Piroxicam Capsules I.P., Piroxicam Dispersible Tablets, Piroxicam Injection (Intramuscular Solution)

DOLONEX®/DOLONEX® DT/DOLONEX® IM

1. NAME OF THE MEDICINAL PRODUCT

DOLONEX®, DOLONEX® DT, DOLONEX® IM

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Capsules:

Each hard gelatin capsule contains Piroxicam IP 20 mg.

Dispersible Tablets:

Each uncoated dispersible tablet contains Piroxicam IP 20 mg.

Intramuscular Solution:

Each ml contains Piroxicam IP 20 mg.

All strengths/presentations mentioned in this document might not be available in the market.

For full list of excipients, please see Section 6.1.

3. PHARMACEUTICAL FORM

Capsule, Dispersible Tablets, Solution for Intramuscular use.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

Piroxicam is a non-steroidal anti-inflammatory drug (NSAID) indicated for a variety of conditions requiring anti-inflammatory and/or analgesic activity, such as rheumatoid arthritis, juvenile rheumatoid arthritis, osteoarthritis (arthrosis, degenerative joint disease), ankylosing spondylitis, pain after operative intervention and following acute trauma, and for the relief of fever and pain associated with acute upper respiratory tract inflammation.

4.2 Posology and Method of Administration

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

Dosage

Rheumatoid Arthritis, Osteoarthritis (Arthrosis, Degenerative Joint Disease), Ankylosing Spondylitis
The recommended starting dose is 20 mg given as a single daily dose. The majority of patients will be maintained on 20 mg daily. A relatively small group of patients may be maintained on 10 mg daily (see section **4.4 Special Warnings and Precautions for Use, Gastrointestinal [GI] Effects**).

Acute Gout
Because of its GI safety profile (see sections **4.3 Contraindications** and **4.4 Special Warnings and Precautions for Use**)

Post-operative and Post-traumatic Pain
The recommended dose is 20 mg, given as a single daily dose.

Upper Respiratory Tract Inflammation
The adult dosage is 10 mg or 20 mg orally once daily for five to seven days.

Use in Children

Juvenile Rheumatoid Arthritis (JRA)
The recommended dosages for children with JRA are based on body weight as follows:

Weight (kg)	Dose (mg)
less than 15	5
16 to 25	10
26 to 45	15
greater than 46	20

The drug should be taken once daily. The dispersible tablet may be used to obtain the exact dose required.

Administration

Oral (Capsules, Dispersible Tablets)
Piroxicam dispersible tablets can be swallowed whole with fluid, or may be dispersed in a minimum of 50 ml of water and then swallowed.

Intramuscular
Piroxicam intramuscular injection is suitable for initial treatment of acute conditions and acute exacerbations of chronic conditions. For continuation of treatment, oral (capsules or tablets) dosage forms should be utilized. Dosage of intramuscular piroxicam is identical with the dosage of piroxicam oral.

Intramuscular injection of piroxicam should be given using aseptic technique into a relatively large muscle. The preferred site is the upper outer quadrant of the buttock (i.e., gluteus maximus). As with all intramuscular injections, aspiration is necessary to help avoid inadvertent injection into a blood vessel.

Combined Administration
The combined total daily dosage of piroxicam, administered as capsules, dispersible tablets, and intramuscular injection should not exceed the maximum recommended daily dosage as indicated above.

4.3 Contraindications

Piroxicam is contraindicated in:

Patients with a history of gastro-intestinal ulceration, bleeding or perforation.

Patients with active peptic ulcerations.

Patients with known hypersensitivity to piroxicam or to any of the excipients. The potential exists for cross sensitivity to aspirin and other NSAIDs. Piroxicam should not be given to

patients in whom aspirin and other NSAIDs induce the symptoms of asthma, nasal polyps, angioedema or urticaria.

Treatment of peri-operative pain in the setting of coronary artery bypass graft (CABG) surgery.

Patients with severe renal and hepatic failure.

Patients with severe heart failure.

