Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Diclofenac 50 mg/Misoprostol 200 micrograms modified release tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet consists of a gastro-resistant core containing 50 mg diclofenac sodium surrounded by an outer mantle containing 200 micrograms misoprostol.

Excipient(s):
Each tablet contains 20.0 mg lactose monohydrate.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Modified Release Tablet

White circular, biconvex uncoated tablets plain one side and embossed with “DM2” on the other side.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Diclofenac/Misoprostol Tablets are indicated for patients who require the non-steroidal anti-inflammatory drug diclofenac together with misoprostol.

The diclofenac component of Diclofenac/Misoprostol Tablets is indicated for the symptomatic treatment of osteoarthritis and rheumatoid arthritis. The misoprostol component of Diclofenac/Misoprostol Tablets is indicated for patients with a special need for the prophylaxis of NSAID-induced gastric and duodenal ulceration.

4.2 Posology and method of administration

Posology
Adults
One tablet to be taken with food, two or three times daily. Tablets should be swallowed whole, not chewed.
Elderly/Renal and Hepatic Impairment
No adjustment of dosage is necessary in the elderly or in patients with hepatic impairment or mild to moderate renal impairment as pharmacokinetics are not altered to any clinically relevant extent. Nevertheless, elderly patients and patients with renal or hepatic impairment should be closely monitored (see section 4.4 and section 4.8).
Paediatric population (under 18 years)
The safety and efficacy of Diclofenac/Misoprostol Tablets in children has not been established.

Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms (see section 4.4).

4.3 Contraindications

Hypersensitivity to the active substance) or to any of the excipients listed in section 6.1.

Diclofenac/Misoprostol Tablets are contraindicated in:

- Patients with active peptic ulcer/haemorrhage or perforation or who have active GI bleeding or other active bleedings e.g. cerebrovascular bleedings,
- Pregnant women and in women planning a pregnancy,

- In women of childbearing potential who are not using effective contraception (see sections 4.4, 4.6 and 4.8),
- Patients with a known hypersensitivity to diclofenac, aspirin, other NSAIDs, misoprostol, other prostaglandins, or any other ingredient of the product,
- Patients in whom, attacks of asthma, urticaria or acute rhinitis are precipitated by aspirin or other non-steroidal anti-inflammatory agents,
- Treatment of peri-operative pain in the setting of coronary artery bypass graft (CABG) surgery,
- Patients with severe renal and hepatic failure,
- Patients with established congestive heart failure (NYHA II-IV), ischaemic heart disease, peripheral arterial disease and/or cerebrovascular disease.

4.4 Special warnings and precautions for use

Warnings
The use of diclofenac/misoprostol with concomitant NSAIDs including COX-2 inhibitors should be avoided.

As with other NSAIDs, allergic reactions, including anaphylactic/anaphylactoid reactions, can also occur in rare cases with diclofenac without earlier exposure to the drug. Hypersensitivity reactions can also progress to Kounis syndrome, a serious allergic reaction that can result in myocardial infarction. Presenting symptoms of such reactions can include chest pain occurring in association with an allergic reaction to diclofenac.

Use in women of childbearing potential (see also section 4.3)
In women of childbearing potential Diclofenac/Misoprostol Tablets must not be used unless they use effective contraception and have been advised of the risks of taking the product if pregnant (see section 4.3 and 4.6).

Precautions
Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms (see section 4.2, and GI and cardiovascular risks below).

Renal/Cardiac/Hepatic
In patients with renal, cardiac or hepatic impairment and in the elderly, caution is required since the use of NSAIDs may result in deterioration of renal function. In the following conditions, Diclofenac/Misoprostol Tablets should be used only in exceptional circumstances and with close clinical monitoring: advanced cardiac failure, advanced kidney failure, advanced liver disease, severe dehydration.

Diclofenac metabolites are eliminated primarily by the kidneys (see section 5.2). The extent to which the metabolites may accumulate in patients with renal failure has not been studied. As with other NSAIDs, metabolites of which are excreted by the kidney, patients with significantly impaired renal function should be more closely monitored.

In rare cases, NSAIDs, including diclofenac/misoprostol, may cause interstitial nephritis, glomerulitis, papillary necrosis and the nephrotic syndrome. NSAIDs inhibit the synthesis of renal prostaglandin which plays a supportive role in the maintenance of renal perfusion in patients whose renal blood flow and blood volume are decreased. In these patients, administration of an NSAID may precipitate overt renal decompensation, which is typically followed by recovery to pre-treatment state upon discontinuation of NSAID therapy. Patients at greatest risk of such a reaction are those with congestive heart failure, liver cirrhosis, nephrotic syndrome and overt renal disease. Such patients should be carefully monitored while receiving NSAID therapy.

