1.3.1.1 PROFESSIONAL INFORMATION FOR MEDICINES FOR HUMAN USE

SCHEDULING STATUS S4

PROPRIETARY NAME AND DOSAGE FORM

ASPEN WARFARIN 5 mg (tablets)

COMPOSITION

Each ASPEN WARFARIN 5 mg tablet contains 5 mg warfarin sodium as warfarin sodium clathrate.

Excipients

Dye P/B pink PB, lactose monohydrate, magnesium stearate, sodium starch glycollate, starch (maize).

Contains sugar: Lactose monohydrate 130,375 mg

CATEGORY AND CLASS

A 8.2 Anticoagulants

PHARMACOLOGICAL ACTION

Pharmacodynamic properties

Warfarin is a coumarin-type anticoagulant and acts by depressing synthesis of Vitamin-K dependent coagulation factors in the liver. The resultant *in vivo* effect is a sequential depression of Factors VII, IX, X and II.

Pharmacokinetic properties

After oral administration, absorption is essentially complete and maximal plasma concentrations are reached in 2 to 8 hours. Approximately 99 % is bound to albumin in the plasma. The half-life ranges from 20 to 60 hours with a mean of 40 hours. The duration of action is 2 to 5 days. Food in the gastrointestinal tract can decrease the rate of absorption. Warfarin is transformed to inactive metabolites by the liver and kidneys and these are excreted in the urine and stool.

INDICATIONS

ASPEN WARFARIN 5 mg is indicated for:

Prevention and management of deep venous thrombosis and pulmonary embolism.

Prevention of thromboembolism in:

- atrial fibrillation.
- prosthetic heart valves.
- post myocardial infarction.
- the treatment of transient ischaemic attacks.

CONTRAINDICATIONS

ASPEN WARFARIN 5 mg is contraindicated in:

- Hypersensitivity to warfarin or any of the excipients in the formulation (see COMPOSITION).
- Haemorrhagic stroke.
- Clinically significant bleeding.
- Within 72 hours of major surgery with risk of severe bleeding (see WARNINGS AND SPECIAL PRECAUTIONS).
- Peptic ulcers or other gastrointestinal disease involving bleeding.
- Conditions involving bleeding from respiratory or genito-urinary tract.

- Severe wounds (including surgical).
- Infective endocarditis.
- Impaired liver function.
- Impaired kidney function.
- Hypertension.
- Cerebrovascular haemorrhage.
- Aneurysm - cerebral, aortic.
- Pericarditis, pericardial effusion.
- Neuro- or ophthalmic surgery - recent or contemplated.
- Surgery involving large exposed raw surfaces.
- Within 48 hours postpartum.
- Polyarthritis.
- Vitamin C deficiency.
- Major regional block anaesthesia.
- Inadequate laboratory facilities or lack of patient co-operation.
- Threatened abortion.
- Safety in children younger than 18 years has not been established.
- Medicines where interactions may lead to a significantly increased risk of bleeding (see INTERACTIONS).
- Fibrinolytic medicines (see INTERACTIONS).
- Patients using over-the-counter miconazole oral gel (see INTERACTIONS).
- Pregnancy and lactation (see HUMAN REPRODUCTION).

WARNINGS AND SPECIAL PRECAUTIONS

Abrupt cessation of ASPEN WARFARIN 5 mg therapy is not recommended except when bleeding occurs.

The dose should be tapered over three to four weeks.

Most adverse events reported with ASPEN WARFARIN 5 mg are a result of over-anticoagulation. Therefore, it is important that the need for therapy is reviewed on a regular basis and therapy discontinued when no longer required.

Commencement of therapy

Monitoring

When therapy with ASPEN WARFARIN 5 mg is started using a standard dosing regimen, the international normalisation ratio (INR) should be determined daily or on alternate days in the early days of treatment. Once the INR has stabilised in the target range the INR can be determined at longer intervals.

INR should be monitored more frequently in patients at an increased risk of over-coagulation, e.g. patients with severe hypertension and liver or renal disease.

Patients for whom adherence may be difficult should be monitored more frequently.

Thrombophilia

Patients with protein C-deficiency are at risk of developing skin necrosis when starting ASPEN WARFARIN 5 mg treatment. In patients with protein C-deficiency, therapy should be introduced without a loading dose of ASPEN WARFARIN 5 mg even if heparin is given. Patients with protein S-deficiency may also be at risk and it is advisable to introduce ASPEN WARFARIN 5 mg therapy slowly in these circumstances.

