Konakion
Trade Mark

COMPOSITION
Phytomenadione: synthetic vitamin K₁.

PROPERTIES, EFFECTS
Vitamin K₁, the active ingredient of Konakion, is a coagulation-promoting factor. As a component of a liver carboxylate system, it is involved in the carboxylation of the coagulation factors II (prothrombin), VII, IX and X and of the coagulation inhibitors protein C and protein S in the postribosomal phase. Anticoagulants of the dicoumarol type inhibit reduction of vitamin K₁ (quinone form) to vitamin K₁ hydroquinone and also prevent the vitamin K₁ epoxide which arises after the carboxylation reaction from being reduced to the quinone form.

Konakion is thus an antagonist of Marcumar™ and similar anticoagulants. It does not, however, inhibit the action of heparin Liquemin™, for this purpose Protamine should be used.

In the mixed-micelles solution, vitamin K₁ is solubilized by means of a micelle colloidal system consisting of lecithin and bile acid, based on a physiological principle also found in the human body. Owing to the absence of organic solvents, venous tolerance to Konakion mixed-micelle solution is good.

INDICATIONS
Hemorrhage or threatened hemorrhage as a result of severe 'hypoprothrombinemia' (i.e. deficiency of coagulation factors II, VII, IX and X) due, for instance, to overdosage of anticoagulants of the dicoumarol type or their combination with phenylbutazone, or to other forms of hypovitaminosis K (e.g. obstructive jaundice, liver and intestinal disorders, prolonged administration of antibiotics, sulfonamides or salicylates).

Hemorrhage in the newborn: prophylaxis and therapy.

DOSAGE
Konakion MM ampoules are for i.v. injection or oral use.

The ampoule solution should not be mixed with other parenteral medications, but may be injected, where appropriate, into the lower part of the infusion set. Mild hemorrhage or tendency to hemorrhage: 5 – 10 drops of Konakion. A second, possibly larger, dose should be given if there is no effect within eight to twelve hours. In general, temporary withdrawal of oral anticoagulant therapy is recommended.

Severe, life-threatening hemorrhage during anticoagulant therapy: 10 mg (up to 20 mg) Konakion (1-2 MM ampoules 10 mg) by slow i.v. injection, or, where appropriate, with continuous infusion of dextrose 5% into the lower section of the infusion set. In life-threatening gastrointestinal or intracranial bleeding, coagulation factor concentrates should be administered, possibly together with Konakion.

Hemorrhage or threatened hemorrhage in newborn or premature infants: prophylaxis: 1 mg (1 ampoule 1 mg) i.m. immediately post-partum. Therapy: 1 mg per kg (1-5 ampoules 1 mg) daily i.m. for one to three days (may be given orally in the milk on the second and third days).

SPECIAL DOSAGE INSTRUCTIONS
Acute intoxications with oral anticoagulants: 10 – 20 mg Konakion (1-2 MM ampoules 10 mg) daily i.v., and later orally, with regular monitoring of prothrombin values until coagulation returns to normal.

If a patient receiving anticoagulants of the dicoumarol type has to undergo surgery, the anticoagulant effect can be counteracted by Konakion (unless anticoagulation protection is desired). If there is a recurrence of thrombosis while Konakion is being used, the anti-coagulant therapy must initially be continued with i.v. administration of Liquemin.

If the patient is referred to another physician, the latter must be notified that Konakion has been prescribed.

ADMINISTRATION
The drops are best diluted in a cold drink such as fruit juice, which should then be drunk immediately. Any unpleasant aftertaste can be avoided by drinking sufficient fluid after the dose.

Instructions for use of drop counter
The dropper makes it easy to measure the dose (1 drop ≈ 1 mg vitamin K₁). Hold the bottle vertically, upside-down. If the drops do not fall immediately, shake or tap the bottle gently or tip repeatedly.

RESTRICTIONS ON USE
Konakion ampoules should not be used for patients with pronounced allergic diathesis.

When treating patients with severely impaired liver function, it must be borne in mind that one MM ampoule contains 54.6 mg glycocholic acid. The limited experience gained to date suggests, however, that liver function is unlikely to deteriorate.

The 10 mg per ml mixed-micelle ampoule must not be given to infants less than one year old, since no data are available as yet on this patient group. Because of the lower doses required, Konakion MM paediatric should be used in neonates and infants under one year of age.

The dosage in neonates should not exceed 5 mg during the first few days of life on account of the immaturity of the hepatic enzyme systems. Only 1 mg ampoules may be used in these patients.

At the time of use, the contents of the MM ampoules (10 mg/ ml) should be clear. Following incorrect storage, the contents may become turbid or phaseseparated. In this event the ampoule must not be used.

UNDESIRABLE EFFECTS
Intravenous injection of Konakion may, in rare cases, cause severe, shock-like reactions. The preparation should therefore be given by very slow i.v. injection, or, where appropriate, with continuous infusion of dextrose 5% into the lower section of the infusion set. Should an anaphylactoid reaction nevertheless occur, i.v. epinephrine should be injected without delay, followed by i.v. administration of glucocorticoids. As an additional measure, volume replacement may be performed.

Local intravenous tolerability of Konakion mixed-micelle solution (10 mg/ ml) is good. Very rarely, however, the veins may become irritated or phlebitis may develop. Intramuscular administration may cause local pain, sometimes with erythema at the injection site. There may also be tenderness.

INTERACTIONS
Dicoumarol and its derivatives antagonize the effect of vitamin K₁ on postribosomal carboxylation of certain coagulation factors and inhibitors.

OVERDOSAGE
Hypervitaminosis of vitamin K₁ is unknown.

STABILITY
This medicine should not be used after the expiry date (EXP) shown on the pack. Konakion (MM) ampoule solution should not be stored above 25°C.

Keep the glass ampoule(s) in the outer carton in order to protect from light.

PACKS
| Drops 2% (1 drop ≈ 1 mg; 1 ml ≈ 20 drops) | 2.5 ml |
|-Amplexes 1 mg in 0.5 ml | 5 |
| Ampoules 10 mg in 1 ml | 5 |
| Ampoules MM 10 mg in 1 ml | 5 |

Medicine: keep out of reach of children

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