SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Piroxicam 20mg Capsules BP

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains 20 mg of Piroxicam PhEur. Also contains lactose.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Capsules hard

Appearance: Hard gelatin, maroon coloured capsule printed with the company logo " PV "and printed with 'P20', or printed with 'PIROXICAM 20'.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Piroxicam is indicated for symptomatic relief of osteoarthritis, rheumatoid arthritis or ankylosing spondylitis.

Due to its safety profile (see sections 4.2, 4.3 and 4.4), Piroxicam is not a first line option should an NSAIDs be indicated. The decision to prescribe Piroxicam should be based on an assessment of the individual patient's overall risks (see sections 4.3 and 4.4).

4.2. Posology and method of administration

The prescription of Piroxicam should be initiated by physicians with experience in the diagnostic evaluation and treatment of patients with inflammatory or degenerative rheumatic diseases.

The maximum recommended daily dose is 20 mg.

Undesirable effects may be minimised by using the minimum effective dose for the shortest duration necessary to control symptoms. The benefit and

tolerability of treatment should be reviewed within 14 days. If continued treatment is considered necessary, this should be accompanied by frequent review.

Given that Piroxicam has been shown to be associated with an increased risk of gastrointestinal complications, the possible need for combination therapy with gastro-protective agents (e.g. misoprostol or proton pump inhibitors) should be carefully considered, in particular for elderly patients.

Use in elderly:
Elderly, frail or debilitated patients may tolerate side effects less well and such patients should be carefully supervised. As with other NSAIDs caution should be used in the treatment of elderly patients who are more likely to be suffering from impaired renal, hepatic or cardiac function.

Use in children: Dosage recommendations and indications for use in children have not been established.

Administration: Oral
To be taken preferably with or after food.

4.3. Contra-indications

History of gastro-intestinal ulceration, bleeding or perforation.

Patient history of gastrointestinal disorders that predispose to bleeding disorders such as ulcerative colitis, Crohn's disease, gastrointestinal cancers or diverticulitis.

Patients with active peptic ulcer, inflammatory gastrointestinal disorder or gastrointestinal bleeding.
Concomitant use with other NSAIDs, including COX-2 selective NSAIDs and acetyl-salicylic acid at analgesic doses.

Concomitant use with anticoagulants.

History of previous serious allergic drug reaction of any type, especially cutaneous reactions such as erythema multiform, Stevens-Johnson syndrome, toxic epidermal necrolysis.

Hypersensitivity to the active substance and excipients, previous skin reaction (regardless of severity) to piroxicam, other NSAIDs and other medications.

Piroxicam should not be given to patients in whom aspirin and other non-steroidal anti-inflammatory drugs induce the symptoms of asthma, rhinitis, angioedema or urticaria.

Piroxicam should be avoided in patients with porphyria.

Severe heart failure.

Last trimester of pregnancy.

4.4 Special warnings and precautions for use

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

The clinical benefit and tolerability should be re-evaluated periodically and treatment should be immediately discontinued at the first appearance of cutaneous reactions or relevant gastrointestinal events.

Gastrointestinal (GI) Effects, Risk of GI Ulceration, Bleeding, and Perforation: NSAIDs, including Piroxicam, can cause serious gastrointestinal events including bleeding, ulceration, and perforation of the stomach, small intestine or large intestine, which can be fatal. These serious adverse events can occur at any time, with or without warning symptoms, in patients treated with NSAIDs.

NSAIDs exposures of both short and long duration have an increased risk of serious GI event. Evidence from observational studies suggests that Piroxicam may be associated with a high risk of serious gastrointestinal toxicity, relative to other NSAIDs.

Patients with significant risk factors for serious GI events should be treated with Piroxicam only after careful consideration (See sections 4.3 and below).

The possible need for combination therapy with gastro-protective agents (e.g. misoprostol or proton pump inhibitors) should be carefully considered (See section 4.2) and also for patients requiring concomitant low dose aspirin, or other drugs likely to increase gastrointestinal risk (see below and section 4.5).