Risk of haemorrhage

The most frequently reported adverse effect of all oral anticoagulants is haemorrhage. ASPEN WARFARIN 5 mg should be given with caution to patients where there is a risk of serious haemorrhage (e.g. concomitant NSAID use, recent ischaemic stroke, bacterial endocarditis, previous gastrointestinal bleeding and severe wounds including surgical wounds).

Risk factors for bleeding include high intensity of anticoagulation (INR > 4,0), age ≥ 65, highly variable INRs, history of gastrointestinal bleeding, uncontrolled hypertension, cerebrovascular disease, serious heart disease, risk of falling, anaemia, malignancy, trauma, renal insufficiency, concomitant medicines (see INTERACTIONS).

All patients treated with ASPEN WARFARIN 5 mg should have their INR monitored regularly. Those at high risk of bleeding may benefit from more frequent INR monitoring, careful dose adjustment to desired INR, and a shorter duration of therapy. Patients should be instructed on measures to minimise risk of bleeding and to immediately report signs and symptoms of bleeding to physicians.

Checking the INR and reducing or omitting doses depending on INR level is essential, following consultation with anticoagulation services if necessary. If the INR is found to be too high, reduce dose or stop ASPEN WARFARIN 5 mg treatment. It will be sometimes necessary to reverse anticoagulation. INR should be checked within 2 to 3 days to ensure that it is falling.

Any concomitant anti-platelet medicines should be used with caution due to an increased risk of bleeding.

Haemorrhage

Haemorrhage can indicate an overdose of ASPEN WARFARIN 5 mg has been taken (see KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT). Unexpected bleeding at therapeutic levels should always be investigated and INR should be monitored (see CONTRAINDICATIONS).

Ischaemic stroke

Anticoagulation following an ischaemic stroke increases the risk of secondary haemorrhage into the infarcted brain. In patients with atrial fibrillation long-term treatment with ASPEN WARFARIN 5 mg is beneficial, but there is a risk of early recurrent embolism and therefore a break in treatment after ischaemic stroke is justified. ASPEN WARFARIN 5 mg treatment should be re-started 2 to 14 days following ischaemic stroke, depending on the size of the infarct and blood pressure. In patients with large embolic strokes or uncontrolled hypertension, warfarin treatment should be stopped for 14 days.

Surgery

Where there is no risk of severe bleeding, surgery can be performed with an INR of < 2. ASPEN WARFARIN 5 mg should be stopped prior to surgery to provide for an appropriate INR (± 2) to be attained.

Where it is necessary to continue anticoagulation e.g. risk of life-threatening thromboembolism, ASPEN WARFARIN 5 mg should be stopped and when the INR is reduced to < 2-heparin therapy should be started.

If surgery is required and ASPEN WARFARIN 5 mg cannot be stopped 3 days beforehand, anticoagulation should be reversed with vitamin K to an appropriate INR of < 2.

The timing for re-instating ASPEN WARFARIN 5 mg therapy depends on the risk of post-operative haemorrhage. In most instances ASPEN WARFARIN 5 mg treatment can be re-started as soon as the patient is able to take oral medicine.

Dental surgery

ASPEN WARFARIN 5 mg need not be stopped before routine dental surgery, e.g. tooth extraction.

Active peptic ulceration

Due to a high risk of bleeding, patients with active peptic ulcers should be treated with caution. Such patients should be reviewed regularly and informed of how to recognise bleeding and what to do in the event of bleeding occurring.

Interactions

Many medicines and foods interact with warfarin and affect the INR (see INTERACTIONS). Any change to medication, including self-medication with over-the-counter products, warrants increased monitoring of the INR. Patients should be instructed to inform their doctor before they start to take any additional medication including over-the-counter medicines, herbal remedies or vitamin preparations.

Thyroid disorders

The rate of warfarin metabolism depends on thyroid status. Therefore patients with hyper- or hypothyroidism should be closely monitored when starting ASPEN WARFARIN 5 mg therapy.

Additional circumstances where changes in dose may be required

The following may also exaggerate the effect of ASPEN WARFARIN 5 mg, and necessitate a

dose reduction:

- Loss of weight.
- Acute illness.
- Cessation of smoking.

The following may reduce the effect of ASPEN WARFARIN 5 mg, and require the dosage to be increased:

- Weight gain.
- Prolonged diarrhoea.
- Prolonged vomiting.