4.4 Special Warnings and Precautions for Use

The use of piroxicam with concomitant systemic non-aspirin NSAIDs including cyclooxygenase-2 (COX-2) inhibitors should be avoided. Concomitant use of a systemic NSAID and another systemic NSAID may increase frequency of gastrointestinal ulcers and bleeding.

Cardiovascular Effects

NSAIDs may cause an increased risk of serious cardiovascular (CV) thrombotic events, myocardial infarction, and stroke, which can be fatal. This risk may increase with duration of use. The relative increase of this risk appears to be similar in those with or without known CV disease or CV risk factors. However, patients with known CV disease or CV risk factors may be at greater risk in terms of absolute incidence, due to their increased rate at baseline. To minimize the potential risk for an adverse CV event in patients treated with piroxicam, the lowest effective dose should be used for the shortest duration possible. Physicians and patients should remain alert for the development of such events, even in the absence of previous CV symptoms. Patients should be informed about the signs and/or symptoms of serious CV toxicity and the steps to take if they occur (see section **4.3 Contraindications**).

Hypertension

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

Fluid Retention and Edema

As with other drugs known to inhibit prostaglandin synthesis, fluid retention and edema have been observed in some patients taking NSAIDs, including piroxicam. Therefore, piroxicam should be used with caution in patients with compromised cardiac function and other conditions predisposing to, or worsened by, fluid retention. Patients with pre-existing congestive heart failure or hypertension should be closely monitored.

Gastrointestinal (GI) Effects

NSAIDs, including piroxicam, 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. Administration of doses of greater than 20 mg/day carries an increased risk of gastrointestinal side effects. Evidence from observational studies suggests that piroxicam may be associated with a high risk of serious gastrointestinal toxicity, relative to other NSAIDs. When GI bleeding or ulceration occurs in patients receiving piroxicam, the treatment should be withdrawn. Patients most at risk of developing these types of GI complications with NSAIDs are the elderly, patients with CV disease, patients using concomitant corticosteroids, antiplatelet drugs (such as aspirin), selective serotonin reuptake inhibitors, patients ingesting alcohol or patients with a prior history of, or active, gastrointestinal disease, such as ulceration, GI bleeding or inflammatory conditions. Therefore, piroxicam should be used with caution in these patients (see sections **4.2 Posology and Method of Administration** and **4.3 Contraindications**).

Renal Effects

In rare cases, NSAIDs 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.

Caution should be used when initiating treatment with piroxicam in patients with severe dehydration. Caution is also recommended in patients with kidney disease (see section **4.3 Contraindications**).

Because of extensive renal excretion of piroxicam and its biotransformation products, lower doses of piroxicam should be considered in patients with impaired renal function, and they should be carefully monitored (see sections **4.3 Contraindications** and **5.2 Pharmacokinetic Properties**).

Hepatic Effects

Piroxicam can cause fatal hepatitis and jaundice. Although, such reactions are rare, if abnormal liver function tests persist or worsen, if clinical signs and symptoms consistent with liver disease develop, or if systemic manifestations occur (e.g., eosinophilia, rash, etc.), piroxicam should be discontinued.

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 piroxicam. 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. Piroxicam should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

Ophthalmologic Effects

Because of reports of adverse eye findings with NSAIDs, it is recommended that patients who develop visual complaints during treatment with piroxicam have an ophthalmic evaluation.

Poor Metabolizers of CYP2C9 Substrates

Patients who are known or suspected to be poor CYP2C9 metabolizers based on previous history/experience with other CYP2C9 substrates should be administered piroxicam with caution as they may have abnormally high plasma levels due to reduced metabolic clearance (see section **5.2 Pharmacokinetic Properties,** *Pharmacogenetics*).

Use with Oral Anticoagulants

The concomitant use of NSAIDs, including piroxicam, with oral anticoagulants increases the risk of GI and non-GI bleeding and should be given with caution. Oral anticoagulants include warfarin/coumarin-type and novel oral anticoagulants (e.g., apixaban, dabigatran, rivaroxaban). Anticoagulation/INR should be monitored in patients taking a warfarin/coumarin-type anticoagulant (see section **4.5 Interaction with Other Medicinal Products and Other Forms of Interaction**).