Serious GI complications

Identification at risk subjects:

The risk for developing serious GI complications increases with age. Age over 70 years is associated with high risk of complications. The administration to patients older than 80 years should be avoided.

The risk of GI bleeding, ulceration or perforation is higher with increasing NSAID doses, in patients with a history of ulcer, particularly if complicated with haemorrhage or perforation (see section 4.3), and in the elderly. These patients should commence treatment on the lowest dose available.

When GI bleeding or ulceration occurs in patients receiving piroxicam the treatment should be withdrawn.

NSAIDs should be given with care to patients with a history of gastrointestinal disease (ulcerative colitis, Crohn's disease) as these conditions may be exacerbated (see section 4.8).

Patients taking concomitant oral corticosteroids, selective serotonin reuptake inhibitors (SSRIs) or anti-platelet agents such as low-dose acetylsalicylic acid are at increased risk of serious GI complications (see below and section 4.5).

Patients and physicians should remain alerted for signs and symptoms of GI ulceration and/or bleeding during Piroxicam treatment. Patients should be asked to report any new or unusual abdominal symptom during treatment. If a gastrointestinal complication is suspected during treatment, Piroxicam should be discontinued immediately and additional clinical evaluation and treatment should be considered.

Caution is required if administered to patients suffering from or with a previous history of bronchial asthma.

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 (see section 4.8).

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 NSAIDs therapy.

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

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

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)

Elderly

The elderly have an increased frequency of adverse reactions to NSAIDs, especially gastrointestinal bleeding and perforation which may be fatal (see section 4.2)

Respiratory disorders

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

Skin reactions

Serious skin reactions, some of them fatal, including exfolative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis, have been reported very rarely in association with the use of NSAIDs (see section 4.8). Evidence from observational studies suggests that Piroxicam may be associated with a higher risk of serious skin reactions than other non-oxicam NSAIDs. Patients appear to be at highest risk of 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. Piroxicam should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

Cardiovascular, Renal and Hepatic Impairment

Piroxicam should be used with caution in patients with renal, hepatic and cardiac impairment.. Such agents 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 a non-steroidal anti-inflammatory drug may cause a dose dependent reduction in prostaglandin formation and precipitate renal failure. Patients at greatest risk of such a reaction are those with impaired renal function, cardiac impairment, liver dysfunction, those taking diuretics and the elderly. Renal function should be monitored in these patients (see also section 4.3).

In rare cases, NSAIDs may cause interstitial nephritis, glomerulonephritis, papillary necrosis and the nephrotic syndrome. Due to the renal excretion of piroxicam, patients with severely impaired renal function should be closely monitored.

Because of reports of adverse eye findings with non-steroidal anti-inflammatory drugs it is recommended that patients who develop visual complaints during treatment with piroxicam have ophthalmic evaluation.

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

4.5 Interaction with other medicinal products and other forms of interaction

Antacids: concomitant administration of antacid had no effect on piroxicam plasma levels.

Aspirin and other non-steroidal Anti-inflammatory Drugs: Piroxicam like other non-steroidal anti-inflammatory drugs decreases platelet aggregation and prolongs bleeding time. This effect should be kept in mind when bleeding times are determined. Avoid concomitant use of two or more NSAIDs (including aspirin) as this may increase the risk of adverse effects (see section 4.3). As with other NSAIDs, the use of Piroxicam together with acetylsalicylic acid or concomitant use with other NSAIDs, including other Piroxicam formulations, must be avoided, since data are inadequate to show that such combinations produce greater improvement than that achieved with Piroxicam alone; moreover, the potential for adverse reactions is enhanced (see section 4.4). Human studies have shown that concomitant use of Piroxicam and acetyl-salicylic acid reduces the plasma Piroxicam concentration to about 80% of the usual value.

Cimetidine: Results of two separate studies indicate a slight but significant increase in absorption of piroxicam following Cimetidine administration but no significant changes in elimination rate constants or half-life. The small increase in absorption is unlikely to be clinically significant.

Digoxin, Digitoxin: Concurrent therapy with piroxicam and digoxin, or piroxicam and digitoxin, did not affect the plasma levels of either drug.