Warfarin resistance

Acquired or inherited warfarin resistance should be suspected if larger than usual daily doses of ASPEN WARFARIN 5 mg are required to achieve the desired anticoagulant effect.

Patients should be given detailed instructions concerning their medication, the importance of compliance and advice concerning modification of their life style if necessary.

The possibility of interactions should be explained. The need for modification of therapy before elective operative procedures or in women contemplating pregnancy should be discussed.

Patients should carry an anticoagulant card or other proof that they are on anticoagulant therapy.

Genetic information

Genetic variability particularly in relation to CYP2C9 and VKORC1 can significantly affect dose

requirements for ASPEN WARFARIN 5 mg. If a familial association with these polymorphisms is known, extra care is warranted.

Effects on the blood

In clinical studies the risk of intracranial bleeding is higher in the elderly. Although cumulative risk of bleeding was related to duration of anticoagulation therapy, risk may be highest early in treatment.

Withdrawal of ASPEN WARFARIN 5 mg therapy may lead to rebound hypercoagulability, ASPEN WARFARIN 5 mg should therefore be withdrawn gradually, although there is no clinical evidence to support this.

Effects on the musculoskeletal system

Vitamin K is involved in bone metabolism and vitamin K deficiency is associated with an increased risk of osteoporotic fractures. Patients on long-term treatment with oral anticoagulants such as ASPEN WARFARIN 5 mg that are vitamin K antagonists may be at increased risk of osteoporosis and fractures. Special care is required.

Effects on the reproductive system

There have been reports of priapism in patients taking ASPEN WARFARIN 5 mg. As with warfarin-induced skin necrosis, priapism appears to be associated with protein C-deficiency, and the two conditions frequently occur together.

Dermatological effects

Skin and soft-tissue necrosis is a less frequent but well-established side effect of ASPEN WARFARIN 5 mg. It is characterised by a localised, painful skin lesion, initially erythematous or

haemorrhagic in appearance but which becomes bullous and eventually culminates in gangrenous necrosis. Fatalities have occurred.

Areas of increased subcutaneous fat such as breast, thigh, and buttock have most often been involved. The aetiology is unknown. Patients with protein C-deficiency appear to be at highest risk.

Treatment with ASPEN WARFARIN 5 mg should be stopped if skin lesions appear and vitamin K should be given to reverse this effect.

Heparin should be given to provide anticoagulation. Fresh frozen plasma or protein C concentrates may also have a role in reversing the condition. Surgical intervention is usually required if necrosis does develop.

Effect on eye

Intra-ocular haemorrhage leading to loss of vision can occur in patients with neovascular (wet) age-related macular degeneration receiving ASPEN WARFARIN 5 mg. Caution is advised in such patients.

Effects on ability to drive and use machines

Patients should not drive, use machinery or perform any tasks that require concentration until they are certain that ASPEN WARFARIN 5 mg does not adversely affect their ability to do so safely (see SIDE EFFECTS).

Excipients:

Lactose warning:

ASPEN WARFARIN 5 mg contains lactose which may have an effect on the glycaemic control of patients with diabetes mellitus. Patients with rare hereditary problems of galactose intolerance e.g. galactosaemia, the Lapp lactase deficiency or glucose-galactose malabsorption or fructose intolerance should not take ASPEN WARFARIN 5 mg.

INTERACTIONS

ASPEN WARFARIN 5 mg has a narrow therapeutic range and care is required with all concomitant therapy.

The individual product information for any new concomitant therapy should be consulted for specific guidance on warfarin dose adjustment and therapeutic monitoring. If no information is provided the possibility of an interaction should still be considered.

Increased monitoring should be considered when commencing any new therapy if there is any doubt as to the extent of interaction.

Pharmacodynamic interactions

Medicines which are contraindicated

Concomitant use of medicines used in the treatment or prophylaxis of thrombosis, or other medicines with adverse effects on haemostasis may increase the pharmacological effect of ASPEN WARFARIN 5 mg, increasing the risk of bleeding, including asparaginase and some contrast media.

Fibrinolytic medicines such as streptokinase, urokinase and alteplase are contraindicated in patients receiving ASPEN WARFARIN 5 mg (see CONTRAINDICATIONS).

Over-the-counter miconazole oral gel is contraindicated in patients receiving ASPEN WARFARIN 5 mg (see CONTRAINDICATIONS).

