Prescribing Information

Phenindione 50mg tablets

Composition: Each tablet contains 50mg 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. **Posology and method of administration: For oral administration. Adults:** Initially load with 200mg, then 100mg on 2nd day. Adjust dose from 3rd day, dependent on the results of the appropriate coagulation tests which should be done at regular intervals. Heparin should be stopped at least 6 hours prior first control test. A maintenance dose of 50-150mg/day is satisfactory in most patients, but a "resistant" patient may need 200mg/day or more. A "sensitive" patient may need less than 50mg/day. Therapeutic effect occurs in 36-48 hours after the initial dose and wanes over 48-72 hours after Phenindione is stopped. **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. **Special warnings and precautions for use:** Awareness of occurrence of allergic reactions by the patients is required. A 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. **Active peptic ulceration:** Caution is required in this group of patients. **Thyroid disorders:** Patients with hyper- or hypo-thyroidism should be closely monitored. Suspect acquired or inherited Phenindione resistance if larger than usual daily doses are required. **Interaction with other medicinal products and other forms of interaction:** fibrinolytics like streptokinase and alteplase are contra-indicated in patients receiving Phenindione. Clopidogrel, NSAIDs, sulfinpyrazone, bivalirudin, dabigatran, dipyridamole, heparins, fondaparinux, rivaroxaban, eptifibatide, tirofiban and abciximab, prostacyclin, SSRI and SNRI antidepressants should be avoided or used with caution. ACTH, allopurinol, amitriptyline/nortriptyline, Cimetidine, Dextropro-poxyphene, Glucagon, Hepato-toxic drugs, Phenformin, Thyroid compounds, Tolbutamide, Disulfiram, Amiodarone, metronidazole, anabolic steroids, corticosteroids, and broad spectrum antibiotics potentiate the effect of Phenindione. Carbamazepine, Colestyramine, sucralfate, griseofulvin, rifampicin, and phenytoin antagonise Phenindione. Interactions with herbal products is theoretical but should be avoided. **Interactions with food and food supplements.** Case reports suggest a possible interaction between anticoagulants (e.g. warfarin) and cranberry juice in most cases leading to an increase in INR or bleeding event. INR monitoring should be considered for patients taking Phenindione and regular cranberry juice. Certain foods such as liver, broccoli, brussels sprouts and green leafy vegetables contain large amounts of vitamin K. **Pregnancy:** 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, haematemesis; pancreatitis; diarrhoea; nausea; vomiting; melaena; taste disturbances have also been reported. Unexplained drop in haematocrit; haemoglobin decreased. (***Please refer 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. **Management:** 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.

Legal Category: POM

Basic NHS Cost: £51.84 per 28 tablets.

Marketing Authorization Number: PL 10972/0039

Marketing Authorization Holder: Amdipharm Mercury Company Limited, NLA Tower, Croydon, CR0 0XT.

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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**