purpura, allergic purpura, pruritus.
Renal and urinary disorders	
Very rare	Acute renal failure, haematuria, proteinuria, nephrotic syndrome, interstitial nephritis, renal papillary necrosis.
General disorders and administration site conditions	
Rare	Oedema
Reproductive system and breast disorders	
Very rare	Impotence

* especially in patients with existing autoimmune disorders, such as systemic lupus erythematosus, mixed connective tissue disease, with symptoms such as stiff neck, headache, nausea, vomiting, fever or disorientation.

Clinical trial and epidemiological data consistently point towards an increased risk of arterial thrombotic events (for example myocardial infarction or stroke) associated with the use of diclofenac, particularly at high dose (150mg daily) and in long term treatment.

4.9 OVERDOSAGE

a) Symptoms
There is no typical clinical picture resulting from diclofenac over dosage. Symptoms include headache, nausea, vomiting, epigastric pain, gastrointestinal bleeding, rarely diarrhoea, dizziness, disorientation, excitation, coma, drowsiness, tinnitus, fainting, occasionally convulsions. In rare cases of significant poisoning acute renal failure and liver damage are possible.
b) Therapeutic measure
Patients should be treated symptomatically as required.
Within one hour of ingestion of a potentially toxic amount, activated charcoal should be considered.
Alternatively, in adults, gastric lavage should be considered within one hour of ingestion of a potentially life-threatening overdose.
Good urine output should be ensured. Special measures such as forced diuresis, dialysis or haemo-perfusion are probably of no help in eliminating NSAIDs, including diclofenac, due to high protein binding and extensive metabolism.
Renal and liver function should be closely monitored.
Patients should be observed for at least four hours after ingestion of potentially toxic amounts.
Frequent or prolonged convulsions should be treated with intravenous diazepam. Supportive measures should be given for complications such as hypotension, renal failure, gastrointestinal disorder, and respiratory depression.
Other measures may be indicated by the patient's clinical condition

5. PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMICS PROPERTIES

Pharmacotherapeutic group: Non-steroidal anti-inflammatory drug (NSAID).
ATC code: M01A B05
Diclofenac Potassium tablets contain the potassium salt of diclofenac, a non-steroidal compound with pronounced and clinically demonstrable analgesic, anti-inflammatory and anti-pyretic properties.
Diclofenac is a potent inhibitor of prostaglandin biosynthesis and a modulator of arachidonic acid releaseand uptake.
Diclofenac Potassium tablets have a rapid onset of action and are therefore suitable for the treatment of acute episodes of pain and inflammation.
In migraine attacks Diclofenac Potassium tablets have been shown to be effective in relieving the headache and in improving the accompanying symptom of nausea.
Diclofenac in vitro does not suppress proteoglycan biosynthesis in cartilage at concentrations equivalent to the concentrations reached in human beings.

5.2 PHARMACOKINETIC PROPERTIES

Absorption

Diclofenac is rapidly and completely absorbed from sugar-coated tablets. Food intake does not affect absorption.
Peak plasma concentration after one 50 mg sugar-coated tablet was 3.9 μmol/l after 20-60 minutes. The plasma concentrations show a linear relationship to the size of the dose.
Diclofenac undergoes first-pass metabolism and is extensively metabolised.

Distribution

Diclofenac is highly bound to plasma proteins (99.7%), chiefly albumin (99.4%)
Diclofenac was detected in a low concentration (100ng/mL) in breast milk in one nursing mother. The estimated amount ingested by an infant consuming breast milk is equivalent to a 0.03 mg/kg/day dose.

Elimination

The total systemic clearance of diclofenac in plasma is 263 ± 56 ml/min (mean ± SD).
The terminal half-life in plasma is 1 – 2 hours.
Repeated oral administration of Diclofenac Potassium tablets for 8 days in daily doses of 50 mg t.d.s does not lead to accumulation of diclofenac in the plasma.
Approx. 60% of the dose administered is excreted in the urine in the form of metabolites, and less than 1% as unchanged substance. The remainder of the dose is eliminated as metabolites through the bile in the faeces.

Biotransformation

The biotransformation of diclofenac involves partly glucuronidation of the intact molecule but mainly single and multiple hydroxylation followed by glucuronidation.

5.3 PRECLINICAL SAFETY DATA

The age of the patient has no influence on the absorption, metabolism, or excretion of diclofenac.
In patients suffering from renal impairment, no accumulation of the unchanged active substance can be inferred from the single-dose kinetics when applying the usual dosage schedule. At a creatinine clearance of <10 ml/min the theoretical steady-state plasma levels of metabolites are about four times higher than in normal subjects. However, the metabolites are ultimately cleared through the bile.
In the presence of impaired hepatic function (chronic hepatitis, non-decompensated cirrhosis) the kinetics and metabolism are the same as for patients without liver disease.

6. PHARAMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Starch BP
Lactose BP
Gelatin BP
Starch BP
Colour tartrazine yellow BP
Color brilliant blue BP
Color sunset yellow BP
Color chocolate brown BP
Talcum BP
Magnesium stearate BP
Microcrystalline cellulose BP
Sodium starch glycolate BP

6.2 INCOMPATIBILITY

None such data reported

6.3 SHELF LIFE

36 months (3 years)

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Special Precautions for Storage
Store at temperature below 30°C. Protect from light.

6.5 NATURE AND CONTENTS OF CONTAINER

Available in Aluminum-PVC Blister clinical packs of 1 x 12 Tablets

ADMINISTRATIVE DATA

7 MARKETING AUTHORISATION HOLDER

7.1 Manufactured By:
Me Cure Industries Ltd,
Plot 6, Block H, Oshodi Industrial Scheme
Oshodi, Lagos, Nigeria.

8 **Manufactured For:**
T.O.C. Pharmaceuticals Nig. Ltd.
88, Ilamoye Street, Ijesha,
Surulere, Lagos State.