Some interacting medicines do not produce predictable effects. There have been reports of increased as well as decreased anticoagulant activity with disopyramide, phenytoin, quinidine and oral contraceptives.

Dipyridamole and aspirin can cause bleeding when given to patients taking anticoagulants, but without any alteration in INR.

Medicines which should be avoided

The following medicines should be avoided, or administered with caution with increased clinical and laboratory monitoring:

- Clopidogrel.
- Non-steroidal anti-inflammatory drugs (NSAIDs), including aspirin and cox-2 specific NSAIDs.
- Thrombin inhibitors such as dabigatran.
- Dipyridamole.
- Unfractionated heparins and heparin derivatives, low molecular weight heparins.
- Fondaparinux, rivaroxaban.
- Glycoprotein IIb/IIIa receptor antagonists such as eptifibatide, tirofiban and abciximab.
- Selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs) antidepressants.
- Other medicines which inhibit haemostasis, clotting or platelet action.

A low-dose aspirin with ASPEN WARFARIN 5 mg may have a role in some patients, but the risk

of gastrointestinal bleeding is increased. ASPEN WARFARIN 5 mg may initially be given with heparin in the initial treatment of thrombosis, until the INR is in the correct range.

Metabolic interactions

Warfarin is a mixture of enantiomers which are metabolised by different CYPP450 cytochromes. R-warfarin is metabolised primarily by CYP1A2 and CYP3A4. S-warfarin is metabolised primarily by CYP2C9. The efficacy of warfarin is affected primarily when the metabolism of S-warfarin is altered.

Medicines that compete as substrates for these cytochromes or inhibit their activity may increase warfarin plasma concentrations and INR, potentially increasing the risk of bleeding. When these medicines are co-administered, the dosage of ASPEN WARFARIN 5 mg may need to be reduced and the level of monitoring increased.

Conversely, medicines which induce these metabolic pathways may decrease warfarin plasma concentrations and INR, potentially leading to reduced efficacy. When these medicines are co-administered, the dosage of ASPEN WARFARIN 5 mg may need to be increased and the level of monitoring increased.

There is a small subset of medicines for which interactions are known, however their clinical effect on the INR is variable. In these cases increased monitoring on starting and stopping therapy is advised.

Care should also be taken when stopping or reducing the dose of a metabolic inhibitor or inducer, once patients are stable on this combination (offset effect).

Medicines which potentiate the effect of warfarin

Allopurinol, capecitabine, erlotinib, disulfiram, azole antifungals (fluconazole, itraconazole, ketoconazole, miconazole), omeprazole, paracetamol (prolonged regular use), propafenone, amiodarone, tamoxifen, methylphenidate, zafirlukast, fibrates, statins (predominantly associated with fluvastatin), erythromycin, telithromycin, co-trimoxazole, metronidazole, chloramphenicol, cimetidine, clofibrate, danazol, glucagon, quinidine, thyroid hormones, tramadol.

Medicines which antagonise the effect of warfarin

Barbiturates, primidone, carbamazepine, griseofulvin, oral contraceptives, rifampicin, azathioprine, phenytoin, phytomenadione.

Medicines with variable effect

Corticosteroids, nevirapine, ritonavir.

Other medicine interactions

Broad spectrum antibiotics may potentiate the effect of ASPEN WARFARIN 5 mg by reducing the gut flora which produce vitamin K. Similarly, orlistat may reduce absorption of vitamin K. Cholestyramine and sucralfate potentially decrease absorption of ASPEN WARFARIN 5 mg. Increased INR has been reported in patients taking glucosamine and ASPEN WARFARIN 5 mg. This combination is not recommended.

Interactions with herbal products

Herbal preparations containing St. John's wort (*Hypericum perforatum*) must not be used whilst taking ASPEN WARFARIN 5 mg due to a proven risk of decreased plasma concentrations and reduced clinical effects of warfarin. Many other herbal products have a theoretical effect on ASPEN WARFARIN 5 mg, however most of these interactions are not proven. Patients should

generally avoid taking any herbal medicines or food supplements whilst taking ASPEN WARFARIN 5 mg and should be told to advise their doctor if they are taking any, as more frequent monitoring is advisable.

Alcohol

Acute ingestion of a large amount of alcohol may inhibit the metabolism of warfarin and increase INR. Conversely, chronic heavy alcohol intake may induce the metabolism of ASPEN WARFARIN 5 mg.