General

When used for the relief of pain and inflammation in upper respiratory tract inflammation, it should be remembered that NSAIDs are only a symptomatic therapy. When given to patients with such conditions, appropriate concomitant antibacterial therapy should be considered.

The following statement applies only when benzyl alcohol is included in the formulation:
Piroxicam solution for intramuscular use contains benzyl alcohol. The preservative benzyl alcohol has been associated with serious adverse events, including the "gasping syndrome", and death in pediatric patients. Although normal therapeutic doses of this product ordinarily deliver amounts of benzyl alcohol that are substantially lower than those reported in association with the "gasping syndrome", the minimum amount of benzyl alcohol at which toxicity may occur is not known. The risk of benzyl alcohol toxicity depends on the quantity administered and the liver and kidneys' capacity to detoxify the chemical. Premature and low-birth weight infants may be more likely to develop toxicity.

The amount of benzyl alcohol in the diluent per each mL is 20 mg.

4.5 Interaction with Other Medicinal Products and Other Forms of Interaction

Acetylsalicylic acid:
As with other NSAIDs, the use of piroxicam in conjunction with acetylsalicylic acid or the concomitant use of two NSAIDs is not recommended because data are inadequate to demonstrate that the combination produces greater improvement than that achieved with the drug alone and the potential for adverse reactions is increased.

Studies in man have shown that the concomitant administration of piroxicam and acetylsalicylic acid resulted in a reduction of plasma levels of piroxicam to about 80% of the normal values.

Piroxicam interferes with the antiplatelet effect of low-dose aspirin, and thus may interfere with aspirin's prophylactic treatment of CV disease.

Anti-coagulants:
Bleeding has been reported rarely when piroxicam has been administered to patients on coumarin type anti-coagulants. Patients should be monitored closely if piroxicam and oral anticoagulants are administered together.

Piroxicam, like other NSAIDs, decreases platelet aggregation and prolongs bleeding time. This effect should be kept in mind when bleeding times are determined.

Antacids:
Concomitant administration of antacids had no effect on piroxicam plasma levels.

Anti-hypertensives including diuretics, angiotensin-converting enzyme (ACE) inhibitors, angiotensin II antagonists (AIIA) and beta-blockers:

NSAIDs can reduce the efficacy of diuretics and other anti-hypertensive drugs including ACE inhibitors, AIIA and beta-blockers.

In patients with impaired renal function (e.g., dehydrated patients or elderly patients with the renal function compromised), the co-administration of an ACE inhibitor or an AIIA and/or diuretics 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 piroxicam with an ACE inhibitor or an AIIA and/or diuretics. Therefore, the concomitant administration of these drugs should be done with caution, especially in elderly patients. Patients should be adequately hydrated and the need to monitor the renal function should be assessed in the beginning of the concomitant treatment and periodically thereafter.

Cardiac glycosides (digoxin and digitoxin):
NSAIDs may exacerbate cardiac failure, reduce glomerular filtration rate (GFR) and increase plasma glycoside levels. Concomitant administration of digoxin or digitoxin had no effect on the plasma levels of piroxicam or either drug.

Cimetidine:
Results of two separate studies indicate a slight increase in absorption of piroxicam following cimetidine administration but no significant changes in elimination parameters. Cimetidine increases the area under the curve ($AUC_{0\text{-}120h}$) and C_{max} of piroxicam by approximately 13% to 15%. Elimination rate constants and half-life show no significant differences. The small but significant increase in absorption is unlikely to be clinically significant.

Cholestyramine:
Cholestyramine has been shown to enhance the oral clearance and decrease the half-life of piroxicam. To minimize this interaction, it is prudent to administer piroxicam at least 2 hours before or 6 hours after cholestyramine.

Corticosteroids:
Increased risk of gastrointestinal ulceration or bleeding.

Cyclosporine:
Increased risk of nephrotoxicity.