Diuretics: Non-steroidal anti-inflammatory drugs may cause sodium, potassium and fluid retention and may interfere with the natriuretic action of diuretic agents. These properties should be kept in mind when treating patients with compromised cardiac function or hypertension since they may be responsible for the worsening of those conditions. Reduced diuretic effect. Diuretics can increase the risk of nephrotoxicity of NSAIDs.

Anti-hypertensive: Reduced anti-hypertensive effect.

Cardiac glycosides: NSAIDs may exacerbate cardiac failure, reduce GFR and increase plasma glycoside levels.

Methotrexate: Decreased elimination of methotrexate. Possibly leading to acute toxicity.

Ciclosporin: Increased risk of nephrotoxicity.

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

Corticosteroids: increased risk of gastrointestinal ulceration or bleeding (see section 4.4).

Anti-coagulants: NSAIDs, including Piroxicam, may enhance the effects of anticoagulants, such as warfarin. Therefore, the use of Piroxicam with concomitant anticoagulant such as warfarin should be avoided. (See section 4.3).

Quinolone antibiotics: 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.

Anti-platelet agents and selective serotonin reuptake inhibitors (SSRIs): Increased risk of gastrointestinal bleeding (see section 4.4).

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

Zidovudine: Increased risk of haematological toxicity when NSAIDs are given with zidovudine. There is evidence of an increased risk of has hemarthroses and haematoma in HIV (+) haemophiliacs receiving concurrent treatment with zidovudine and ibuprofen.

Highly protein-bound drugs: 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.

Lithium: Non-steroidal anti-inflammatory drugs including piroxicam have been reported to increase steady state plasma lithium levels. It is recommended that these levels are monitored when initiating, adjusting and discontinuing piroxicam.

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 safety of piroxicam used during pregnancy or during lactation, has not yet been established. Congenital abnormalities have been reported in association with NSAID administration in man; however, these are low in frequency and do not appear to follow any discernible pattern. Piroxicam inhibits prostaglandin synthesis and release through a reversible inhibition of the cyclo-oxygenase enzyme. This effect, as with other non-steroidal anti-inflammatory drugs has been associated with an increased incidence of dystocia and delayed parturition in pregnant animals when drug administration was continued into late pregnancy. In view of the known effects of NSAIDs on the foetal cardiovascular system (risk of closure of the ductus arteriosus), use in the last trimester of pregnancy is contraindicated. The onset of labour may be delayed and the duration increased with an increased bleeding tendency in both mother and child (see section 4.3). 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.

Lactation: A study indicates that piroxicam appears in the breast milk at about 1% to 3% of the maternal plasma concentrations. No accumulation of piroxicam occurred in milk relative to that in plasma during treatment for up to 52 days. Piroxicam is not recommended for use in nursing mothers as clinical safety has not been established.

See section 4.4 Special warnings and precautions for use, regarding female fertility.

4.7. Effects on Ability to Drive and Use Machines

Dizziness , drowsiness , visual disturbances or headaches are possible undesirable effects after taking NSAIDs , if affected, patients should not drive or operate machinery.

4.8 Undesirable effects

Gastro-intestinal: The most commonly-observed adverse events are gastrointestinal in nature. Peptic ulcers, perforation or GI bleeding, sometimes fatal, particularly in the elderly, may occur (see section 4.4). Nausea, vomiting, diarrhoea, flatulence, constipation, dyspepsia, abdominal pain, melaena, haematemesis, ulcerative stomatitis, abdominal discomfort, gastritis, anorexia, epigastric distress, exacerbation of colitis and Crohn's disease (See section 4.4) have been reported following administration. Less frequently, gastritis has been observed. Pancreatitis has been reported very rarely. Objective evaluations of gastric mucosa appearances and intestinal blood loss show that 20mg/day of piroxicam administered either in single or divided

doses is significantly less irritating to the gastro-intestinal tract than aspirin. Peptic ulceration, perforation and gastro-intestinal bleeding in rare cases fatal, have been reported with piroxicam.