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.

As with all NSAIDS, diclofenac/misoprostol can lead to the onset of new hypertension or worsening of pre-existing hypertension, either of which may contribute to the increased incidence of cardiovascular events. NSAIDs, including diclofenac/misoprostol, should be used with caution in patients with hypertension. Blood pressure should be monitored closely during the initiation of therapy with diclofenac/misoprostol and throughout the course of therapy.

Patients with uncontrolled hypertension, congestive heart failure, established ischaemic heart disease, peripheral arterial disease, and/or cerebrovascular disease should only be treated with diclofenac after careful consideration. Patients with significant risk factors for cardiovascular events (eg. hypertension, 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 may be used. The patient's need for symptomatic relief and response to therapy should be re-evaluated periodically.

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 serious arterial thrombotic events (for example myocardial infarction or stroke).

Physicians and patients should remain alert for the development of such events, even in the absence of previous cardiovascular symptoms. Patients should be informed about the signs and/or symptoms of serious cardiovascular toxicity and the steps to take if they occur (see section 4.3).

Blood system/Gastrointestinal
NSAIDs, including diclofenac/misoprostol, can cause serious gastrointestinal (GI) adverse events including inflammation, bleeding, ulceration, and perforation of the stomach, small intestine, or large intestine, which can be fatal. When GI bleeding or ulceration occurs in patients receiving diclofenac/misoprostol, the treatment should be withdrawn. These events can occur at any time during treatment, with or without warning symptoms or in patients with a previous history of serious GI events. NSAIDs, including diclofenac, may be associated with increased risk of gastro-intestinal anastomotic leak. Close medical surveillance and caution are recommended when using diclofenac after gastro-intestinal surgery.

Patients most at risk of developing these types of GI complications with NSAIDs are those treated at higher doses, the elderly, patients with cardiovascular disease, patients using concomitant aspirin, or patients with a prior history of, or active, gastrointestinal disease, such as ulceration, GI bleeding or inflammatory conditions.

Therefore, diclofenac/misoprostol should be used with caution in these patients and commence on treatment at the lowest dose available (see section 4.3).

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. Caution should be advised in patients receiving concomitant medicines which could 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 (see section 4.5).

Diclofenac/Misoprostol Tablets in common with other NSAIDs, may decrease platelet aggregation and prolong bleeding time. Extra supervision is recommended in haematopoietic disorders or in conditions with defective coagulation or in patients with a history of cerebrovascular bleeding.

Caution is required in patients suffering from ulcerative colitis or Crohn's Disease as these conditions may be exacerbated (see section 4.8).

Care should be taken in elderly patients and in patients treated with corticosteroids, other NSAIDs, or anti-coagulants (see section 4.5).

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, including diclofenac/misoprostol (see section 4.8). Patients appear to be at highest risk for these events early in the course of therapy, the onset of the event occurring in the majority of cases within the first month of treatment. Diclofenac/misoprostol should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

Hypersensitivity
NSAIDs may precipitate bronchospasm in patients suffering from, or with a history of bronchial asthma or allergic disease.

Long-term treatment

All patients who are receiving long-term treatment with NSAIDs should be monitored as a precautionary measure (e.g. renal, hepatic function and blood counts). During long-term, high dose treatment with analgesic/anti-inflammatory drugs, headaches can occur which must not be treated with higher doses of the medicinal product.

• Diclofenac/Misoprostol Tablets may mask fever and thus an underlying infection.

• Patients with rare hereditary problems of galactose intolerance, the total lactase deficiency or glucose-galactose malabsorption should not take this medicine.
This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

Visual effects
Visual disturbances such as visual impairment, blurred vision or diplopia appear to be NSAID class effects and are usually reversible on discontinuation. If such symptoms occur during diclofenac treatment, an ophthalmological examination may be considered to exclude other causes.

4.5 Interaction with other medicinal products and other forms of interactions

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

Because of their effect on renal prostaglandins, cyclo-oxygenase inhibitors such as diclofenac can increase the nephrotoxicity of ciclosporin. There is a possible increased risk of nephrotoxicity when NSAIDs are given with tacrolimus.

Steady state plasma lithium and digoxin levels may be increased and ketoconazole levels may be decreased.

Pharmacodynamic studies with diclofenac have shown no potentiation of oral hypoglycaemic and anticoagulant drugs. However, as interactions have been reported with other NSAIDs, caution and adequate monitoring are, nevertheless advised (see statement on platelet aggregation in Precautions).