Lithium and other protein-bound agents:
Piroxicam is highly protein-bound, and therefore might be expected to displace other protein-bound drugs. The physician should closely monitor patients for change in dosage requirements when administering piroxicam to patients on highly protein-bound drugs. NSAIDs, including piroxicam, have been reported to increase steady-state plasma lithium levels. It is recommended that these levels be monitored when initiating, adjusting and discontinuing piroxicam.

Methotrexate:
When methotrexate is administered concurrently with NSAIDs, including piroxicam, NSAIDs may decrease elimination of methotrexate resulting in increased plasma levels of methotrexate. Caution is advised, especially in patients receiving high doses of methotrexate.

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

4.6 Fertility, Pregnancy and Lactation

Fertility
Based on the mechanism of action, the use of NSAIDs, including piroxicam, may delay or prevent rupture of ovarian follicles, which has been associated with reversible infertility in

some women. In women who have difficulties conceiving or who are undergoing investigation of infertility, withdrawal of NSAIDs, including piroxicam, should be considered.

Pregnancy
Although no teratogenic effects were seen in animal testing, the use of piroxicam during pregnancy is not recommended. Piroxicam inhibits prostaglandin synthesis and release through a reversible inhibition of the cyclo-oxygenase enzyme. This effect, as with other NSAIDs have been associated with an increased incidence of dystocia and delayed parturition in pregnant animals when drug administration was continued into late pregnancy. NSAIDs are also known to induce premature closure of the ductus arteriosus in infants. Therefore, piroxicam should be avoided during the third trimester of pregnancy.

Inhibition of prostaglandin synthesis might adversely affect pregnancy. Data from epidemiological studies suggest an increased risk of spontaneous abortion after use of prostaglandin synthesis inhibitors in early pregnancy. In animals, administration of prostaglandin synthesis inhibitors has been shown to result in increased pre- and post-implantation loss.

If used during second or third trimester of pregnancy, NSAIDs may cause fetal renal dysfunction which may result in reduction of amniotic fluid volume or oligohydramnios in severe cases. Such effects may occur shortly after treatment initiation and are usually reversible. Pregnant women on piroxicam should be closely monitored for amniotic fluid volume.

The following statement applies only when benzyl alcohol is included in the formulation: Benzyl alcohol can cross the placenta (see section **4.4 Special Warnings and Precautions for Use**).

Lactation
The presence of piroxicam in breast milk has been determined during initial and long term dosing conditions (52 days). Piroxicam appeared in breast milk at about 1% to 3% of the maternal plasma concentration. No accumulation of piroxicam occurred in milk relative to that in plasma during treatment. Piroxicam is not recommended for use in nursing mothers as the clinical safety has not been established.

4.7 Effects on Ability to Drive and Use Machines

The effect of piroxicam on the ability to drive or operate heavy machinery has not been studied.

4.8 Undesirable Effects

Piroxicam is generally well tolerated. Gastrointestinal symptoms are the most commonly encountered side effects but in most instances do not interfere with the course of therapy.

Objective evaluations of gastric mucosal appearances and intestinal blood loss show that 20 mg/day of piroxicam administered either in single or divided daily doses is significantly less irritating to the gastrointestinal tract than acetylsalicylic acid.

Blood and lymphatic system disorders: Anemia, aplastic anemia, eosinophilia, hemolytic anemia, leucopenia, thrombocytopenia.

Immune system disorders: Anaphylaxis, serum sickness.

Metabolism and nutrition disorders: Anorexia, hyperglycemia, hypoglycemia, fluid retention.

Psychiatric disorders: Depression, dream abnormalities, hallucinations, insomnia, mental confusion, mood alterations, nervousness.

Nervous system disorders: Aseptic meningitis, dizziness, headache, paresthesia, somnolence, vertigo.

Eye disorders: Blurred vision, eye irritations, swollen eyes.

Ear and labyrinth disorders: Hearing impairment, tinnitus.

Cardiac disorders: Palpitations.

Vascular disorders: Vasculitis, hypertension.

Respiratory, thoracic and mediastinal disorders: Bronchospasm, dyspnea, epistaxis.