Some epidemiological studies have suggested that piroxicam is associated with higher risk of gastro-intestinal adverse reactions compared with some NSAIDs, but this has not been confirmed in all studies. Administration of doses exceeding 20mg daily (of more than several days duration) carries an increased risk of gastro-intestinal side effects, but they may also occur with lower doses (See section 4.2 Posology and method of administration).

Long term administration of doses of 30 mg or higher carries an increased risk of gastro-intestinal side effects.

Hypersensitivity reactions: Hypersensitivity reactions have been reported following treatment with NSAIDs. These may consist of (a) non-specific allergic reactions and anaphylaxis rarely, (b) respiratory tract reactivity comprising asthma, aggravated asthma, bronchospasm or dyspnoea rarely, or (c) assorted skin disorders, rarely including rashes of various types, pruritus, urticaria, purpura, angiodema and, more rarely exfoliative and bullous dermatoses (including epidermal necrolysis and erythema multiforme). Vasculitis and serum sickness have been rarely reported.

Cardiac: Oedema, hypertension, and cardiac failure, have been reported in association with NSAIDs treatment. The possibility of precipitating congestive heart failure in elderly patients or those with compromised cardiac function should therefore be borne in mind.

Other adverse reactions reported less commonly include:

Dermal hypersensitivity: Rash and pruritis. Photosensitivity reactions occur infrequently. As with other non-steroidal anti-inflammatory drugs, Stevens Johnson syndrome and Toxic Epidermal Necrolysis (very rare). Vasculo bullous reactions have been reported rarely. Oncholysis and alopecia have rarely been reported.

Renal function: Nephrotoxicity in various forms, including interstitial nephritis, nephrotic syndrome, renal papillary necrosis and renal failure.

Haematological: Thrombocytopenia, non-thrombocytopenic purpura (lenoch-schoenlein), eosinophilia, neutropenia, agranulocytosis, leucopenia, aplastic anaemia and haemolytic anaemia. Reversible elevations of blood urea nitrogen (BUN) and creatinine have been reported. Decrease in haemoglobin and haematocrit, unassociated with obvious gastro-intestinal bleeding have occurred. Epistaxis has rarely been reported.

Liver Function: Changes in different liver function parameters have been observed. As with most other non-steroidal anti-inflammatory drugs, some patients may develop increased serum transaminase levels during treatment with piroxicam. Severe hepatic reactions, including jaundice and cases of fatal

hepatitis have been reported. 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), piroxicam should be discontinued.

Neurological and special senses: Optic neuritis, dizziness, headache. Rarely drowsiness, malaise, fatigue, tiredness, nervousness, mood alterations, hallucinations, paraesthesia, mental confusion, vertigo, dream abnormalities. In isolated cases disturbances of sensation as anxiety, convulsions, confusion, depression, , disorientation, disturbance of vision (blurred vision, diplopia), impaired hearing, insomnia, irritability, memory disturbance, nightmares, psychotic reactions, tinnitus, tremor, reports of aseptic meningitis (especially in patients with existing auto-immune disorders, such as systemic lupus erythematosus, mixed connective tissue disease), with symptoms such as stiff neck, headache, nausea, vomiting, fever or disorientation (see section 4.4). Taste alteration disorders.

Other: The following have been reported rarely, palpitations and dyspnoea, anecdotal cases of positive ANA, anecdotal cases of hearing abnormalities, metabolic abnormalities such as hypoglycaemia, hyperglycaemia, weight increase or decrease.

Swollen eyes, blurred vision and eye irritations have been reported. Routine ophthalmoscopy and slit-lamp examination have revealed no evidence of ocular changes. Malaise and tinnitus may occur.

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

4.9. Overdose

In the event of overdose with piroxicam, supportive and symptomatic therapy is indicated.

Symptoms:
Symptoms include headache, nausea, vomiting, epigastric pain, gastrointestinal bleeding, rarely diarrhoea, disorientation, excitation, coma, drowsiness, dizziness, tinnitus, fainting, occasionally convulsions. In cases of significant poisoning acute renal failure and liver damage are possible.