Because of decreased platelet aggregation, caution is advised when using Diclofenac/Misoprostol Tablets with anti-coagulants. NSAIDs may enhance the effects of anti-coagulants, such as warfarin, antiplatelet agents, such as aspirin, and serotonin re-uptake inhibitors (SSRIs) thereby increasing the risk of gastrointestinal bleeding (see section 4.4). Close monitoring of such patients is therefore recommended.

Antidiabetics: Clinical studies have shown that diclofenac can be given together with oral antidiabetic agents without influencing their clinical effect. However, there have been isolated reports of both hypoglycaemic and hyperglycaemic effects necessitating changes in the dosage of the antidiabetic agents during treatment with diclofenac. For this reason, monitoring of the blood glucose level is recommended as a precautionary measure during concomitant therapy. There have also been isolated reports of lactic acidosis when diclofenac was coadministered with metformin, especially in patients with pre-existing renal impairment.

Caution is advised when methotrexate is administered concurrently with NSAIDs because of possible enhancement of its toxicity by the NSAID as a result of increase in methotrexate plasma levels.

Concomitant use with other NSAIDs or with corticosteroids may increase the frequency of gastrointestinal ulceration or bleeding and of side effects generally.

Anti-hypertensives including diuretics, angiotensin-converting enzyme (ACE) inhibitors and angiotensin II antagonists (AIIA): NSAIDs can reduce the efficacy of diuretics and other antihypertensive drugs.

In patients with impaired renal function (e.g. dehydrated patients or elderly patients with compromised renal function), the co-administration of an ACE inhibitor or an AIIA with a cyclo-oxygenase inhibitor can increase the deterioration of the renal function, including the possibility of acute renal failure, which is usually reversible. The occurrence of these interactions should be considered in patients taking diclofenac/misoprostol with an ACE inhibitor or an AIIA.

Antacids may delay the absorption of diclofenac. Magnesium-containing antacids have been shown to exacerbate

misoprostol-associated diarrhoea.

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

NSAIDs should not be used for 8-12 days after mifepristone administration as NSAIDs can reduce the effect of mifepristone.

4.6 Fertility, pregnancy and lactation

Womenofchildbearingpotential
Women of childbearing potential must be informed about the risk of teratogenicity prior to treatment with Diclofenac/Misoprostol Tablets. Treatment must not be initiated until pregnancy is excluded, and women should be fully counselled on the importance of adequate contraception while undergoing treatment. If pregnancy is suspected, treatment must be immediately discontinued (see sections 4.3, 4.4 and 4.8).

Pregnancy
Diclofenac/Misoprostol Tablets are contraindicated in pregnant women and in women planning a pregnancy.

Misoprostol:
Misoprostol induces uterine contractions and is associated with abortion, premature birth, and foetal death and foetal malformations.

Approximately a 3-fold increased risk of malformations was reported in pregnancies exposed to misoprostol during the first trimester, compared to a control group incidence of 2%. In particular, prenatal exposure to misoprostol has been associated with Moebius syndrome (congenital facial paralysis leading to hypomimia, troubles of sucking and deglutition and eye movements, with or without limb defects); amniotic band syndrome (limb deformities/ amputations, especially clubfoot, acheiria, olygodactyly, cleft palate inter alia) and central nervous system anomalies (cerebral and cranial anomalies as anencephaly, hydrocephaly, cerebellar hypoplasia, neural tube defects). Other defects including arthrogryposis have been observed.

Consequently:
- Women should be informed of the risk of teratogenicity.
- Should the patient wish to continue with her pregnancy after exposure of misoprostol in utero, a careful ultrasound scan monitoring of the pregnancy, with a special attention to the limbs and head must be carried out.

Diclofenac:

Inhibition of prostaglandin synthesis might adversely affect pregnancy and/or the embryo/foetal development. Data from epidemiological studies suggest an increased risk of miscarriage and of cardiac malformation and gastroschisis after use of prostaglandin synthesis inhibitors 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 prostaglandin synthesis inhibitors has been 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 the organogenetic period.

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 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.

Breast-feeding
Misoprostol is rapidly metabolised in the mother to misoprostol acid, which is biologically active and is excreted in breast milk. Diclofenac is excreted in breast milk in very small quantities. In general, the potential effects on the infant from any exposure to misoprostol and its metabolites via breast feeding are unknown. However, diarrhoea is a recognised side effect of misoprostol

and could occur in infants of nursing mothers. Diclofenac/Misoprostol Tablets should therefore not be administered to nursing mothers.

