Konakion® MM Paediatric

Phytomenadione

COMPOSITION

Active substance: phytomenadione (synthetic vitamin K_1)

Excipients: glycocholic acid, sodium hydroxide, lecithin, hydrochloric acid, water for injection

GALENICAL FORM AND AMOUNT OF ACTIVE INGREDIENT PER UNIT

MM paediatric ampoules (0.2 ml) containing 2 mg.

Each amber-glass ampoule contains 0.2 ml of a clear mixed micelle solution with 2 mg vitamin K_1 (filling volume 0.3 ml) for oral or parenteral administration.

INDICATIONS AND POTENTIAL USES

Prophylaxis and treatment of hemorrhagic disease of the newborn.

DOSAGE AND ADMINISTRATION

Prophylaxis

For all healthy neonates: 2 mg orally at birth or shortly after birth, followed by 2 mg four to seven days later.

Breast-fed infants should be given an additional 2 mg dose orally after four to six weeks.

If the product cannot be given orally, neonates should receive 1 mg i.m. or i.v. at birth or shortly after birth.

Where a second oral dose after four to seven days (and, in breast-fed children, an additional oral dose after four to six weeks) cannot be guaranteed, a single i.m. dose of 1 mg (0.1 ml) is recommended at birth or shortly after birth.

Neonates at special risk (e.g. premature infants, birth asphyxia, neonates with obstructive jaundice, newborn of mothers treated with anticoagulants or antiepileptics):

Intramuscular and intravenous doses should not exceed 0.4 mg/kg (equivalent to 0.04 ml/kg) in premature infants weighing less than 2.5 kg (see “Warnings and Precautions”).

The size and frequency of further doses should be based on coagulation status.

Treatment

Initial dose: 1 mg i.v.; further doses as required, depending on clinical picture and coagulation status. Treatment with Konakion MM paediatric may need to be accompanied by more immediate effective therapy such as transfusion of whole blood or blood clotting factors in order to compensate for severe blood loss and delayed response to vitamin K_1.

CONTRAINDICATIONS

Hypersensitivity to phytomenadione or any of the excipients listed under "Composition".

WARNINGS AND PRECAUTIONS

Parenteral administration, particularly if rapid, is associated with a risk of kernicterus in premature infants weighing less than 2.5 kg and especially in acidotic premature infants.

INTERACTIONS

Dicoumarol and its derivatives antagonise the effect of vitamin K_1 on postribosomal carboxylation of certain clotting factors and inhibitors. Coadministration of anticonvulsants can impair the action of phytomenadione.

UNDESIRABLE EFFECTS

Immune system

Anaphylactoid reactions occur in rare cases after parenteral use of phytomenadione.

Administration site reactions

Parenteral use of Konakion MM paediatric may lead in very rare cases to local irritation.

OVERDOSAGE

Hypervitaminosis K_1 is unknown. The following undesirable effects have been reported in connection with overdose during use of Konakion in neonates and infants: jaundice, hyperbilirubinemia, increased AST (GOT) and GGT, abdominal pain, constipation, soft stools, malaise, motor restlessness and skin rash. Causality has not been established. The majority of these undesirable effects were considered non-serious and resolved without any treatment.

Treatment should be aimed at alleviating symptoms.

PROPERTIES/EFFECTS

ATC code: B02BA01

Mechanism of action

Vitamin K_1 is a procoagulant factor. As a cocarboxylase, phytomenadione is involved in the formation of prothrombin, factor VII, factor IX and factor X, and of the clotting inhibitors protein C and protein S.

Vitamin K_1 does not readily cross the placental barrier from mother to child and is excreted only in small amounts in breast milk.

Vitamin K_1 deficiency leads to an increased tendency to hemorrhagic disease of the newborn. Administration of vitamin K_1, which promotes synthesis of the above-mentioned clotting factors in the liver, can reverse an abnormal coagulation status and bleeding due to vitamin K_1 deficiency.

PHARMACOKINETICS

In the mixed micelle solution, vitamin K_1 is solubilised by means of a physiological colloidal system consisting of lecithin and bile acid.

Absorption

Bioavailability is approximately 50%.

Distribution

Phytomenadione accumulates mainly in the liver, is up to 90% bound to lipoproteins in the plasma and is stored in the body only for short periods of time. It crosses the placenta only in small amounts.

Metabolism

Vitamin K_1 is converted to more polar metabolites such as phytomenadione-2,3-epoxide.

Elimination

The half-life of vitamin K_1 in plasma is approximately 1.5 to 3 hours. Vitamin K_1 is excreted in bile and urine as glucuronide and sulphate conjugates.

PRECLINICAL DATA

No mutagenic or carcinogenic effects have been reported to date.

Injection of vitamin K_1 from day 6 to day 11 of gestation produced teratogenic effects in mice.

SPECIAL REMARKS

Stability

This medicinal product must not be used after the expiry date (EXP) shown on the container.

Special precautions for storage

Store in original container, protect from light. Do not store above 25°C.

The ampoule solution must be clear at the time of use. Incorrect storage can result in turbidity or phase separation. In such cases the ampoule must not be used.

Instructions for handling

Oral administration

With the dispensers included in the pack: after breaking the ampoule, place the dispenser vertically into the ampoule;

withdraw the solution until it reaches the mark (= 2 mg vitamin K_1);

inject the contents of the dispenser directly into the neonate's mouth.

Parenteral administration

Konakion MM paediatric should not be diluted or mixed with other parenteral medications. It may, however, be injected into the lower part of an infusion set.

PACKS

MM paediatric ampoules (0.2 ml) containing 2 mg:	5
Dispenser for oral administration:	5

This is a medicament

A medicament is a product which affects your health, and its consumption contrary to instructions is dangerous for you.

Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacist who sold the medicament.

The doctor and the pharmacist are experts in medicine, its benefits and risks.

Do not by yourself interrupt the period of treatment prescribed for you.

Do not repeat the same prescription without consulting your doctor.

Medicine: keep out of reach of children

Council of Arab Health Ministers

Union of Arab Pharmacists

Current at September 2009

Made for F. Hoffmann-La Roche Ltd, Basel, Switzerland by CENEXI SAS, Fontenay-sous-Bois, France