Gastrointestinal disorders: Abdominal discomfort, abdominal pain, constipation, diarrhea, epigastric distress, flatulence, gastritis, gastrointestinal bleeding (including hematemesis and melena), indigestion, nausea, pancreatitis, perforation, stomatitis, ulceration, vomiting (see section **4.4 Special Warnings and Precautions for Use, Gastrointestinal (GI) Effects**).

Hepatobiliary disorders: Fatal hepatitis, jaundice.

Reproductive system and breast disorders: Female fertility decreased.

Skin and subcutaneous tissue disorders: Alopecia, angioedema, dermatitis exfoliative, erythema multiforme, non-thrombocytopenic purpura (Henoch-Schoenlein), onycholysis, photoallergic reactions, pruritus, skin rash, Stevens-Johnson syndrome, toxic epidermal necrolysis (Lyell's disease), urticaria, vesiculo bullous reactions (see section **4.4 Special Warnings and Precautions for Use, Skin Reactions**).

Renal and urinary disorders: Nephrotic syndrome, glomerulonephritis, interstitial nephritis; renal failure.

General disorders and administration site conditions: Edema (mainly of the ankle), local adverse reactions (burning sensations) or tissue damage (sterile abscess formation, fatty tissue necrosis) at the site of injection, malaise, transient pain upon injection.

Investigations: Positive ANA, reversible elevations of BUN and creatinine, decreases in hemoglobin and hematocrit unassociated with obvious gastro-intestinal bleeding, increased serum transaminase levels, weight decrease, weight increase.

4.9 Overdose

In the event of overdosage with piroxicam, supportive and symptomatic therapy is indicated. Studies indicate that administration of activated charcoal may result in reduced absorption and re-absorption of piroxicam thus reducing the total amount of active drug available.

Although there are no studies to date, hemodialysis is probably not useful in enhancing elimination of piroxicam since the drug is highly protein-bound.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

Piroxicam is a non-steroidal anti-inflammatory agent, which also possesses analgesic and antipyretic properties. Edema, erythema, tissue proliferation, fever, and pain can all be inhibited in laboratory animals by the administration of piroxicam. It is effective regardless of the etiology of the inflammation. While its mode of action is not fully understood, independent studies *in vitro* as well as *in vivo* have shown that piroxicam interacts at several steps in the immune and inflammation responses through:

- -Inhibition of prostanoid synthesis, including prostaglandins, through a reversible inhibition of the cyclo-oxygenase enzyme.
- -Inhibition of neutrophil aggregation.
- -Inhibition of polymorphonuclear cell and monocyte migration to the area of inflammation.
- -Inhibition of lysosomal enzyme release from stimulated leucocytes.
- -Inhibition of superoxide anion generation by the neutrophil.
- -Reduction of both systemic and synovial fluid rheumatoid factor production in patients with seropositive rheumatoid arthritis.

It is established that piroxicam does not act by pituitary-adrenal axis stimulation. *In vitro* studies have not revealed any negative effects on cartilage metabolism.

In clinical studies piroxicam has been found effective as an analgesic in pain of various etiologies (post-traumatic pain, post-episiotomy pain and post-operative pain). The onset of analgesia is prompt.

5.2 Pharmacokinetic Properties

Absorption and Distribution

Piroxicam is well absorbed following oral administration. With food there is a slight delay in the rate but not the extent of absorption following oral administration. Stable plasma concentrations are maintained throughout the day on once-daily dosage. Continuous treatment with 20 mg/day for periods of 1 year produces similar blood levels to those seen when steady state is first achieved.

Drug plasma concentrations are proportional for 10 mg and 20 mg doses and generally peak within three to five hours after administration. A single 20 mg dose generally produces peak piroxicam plasma levels of 1.5 to 2 mcg/ml while maximum drug plasma concentrations, after repeated daily ingestion of 20 mg piroxicam, usually stabilize at 3 to 8 mcg/ml. Most patients approximate steady state plasma levels within 7 to 12 days.