4.7 Effects on ability to drive and use machines

Patients who experience dizziness or other central nervous system disturbances while taking NSAIDs should refrain from driving or operating machinery.

4.8 Undesirable effects

In the table below the incidence of adverse drug reactions reported in controlled clinical studies where diclofenac/misoprostol was administered to more than 2000 patients are listed. Additionally, adverse drug reactions reported during post- marketing surveillance are whose frequency cannot be estimated from the available data, such as spontaneous reports, have been listed at frequency 'unknown'. The most commonly observed adverse events are gastrointestinal in nature.

Organ System	Very Common (≥1/10)	Common (≥1/100 and <1/10)	Uncommon (≥1/1,000 and <1/100)	Rare (≥1/10,000, and <1/1,000)	Frequency: Unknown (Post-marketing experience)
Infections and infestations					Aseptic meningitis1
Bloodand lymphatic system disorders			Thrombo-cytopaenia		Aplastic anaemia, agranulocytosis, haemolytic anaemia, leucopenia
Immune system disorders				Anaphylactic reaction	Hypersensitivity
Metabolis m and nutrition disorders					Anorexia
Psychiatric disorders		Insomnia			Psychotic reaction, disorientation, depression, anxiety, nightmares, mood change, irritability
Nervous system disorders		Headache, dizziness			Convulsions, memory disturbance, drowsiness, tremor, taste disturbance, paraesthesia
Eyes disorders					Visual disturbances, blurred vision
Earand labyrinth disorders					Tinnitus
Cardiac disorders					Cardiac failure,palpitations, Kounis syndrome
Vascular disorders					Shock, hypertension, hypotension, vasculitis
Respiratory, thoracic and mediastinal disorders					Asthma, pneumonitis, dyspnoea
Gastrointestinal disorders	Abdominal pain, diarrhoea[2], nausea, dyspepsia	Gastritis, vomiting, flatulence, eructation, constipation, peptic ulcer	Stomatitis		GI perforation[3], gastrointestinal bleeding[3], melaena, haematemesis, colitis, Crohn's disease, oesophageal disorder, mouth ulceration, glossitis, tongue odema, dry mouth, Ischaemic colitis, Gastrointestinalstenosis(as a consequence of gastro intestinalulcer),
					peritonitis(as a consequence of gastro intestinalulcer with perforation, which may lead to peritonitis)

Hepato- biliary disorders		Alanine amino-transferase increased		Hepatitis, jaundice	Hepatitis fulminant, aspartate aminotransferase increased, blood bilirubin increased
Skinand subcutaneous tissue disorders		Erythema multiforme, rash, pruritus	Purpura, urticaria	Angioedema	Toxic epidermal necrolysis[4] , Stevens-Johnson syndrome[4] , dermatitis exfoliative[4] , dermatitis bullous, Henoch Schönlein purpura, mucocutaneous rash, rash vesicular, photosensitivity reaction, alopecia, urticaria
Renaland urinary disorders					Renal failure, acute renal failure, renal papillary necrosis, nephritis interstitial, nephrotic syndrome, proteinuria, haematuria
Pregnancy, puerperium and perinatal conditions				uterine rupture**	Intra-uterine death, incomplete abortion, premature baby, anaphylactoid syndrome of pregnancy, retained placenta or membranes, uterine contractions abnormal
Reproductive system and breast disorders			Menorrhagia, metrorrhagia, vaginal haemorrhage, postmenopausal haemorrhage		Uterine haemorrhage
Congenital,familial and genetic disorders		Foetal malformation			
General disorders and administration site conditions					Oedema[5] , chest pain, face oedema, fatigue, pyrexia, chills, inflammation
Investigations		Blood alkaline phosphatase increased			Decreased haemoglobin
Injury, poisoning and procedural complications					Uterine perforation

[1] Symptoms of aseptic meningitis (stiff neck, headache, nausea, vomiting, fever or impaired consciousness) have been reported during treatment with NSAIDs. Patients suffering from autoimmune disease (e.g. lupus erythematosus, mixed connective tissue disorders) seem to be more susceptible.
[2] Diarrhoea is usually mild to moderate and transient and can be minimised by taking Diclofenac/Misoprostol Tablets with food and by avoiding the use of predominantly magnesium-containing antacids.
[3] GI perforation or bleeding can sometimes be fatal, particularly in the elderly (see section 4.4).
[4] Serious skin reactions, some of them fatal, have been reported very rarely (see section 4.4).
[5] Especially in patients with hypertension or impaired renal function (see section 4.4).

**Uterine rupture has been uncommonly reported after prostaglandin intake during the second or third trimester of pregnancy. Uterine ruptures occurred particularly in multiparous women or in women with a caesarean section scar.