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. 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. Other measures may be indicated by the patient's clinical condition.
Although there are no studies to date, haemodialysis is probably not useful in enhancing elimination of piroxicam since the drug is highly protein bound.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Piroxicam has analgesic, anti-inflammatory and antipyretic properties. It is used in rheumatic disorders such as ankylosing spondylitis, osteoarthritis and rheumatoid arthritis. Oedema, erythema, tissue proliferation, fever and pain can all be inhibited in laboratory animals by the administration of piroxicam. It is effective regardless of the aetiology 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.
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.

5.2 Pharmacokinetic properties

Piroxicam is well absorbed from the gastro-intestinal tract. It is metabolised in the liver by hydroxylation and conjugation with glucuronic acid and excreted predominantly in the urine with smaller amounts in the faeces. Less than 5% of the dose is excreted unchanged. Piroxicam is extensively bound to plasma proteins (about 99%) and has a long plasma half-life of approximately 50 hours, which allows a dosage, for the majority of patients, of 20 mg to be taken once daily. This will provide continuous relief of pain and inflammation over the 24 hour period.

Drug plasma concentrations are proportional for 10 and 20mg doses and generally peak within 3 to 5 hours after medication. A single 20mg dose generally produces peak piroxicam plasma levels of 1.5 to 2 microgram/ml while maximum plasma concentrations, after repeated daily ingestion of 20mg

piroxicam, usually stabilise at 3 to 8 microgram/ml. Most patients approximate steady state plasma levels within 7 to 12 days.

Treatment with a loading dose regimen of 40mg daily for the first 2 days followed by 20mg daily thereafter allows a high percentage (approximately 76%) of steady state levels to be achieved immediately following the second dose. Steady state levels, area under the curves and elimination half-life are similar to that following a 20mg daily dose regimen.

A multiple dose comparative study of the bioavailability of the injectable forms 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.

A multiple dose comparative study of the pharmacokinetics and the bioavailability of Piroxicam with the oral capsule have shown that after once daily administration for 14 days, the mean plasma piroxicam concentration time profiles for capsules and Piroxicam were nearly super imposable. There were no significant differences between the mean steady state C_{max} values, C_{min} values, T½, or T_{max} values. This study concluded that Piroxicam is bioequivalent to the capsule after once daily dosing. Single dose studies have demonstrated bioequivalence as well when the tablet is taken with or without water.

Piroxicam is extensively metabolised and less than 5% of the daily dose is excreted unchanged in urine and faeces. 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.

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.

5.3. Preclinical Safety Data

There are no pre- clinical data of any relevance additional to that already included in other sections of the SPC.

6. PHARMACEUTICAL PARTICULARS

6.1. List of Excipients

Contents of capsules:
Lactose
Maize Starch
Sodium Lauryl Sulphate
Crospovidon (Kollidon CL)
Magnesium Stearate

Capsule Shell:
Amaranth (E123)
Titanium Dioxide (E171)
Gelatin

Printing ink:
Shellac
Soya Lecithin (E322)
Dimeticone
Titanium dioxide (E171)

6.2. Incompatibilities

Not Applicable

6.3. Shelf Life

3 years.

6.4. Special Precautions for Storage

Do not store above 30°C.

6.5 Nature and contents of container

1. Polypropylene tubes with low density polyethylene caps.
   Pack sizes: 28,30,56,60, Dispensing packs: 100,250 and 500 capsules

2. Blister packs consisting of clear PVC and hard temper aluminium foil contained in a carton.
   Pack sizes: 28, 30, 56 and 60 capsules

3. Tracer Packs: Child resistant containers consisting of polypropylene tubes with high density polyethylene caps.

Pack sizes: 28, 30, 56 and 60 capsules.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Not applicable.

7 MARKETING AUTHORISATION HOLDER

Pharmvit Limited
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8. MARKETING AUTHORISATION NUMBER

PL 04556/0050

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 13 January 2004
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10 DATE OF REVISION OF THE TEXT

13/06/2017