Interactions with food and food supplements

Case reports suggest an interaction between ASPEN WARFARIN 5 mg and cranberry juice, in most cases leading to an increase in INR or bleeding event. Patients should be advised to avoid cranberry products. Increased supervision and INR monitoring should be considered for any patient taking ASPEN WARFARIN 5 mg and regular cranberry juice.

Limited evidence suggests that grapefruit juice may cause a modest rise in INR in some patients taking ASPEN WARFARIN 5 mg.

Certain foods such as liver, broccoli, Brussels sprouts and green leafy vegetables contain large amounts of vitamin K. Sudden changes in diet can potentially affect control of anticoagulation. Patients should be informed of the need to seek medical advice before undertaking any major changes in diet.

Many other food supplements have a theoretical effect on ASPEN WARFARIN 5 mg; however most of these interactions are not proven. Patients should generally avoid taking any food supplements whilst taking ASPEN WARFARIN 5 mg, and should be told to advise their doctor if

they are taking any, as more frequent monitoring is advisable.

Laboratory tests

Heparins may prolong the INR, therefore a sufficient time interval should be allowed after administration before performing the test.

HUMAN REPRODUCTION

ASPEN WARFARIN 5 mg is contraindicated in pregnancy and lactation as ASPEN WARFARIN 5 mg is teratogenic in animals and humans (see CONTRAINDICATIONS).

Pregnancy

Warfarin is a recognised teratogen. Based on human experience warfarin causes foetal warfarin syndrome (warfarin embryopathy) characterised by bone stippling (chondrodysplasia punctata) and nasal hypoplasia when administered in the first trimester of pregnancy.

CNS abnormalities may develop after use in any trimester, but appear most likely when used in the second or third trimester. The use in the late stages of pregnancy is associated with foetal haemorrhage. ASPEN WARFARIN 5 mg has also been associated with an increased rate of abortion and foetal death. Women of child-bearing age who are taking ASPEN WARFARIN 5 mg should use effective contraception during treatment.

Lactation

Warfarin is excreted in breast milk in small amounts. Women on ASPEN WARFARIN 5 mg should not breastfeed.

Women of childbearing potential

Females of childbearing potential must be advised to use effective contraception during treatment, and for at least 1 month after the final dose of ASPEN WARFARIN 5 mg.

DOSAGE AND DIRECTIONS FOR USE

The administration and dosage of ASPEN WARFARIN 5 mg must be individualised for each patient according to the patient's sensitivity as indicated by the international normalised ratio (INR).

INR measurements should be carried out before treatment, on the 2nd and 3rd days of treatment and then on alternate days until the maintenance dose is established. Thereafter the patient should be monitored monthly.

Satisfactory levels of INR for maintenance, vary with the condition treated and the risk of thromboembolism.

INR 2,0 to 2,5 (PT ratio 1,3 to 1,5)

Prophylaxis of DVT including surgery in high risk patients.

INR 2,0 to 3,0 (PT ratio 1,3 to 1,5)

Prophylaxis of DVT in hip surgery and fractured femur operations.

Prevention of thromboembolism in myocardial infarction, mitral stenosis with embolism, atrial fibrillation, tissue prosthetic heart valves.

Treatment of DVT, pulmonary embolism, transient ischaemic attacks, systemic embolism.

INR 3,0 to 4,5 (PT ratio 1,5 to 2,0)

Recurrent DVT and pulmonary embolism. Arterial disease including myocardial infarction. Prosthetic heart valves. The correlation between the INR and the PT ratio is based on thromboplastin with an International sensitivity index of 2,3.

Treatment should be commenced with a 5 mg dose once daily. The dose should be titrated according to INR results, to the desired INR, according to the condition. Maintenance doses usually range from 2,5 to 10 mg daily.

Doses should be given at the same time each day.

SIDE EFFECTS

Blood and the lymphatic system disorders

Less frequent: Anaemia

Immune system disorders

Less frequent: Hypersensitivity reactions

Vascular disorders

Frequent: Haemorrhage from almost any organ of the body with the consequent effects of haematomas

Less frequent: Intracranial haemorrhage, including cerebral subdural haematoma, haemothorax, epistaxis, gastrointestinal haemorrhage, rectal haemorrhage, haematemesis.