Given the lack of precise and/or reliable denominator and numerator figures, the spontaneous adverse event reporting system through which post marketing safety data are collected does not allow for a medically meaningful frequency of occurrence of any undesirable effects.

With regard to the relative frequency of reporting of adverse reactions during post marketing surveillance, the undesirable effects at the gastrointestinal level were those received most frequently followed by cutaneous/hypersensitivity-type reactions, which is in agreement with the known side effects profile of the NSAIDs drug class.

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. (see section 4.3 and 4.4 for Contraindications and Special warnings and special precautions for use).

Reportingofsuspectedadversereactions
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. You can also report side effects directly at:
HPRA Pharmacovigilance
Earlsfort Terrace
IRL - Dublin 2
Tel: +353 1 6764971
Fax: +353 1 6762517
Website: www.hpra.ie
e-mail: medsafety@hpra.ie

4.9 Overdose

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

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Anti-inflammatory and antirheumatic products,
ATC code: M01BX

Diclofenac/Misoprostol Tablet is a non-steroidal, anti-inflammatory drug, which is effective in treating the signs and symptoms of arthritic conditions.

Mechanism of action
This activity is due to the presence of diclofenac, which has been shown to have anti-inflammatory and analgesic properties.

Diclofenac/Misoprostol Tablets also contain the gastroduodenal mucosal protective component misoprostol, which is a synthetic prostaglandin E1 analogue that enhances several of the factors that maintain gastroduodenal mucosal integrity.

5.2 Pharmacokinetic properties

The pharmacokinetic profiles following oral administration of a single dose or multiple doses of diclofenac sodium and misoprostol administered as Diclofenac/Misoprostol Tablets are similar to the profiles when the two drugs are administered as separate tablets. There are no pharmacokinetic interactions between the two components.

Diclofenac sodium is completely absorbed from the gastrointestinal (GI) tract after fasting oral administration. Only 50 % of the absorbed dose is systemically available due to first pass metabolism. Peak plasma levels are achieved in 2 hours (range 1-4 hours), when given as a single dose under fasting conditions. The area-under-the plasma-concentration curve (AUC) is dose proportional within the range of 25 mg to 150 mg.
The terminal half-life is approximately 2 hours. Clearance and volume of distribution are about 350 ml/min and 550 ml/kg, respectively. More than 99 % of diclofenac sodium is reversibly bound to human plasma albumin, and this has been shown not to be age dependent.

Diclofenac sodium is eliminated through metabolism and subsequent urinary and biliary excretion of the glucuronide and the sulfate conjugates of the metabolites. Approximately 65 % of the dose is excreted in the urine and 35 % in the bile. Less than 1% of the parent drug is excreted unchanged.

Misoprostol is rapidly and extensively absorbed, and it undergoes rapid metabolism to its active metabolite, misoprostol acid, which is eliminated with an elimination t½ of about 30 minutes. No accumulation of misoprostol acid was found in multiple-dose studies, and plasma steady state was achieved within 2 days. The serum protein binding of misoprostol acid is less than 90 %. Approximately 70 % of the administered dose is excreted in the urine, mainly as biologically inactive metabolites.

5.3 Preclinical safety data

In co-administration studies in animals, the addition of misoprostol did not enhance the toxic effects of diclofenac. The combination was also shown not to be teratogenic or mutagenic. The individual components show no evidence of carcinogenic potential.

Misoprostol in multiples of the recommended therapeutic dose in animals has produced gastric mucosal hyperplasia. This characteristic response to E-series prostaglandins reverts to normal on discontinuation of the compound.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Core:
lactose monohydrate
microcrystalline cellulose
maize starch
povidone K-30
magnesium stearate
purified talc

Mantle/Coat:
hypromellose
methylacrylic acid copolymer type C
purified talc
triethylcitrate
sodium starch glycolate
hydrogenated castor oil
microcrystalline cellulose

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years

6.4 Special precautions for storage

This medicine product does not require any special storage instructions.

6.5 Nature and contents of container

Diclofenac/Misprostol Tablets are presented in packs composed of OPA-ALU-PVC blisters with aluminium foil.
Pack size: 6, 7, 56, 60, 84, 100, 120 and 140 tablets

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.
Any unused product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Morningside Healthcare Limited
Unit C, Harcourt Way
Leicester, LE19 1 WP
United Kingdom

8 MARKETING AUTHORISATION NUMBER

PA1333/014/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 18th January 2013
Date of last renewal: 16th August 2017

10 DATE OF REVISION OF THE TEXT

January 2020