

Prescribing Information

Pheninidone 10mg & 25mg tablets (phenindione)

Presentation: Each tablet contains 10mg or 25mg phenindione.

Indications: Anticoagulation. Therapy can be initiated with heparin and phenindione together. Anticoagulant therapy in the prophylaxis of systemic embolisation in patients with rheumatic heart disease and atrial fibrillation. Prophylaxis after insertion of prosthetic heart valves. Prophylaxis and treatment of venous thrombosis and pulmonary embolism.

Dosage and administration: Oral administration. *Adults:* Initially 200mg, then 100mg on 2nd day. Adjust dose from 3rd day, dependent on the results of the appropriate coagulation tests. Heparin should be stopped at least 6 hours prior first control test. A maintenance dose of 50-150mg/day is satisfactory in most patients.

Contraindications: Hypersensitivity to the product or any of the excipients, haemorrhagic stroke, clinically significant bleeding risk of severe bleeding after major surgery, within 48 hours postpartum, concomitant use with drugs which lead to increased risk of severe renal or hepatic disease, bacterial endocarditis, uncontrolled hypertension, galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption.

Precautions and warnings: Hypersensitivity to phenindione or any of the excipients. Caution in active peptic ulceration and thyroid disorders. Reduction of dosage may be required in cases of loss of weight, the elderly, acute illnesses, deficient renal function, and decreased dietary intake of Vitamin K. Dose may need to be increased with weight gain, diarrhoea and vomiting, increased intake of Vitamin K, fats or oils. *Monitoring:* INR should be determined daily or on alternate days in the early days of treatment and at longer intervals once stabilized in the target range. More frequent monitoring recommended for patients at increased risk of over coagulation e.g. those with severe hypertension, liver or renal disease or those with poor adherence. Patients with protein C and protein S deficiency are at risk of developing skin necrosis. Caution in patients with risk of serious haemorrhage (e.g. NSAID use, anti-platelet drugs, recent ischaemic stroke, bacterial endocarditis, previous gastrointestinal bleeding). Unexpected bleeding at therapeutic levels should always be investigated. A break in treatment after ischaemic stroke is justified. Re-start treatment 2-14 days following ischaemic stroke. With large embolic strokes, or uncontrolled hypertension, Phenindione should be stopped for 14 days. *Surgery:* If no risk of severe bleeding, surgery can be performed with an INR of <2.5. With risk of severe bleeding, phenindione should be stopped 3 days prior to surgery; if this is not possible then anticoagulation should be reversed with low-dose vitamin K. Vitamin K can lead to resistance to the action of phenindione.

Interactions: Fibrinolytics, clopidogrel, NSAIDs, sulfapyrazone, bivalirudin, dabigatran, dipyrindamole, heparins, fondaparinux,

rivaroxaban, eptifibatide, tirofiban and abciximab, prostacyclin, SSRI and SNRI antidepressants, ACTH, allopurinol, amitriptyline/nortriptyline, cimetidine, dextropro-poxyphene, glucagon, hepato-toxic drugs, phenformin, thyroid compounds, tolbutamide, disulfiram, amiodarone, metronidazole, anabolic steroids, corticosteroids, broad spectrum antibiotics, carbamazepine, colestyramine, sucralfate, griseofulvin, rifampicin, phenytoin, some herbal products (theoretical). INR monitoring should be considered for patients taking phenindione and regular cranberry juice or foods containing large amounts of vitamin K.

Pregnancy and lactation: Oral anticoagulant therapy is contraindicated in pregnancy and lactation.

Undesirable effects: Hypersensitivity including skin rashes, alopecia, exanthema, skin necrosis, exfoliative dermatitis, leucopenia and agranulocytosis, hepatitis and renal damage with tubular necrosis. Micro-adenopathy, jaundice, albuminuria, eosinophilia, a leucaemoid blood picture, and cytopenia may be observed. Fever, nervous system disorders, cerebral haemorrhage; cerebral subdural haematoma, haemorrhage, haemothorax, epistaxis, gastrointestinal haemorrhage, haematuria, rectal haemorrhage, haematemeses; pancreatitis; diarrhoea; nausea; vomiting; melaena; taste disturbances have also been reported. Unexplained drop in haematocrit; haemoglobin decreased.

(Please refer to the Summary of Product Characteristics for detailed information)

Overdose: The onset of bleeding may be delayed and patients may remain profoundly anti-coagulated for several days. Spontaneous bruising, haematomas, haematuria, rectal bleeding and haemorrhage into any internal organ may occur. The benefit of gastric decontamination is uncertain. If the patient presents within one hour of ingestion of more than 0.25mg/kg or more than the patient's therapeutic dose, consider activated charcoal (50g for adults; 1g/kg for children). Measure the prothrombin time at presentation and sequentially every 24-48 hours after ingestion depending on the initial dose and initial INR.

Basic NHS Cost: £79.01 10mg x 28 tablets; £99.89 25mg x 28 tablets

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Marketing Authorisation Holder: Amdipharm Mercury Company Limited (AMCo), 1st Floor, Capital House, 85 King William Street, London, EC4N 7BL.

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Adverse events should be reported to the local regulatory authority.

Reporting forms and information can be found at <http://www.mhra.gov.uk/yellowcard>.

Adverse events should also be reported to **Amdipharm Mercury Medical Information** at **08700 70 30 33** or by email to medicalinformation@amcolimited.com