Gastrointestinal disorders

Less frequent: Pancreatitis, diarrhoea, nausea, vomiting, melaena

Hepatobiliary disorders

Less frequent: Jaundice, hepatic dysfunction

Skin and subcutaneous tissue disorders

Less frequent: Rash, alopecia, purpura, purple toe syndrome, erythematous swollen skin patches leading to ecchymosis, infarction and skin necrosis, skin reactions

Musculoskeletal, connective tissue and bone disorders

Less frequent: Osteoporosis

Renal and urinary disorders

Less frequent: Haematuria

Reproductive system and breast disorders

Less frequent: Priapism

General disorders and administrative site conditions

Less frequent: Fever

Investigations

Less frequent: Unexplained drop in haematocrit, decreased haematocrit

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT

See SIDE EFFECTS.

Symptoms

Excessive bleeding may occur.

Treatment

The benefit of gastric decontamination is uncertain. If the patient presents within 1 hour of ingestion of more than 0,25 mg/kg or more than the patient's therapeutic dose, consider activated charcoal (50 g for adults; 1 g/kg for children).

In cases of life-threatening haemorrhage

Stop warfarin treatment, give prothrombin complex concentrate (Factors II, VII, IX, and X) 30 to 50 units/kg or (if no concentrate available) fresh frozen plasma 15 ml/kg.

Non-life threatening haemorrhage

Where anticoagulation can be suspended, give slow intravenous injection of phytomenadione (vitamin K_1) 10 mg to 20 mg for adults (250 micrograms/kg for a child).

Where rapid re-anticoagulation is desirable (e.g. valve replacements) give prothrombin complex concentrate (Factors II, VII, IX, and X) 30 to 50 units/kg or (if no concentrate available) fresh frozen plasma 15 ml/kg.

Monitor INR to determine when to restart normal therapy. Monitor INR for at least 48 hours post overdose.

For patients on long-term warfarin therapy without major haemorrhage

- INR > 8,0 with no bleeding or minor bleeding - stop warfarin, and give phytomenadione (vitamin K_1) 0,5 mg to 1 mg for adults, 0,015 to 0,030 mg/kg (15 to 30 micrograms/kg) for

children by slow intravenous injection or 5 mg by mouth (for partial reversal of anticoagulation give smaller oral doses of phytomenadione e.g. 0,5 mg to 2,5 mg using the intravenous preparation orally); repeat dose of phytomenadione if INR still too high after 24 hours. Large doses of phytomenadione may completely reverse the effects of warfarin and make re-establishment of anticoagulation difficult.

- INR 6,0 to 8,0, no bleeding or minor bleeding - stop warfarin, restart when INR is below appropriate target value.
- INR < 6,0 but more than 0,5 units above target value - reduce dose or stop warfarin, restart when INR is below target value.

For patients not on long-term anticoagulants without major haemorrhage

Measure the INR at presentation and sequentially every 24 to 48 hours after ingestion depending on the initial dose and initial INR.

- If the INR remains normal for 24 to 48 hours and there is no evidence of bleeding, there should be no further monitoring necessary.
- Give vitamin K_1 (phytomenadione) if:
  a) there is no active bleeding and the patient has ingested more than 0,25 mg/kg or
  b) the INR is already significantly prolonged (INR > 4,0).

The adult dose of vitamin K_1 is 10 mg to 20 mg orally (250 micrograms/kg body weight for a child). Delay oral vitamin K_1 at least 4 hours after any activated charcoal has been given. Repeat INR at 24 hours and consider further vitamin K_1.

IDENTIFICATION

8,0 mm diameter, flat, pink speckled, circular, bevelled edged tablet with a breakline on one side

PRESENTATION

100 or 500 tablets are packed into a white polypropylene securitainer, together with a silica gel desiccant and a foam insert of polyurethane or cotton wool balls and sealed with a white low density polyethylene (LDPE) closure.

100 tablets are packed into a white high density polyethylene (HDPE) securitainer, together with a silica gel desiccant and a foam insert of polyurethane or cotton wool balls and sealed with a white low density polyethylene (LDPE) tamper evident cap.

100 tablets are packed into a white high density polyethylene (HDPE) securitainer, together with a silica gel desiccant and a foam insert of polyurethane or cotton wool balls and sealed with a white low density polyethylene (LDPE) tamper evident handycap.

Not all packs and pack sizes are necessarily marketed.

STORAGE INSTRUCTIONS

Store at or below 25 °C.

Protect from light.

Keep in original packaging until required for use.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER

H/8.2/0742

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION

PHARMACARE LIMITED

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DATE OF PUBLICATION OF THE PROFESSIONAL INFORMATION FOR MEDICINES FOR HUMAN USE

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