A multiple dose comparative study of the bioavailability of the injectable form with the oral capsule has shown that after intramuscular administration of piroxicam, plasma levels are significantly higher than those obtained after ingestion of capsules during the 45 minutes following administration the first day, during 30 minutes the second day, and 15 minutes the seventh day. Bioequivalence exists between the two dosage forms.

Metabolism and Elimination

Piroxicam is extensively metabolized and less than 5% of the daily dose is excreted unchanged in urine and feces. Piroxicam metabolism is predominantly mediated via cytochrome P450 CYP 2C9 in the liver. One important metabolic pathway is hydroxylation of the pyridyl ring of the piroxicam side chain, followed by conjugation with glucuronic acid and urinary elimination. The plasma half-life is approximately 50 hours in man.

Patients who are known or suspected to be poor CYP2C9 metabolizers based on previous history/experience with other CYP2C9 substrates should be administered piroxicam with caution as they may have abnormally high plasma levels due to reduced metabolic clearance (see section **4.4 Special Warnings and Precaution for Use, Poor Metabolizers of CYP2C9 Substrates**).

Pharmacogenetics

CYP2C9 activity is reduced in individuals with genetic polymorphisms, such as the CYP2C9*2 and CYP2C9*3 polymorphisms. Limited data from two published reports showed that subjects with heterozygous CYP2C9*1/*2 (n=9), heterozygous CYP2C9*1/*3 (n=9), and homozygous CYP2C9*3/*3 (n=1) genotypes showed 1.7-, 1.7-, and 5.3-fold higher piroxicam systemic levels, respectively, than the subjects with CYP2C9*1/*1 (n=17, normal metabolizer genotype) following administration of an oral single dose. The mean elimination half life values of piroxicam for subjects with CYP2C9*1/*3 (n=9) and CYP2C9*3/*3 (n=1) genotypes were 1.7- and 8.8-fold higher than subjects with CYP2C9*1/*1 (n=17). It is estimated that the frequency of the homozygous*3/*3 genotype is 0% to 5.7% in various ethnic groups.

5.3 Preclinical Safety Data

Subacute and chronic toxicity studies have been carried out in rats, mice, dogs, and monkeys, using doses which ranged from 0.3 mg/kg/day to 25 mg/kg/day. The latter dose is approximately 90 times the recommended human dose level. The only pathology seen was that characteristically associated with the animal toxicology of non-steroidal anti-inflammatory agents; namely, renal papillary necrosis and gastrointestinal lesions. With regard to the latter, the monkey proved to be quite resistant to this effect and the dog unusually sensitive.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Capsules: Lactose, maize starch, magnesium stearate, and sodium lauryl sulphate.

Dispersible Tablets: Lactose IP, dibasic calcium phosphate IP, microcrystalline cellulose IP, hydroxy propyl cellulose NF, and sodium stearyl fumarate NF.

Intramuscular Solution: Sodium dihydrogen phosphate dihydrate, nicotinamide, propylene glycol, ethanol (95%), benzyl alcohol IP, sodium hydroxide, hydrochloric acid, and water for injection.

6.2 Incompatibilities

Solution for intramuscular use should not be mixed with other medications.

6.3 Shelf-life

Capsules: 24 Months.

Dispersible Tablets: 36 Months.

Intramuscular Solution: 36 Months.

6.4 Special Precautions for Storage

Capsules: Store protected from light and moisture.

Dispersible Tablets: Store in a dry place at a temperature not exceeding 40°C.

Intramuscular Solution: Store protected from light and excessive heat.

6.5 Nature and Contents of Container

Capsules (20 mg): Blister pack of 10 Capsules, 15 strips of 10 capsule each.

Dispersible Tablets (20 mg): Blister pack of 10 Tablets, 2 strips per Combistrip, 10 Combistrips per carton Or Blister pack of 15 Tablets, and such 30 Blister packs per carton.

Intramuscular Solution (20 mg/ml): 1 ml and 2 ml in Amber coloured ampoules. 5 Ampoules in a blister strip. 20 Blister in a carton.

6.6 Special Precautions for Disposal and Other Handling

None specific.