monitored closely in patients receiving concomitant treatment.

- **CONTRA-INDICATIONS** Avoid use within 48 hours postpartum · haemorrhagic stroke · significant bleeding
- **CAUTIONS** Bacterial endocarditis (use only if warfarin otherwise indicated) · conditions in which risk of bleeding is increased · history of gastrointestinal bleeding · hyperthyroidism · hypothyroidism · peptic ulcer · postpartum (delay warfarin until risk of haemorrhage is low—usually 5–7 days after delivery) · recent ischaemic stroke · recent surgery · uncontrolled hypertension
- **SIDE-EFFECTS**
  - **Common or very common** Haemorrhage
  - **Rare or very rare** Alopecia · nausea · vomiting
  - **Frequency not known** Blue toe syndrome · CNS haemorrhage · diarrhoea · fever · haemothorax · jaundice · pancreatitis · skin necrosis (increased risk in patients with protein C or protein S deficiency) · skin reactions
- **CONCEPTION AND CONTRACEPTION** Women of child-bearing age should be warned of the danger of teratogenicity.
- **PREGNANCY** Should not be given in the first trimester of pregnancy. Warfarin, acenocoumarol, and phenindione cross the placenta with risk of congenital malformations, and placental, fetal, or neonatal haemorrhage, especially during the last few weeks of pregnancy and at delivery. Therefore, if at all possible, they should be avoided in pregnancy, especially in the first and third trimesters (difficult decisions may have to be made, particularly in women with prosthetic heart valves, atrial fibrillation, or with a history of recurrent venous thrombosis or pulmonary embolism). Stopping these drugs before the sixth week of gestation may largely avoid the risk of fetal abnormality.
- **HEPATIC IMPAIRMENT** In general, manufacturers advise caution in mild to moderate impairment; avoid in severe impairment.
- **MONITORING REQUIREMENTS**
  - The base-line prothrombin time should be determined but the initial dose should not be delayed whilst awaiting the result.
  - It is essential that the INR be determined daily or on alternate days in early days of treatment, *then* at longer intervals (depending on response), *then* up to every 12 weeks.
  - Change in patient's clinical condition, particularly associated with liver disease, intercurrent illness, or drug administration, necessitates more frequent testing.
- **PATIENT AND CARER ADVICE** Anticoagulant treatment booklets should be issued to all patients or their carers; these booklets include advice for patients on anticoagulant treatment, an alert card to be carried by the patient at all times, and a section for recording of INR results and dosage information. In **England**, **Wales**, and **Northern Ireland**, they are available for purchase from:
  3M Security Print and Systems Limited
  Gorse Street, Chadderton
  Oldham
  OL9 9QH
  Tel: 0845 610 1112
  GP practices can obtain supplies through their Local Area Team stores. NHS Trusts can order supplies from www.nhsforms.co.uk or by emailing nhsforms@spsl.uk.com.
  In **Scotland**, treatment booklets and starter information packs can be obtained by emailing stockorders.DPPAS@apsgroup.co.uk or by fax on (0131) 6299 967
  Electronic copies of the booklets and further advice are also available at www.npsa.nhs.uk/nrls/alerts-and-directives/alerts/anticoagulant.

Warfarin sodium

10-Oct-2016

- **INDICATIONS AND DOSE**

Treatment and prophylaxis of thrombotic episodes (induction)

▸ BY MOUTH

- Neonate (initiated under specialist supervision): Initially 200 micrograms/kg for 1 dose on day 1, then reduced to 100 micrograms/kg once daily for the following 3 days, subsequent doses dependent on INR levels, induction dose may need to be altered according to condition (e.g. abnormal liver function tests, cardiac failure), concomitant interacting drugs, and if baseline INR above 1.3.
- Child: Initially 200 micrograms/kg (max. per dose 10 mg) for 1 dose on day 1, then reduced to 100 micrograms/kg once daily (max. per dose 5 mg) for the following 3 days, subsequent doses adjusted according to INR levels, induction dose may need to be altered according to condition (e.g. abnormal liver function tests, cardiac failure), concomitant interacting drugs, and if baseline INR above 1.3

Treatment and prophylaxis of thrombotic episodes following induction dose (if INR still below 1.4)

▸ BY MOUTH

- Neonate (under expert supervision): 200 micrograms/kg once daily.
- Child: 200 micrograms/kg once daily (max. per dose 10 mg)

Treatment and prophylaxis of thrombotic episodes following induction dose (if INR above 3.0)

▸ BY MOUTH

- Neonate (under expert supervision): 50 micrograms/kg once daily.
- Child: 50 micrograms/kg once daily (max. per dose 2.5 mg)

Treatment and prophylaxis of thrombotic episodes following induction dose (if INR above 3.5)

▸ BY MOUTH

- Neonate (under expert supervision): Dose to be omitted.
- Child: Dose to be omitted

Treatment and prophylaxis of thrombotic episodes (usual maintenance)

▸ BY MOUTH

- Neonate (under expert supervision): Maintenance 100–300 micrograms/kg once daily, doses up to 400 micrograms/kg once daily may be required especially if bottle fed, to be adjusted according to INR.
- Child: Maintenance 100–300 micrograms/kg once daily, doses up to 400 micrograms/kg once daily may be required especially if bottle fed, to be adjusted according to INR

- **UNLICENSED USE** Not licensed for use in children.

IMPORTANT SAFETY INFORMATION

MHRA/CHM ADVICE: WARFARIN: REPORTS OF CALCIPHYLAXIS (JULY 2016)

An EU-wide review has concluded that on rare occasions, warfarin use may lead to calciphylaxis—patients should be advised to consult their doctor if they develop a painful skin rash; if calciphylaxis is diagnosed, appropriate treatment should be started and consideration should be given to stopping treatment with warfarin. The MHRA has advised that calciphylaxis is most commonly observed in patients with known risk