Optimal absorption requires the presence of bile and pancreatic juice. Systemic availability following oral or intramuscular dosing is approximately 50%, with a wide range of interindividual variability. Onset of action occurs approximately 1-3 hours after intravenous administration and 4-6 hours after intramuscular or oral doses.

**Distribution**
The primary distribution compartment corresponds to the plasma volume. In blood plasma 90% of phytomenadione is bound to lipoproteins (VLDL fraction). Normal plasma concentrations of phytomenadione range from 0.4 to 1.2 µg per litre. Plasma concentrations between 10 and 20 µg per litre are achieved following intramuscular doses of 10 g phytomenadione. Phyotomenadione does not readily cross the placenta and is poorly distributed into breast milk.

**Metabolism**
Phytomenadione is rapidly converted into more polar metabolites, including phytomenadione-2,3-epoxide. Some of this metabolite is reconverted into phytomenadione.

**Elimination**
Following metabolic degradation, phytomenadione is excreted in the bile and urine as glucuronide and sulfate conjugates. Less than 10% of a dose is excreted unchanged in the urine. The elimination half-life has been reported to be between 1.5 and 3 hours.

**Pharmacokinetics in Special Clinical Situations**
Absorption of phytomenadione is impaired by various conditions, including malabsorption syndromes, short bowel syndrome, biliary atresia and pancreatic insufficiency. Elderly anticoagulated patients are more sensitive than younger ones to parenteral phytomenadione.

**Indications**
Hemorrhage or risk of hemorrhage as a result of
severe hypoprothrombinemia’ (i.e. deficiency of clotting factors II, VII, IX and X) of various etiologies, including overdosage of coumarin-type anticoagulants, their combination with phenylbutazone and other forms of hypovitaminosis K (e.g. in obstructive jaundice and liver and intestinal disorders, and after prolonged treatment with antibiotics, sulfonamides or salicylates).

**Contraindications**
Hypersensitivity to phytomenadione or any of the excipients (see Composition).

**Side Effects**
There are isolated, unconfirmed reports of anaphylactoid reactions occurring after intravenous injection of Konakion MM.

Very rarely, venous irritation or phlebitis has been reported in association with intravenous administration of Konakion mixed micelle solution (10 mg/ml). Localized pain, sometimes accompanied by erythema at the injection site, has occasionally occurred to children given Konakion by intramuscular injection. Tenderness to pressure may also be observed.

**Precautions**
The MM ampoules containing 10 mg/ml must not be administered to infants under one year of age. Konakion MM paediatric is the only formulation that should be used in these patients. The contents of the 10 mg/MM ampoules must be clear when used. Turbidity or phase separation can occur if ampoules are stored improperly. The ampoules must not be used in such cases.

**Pregnancy and Lactation**
No controlled studies of Konakion have been performed in animals or pregnant women. On the basis of many years’ clinical experience, however, it is safe to assume that neither phytomenadione nor the excipients contained in the various Konakion formulations have any reproductive toxicological effects when the drug is given at the recommended dosages. As with all medications, however, Konakion should be given to pregnant women only if clearly needed.

Only a small fraction of administered vitamin K₁ enters the breast milk. At therapeutic doses, administration of Konakion to nursing mothers accordingly does not pose a risk to their infants.

**Overdosage**
Hypervitaminosis K₁ is unknown.

**Stability**
This medicine should not be used after the expiry date (EXP) shown on the pack.

**Drug Interactions**
Coumarin and its derivatives antagonize the effect of vitamin K₁ on the post-translational carboxylation of certain clotting factors and inhibitors. Coadministration of anticonvulsants can impair the action of phytomenadione.

**Dosage and Administration**
The most suitable route of administration (oral, intramuscular, intravenous), dose, dosage interval and duration of treatment depend on the severity of the patient’s hypoprothrombinemia and his or her response.

**Standard Dosage**
Mild Hemorrhage or Hemorrhagic Tendency: 1 chewable dragée. This should be followed by a second, possibly larger, dose if no effect is seen within 8-12 hours. Generally speaking, oral anticoagulants should be discontinued temporarily.

Severe, Life-threatening Hemorrhage during Anticoagulant Therapy: 10-20 mg Konakion (one to two 10 mg Konakion MM ampoules) by slow intravenous injection (at least 30 seconds). If necessary, the drug can be injected into the lower chamber of an LV, set during an infusion of 0.9% sodium chloride or 5% glucose. See special dosage instructions.

**Special Dosage Instructions**
Acute intoxication with oral anticoagulants: 10-20 mg vitamin K₁ (one to two 10 mg Konakion MM ampoules) daily by intravenous injection, followed by oral treatment and continuous monitoring of prothrombin time until the patient’s coagulation status normalizes.
Konakion can be used to reverse the action of coumarin-type anticoagulants prior to surgery (provided anticoagulant protection is not desired). If thrombosis recurs, anticoagulation must be reinstituted, initially by giving intravenous heparin.

When patients who have received Konakion are referred to another physician for further care, the latter should be informed that the drug was prescribed.

In life-threatening intracranial or gastrointestinal hemorrhage, clotting factor replacement should be instituted as a first-line measure, accompanied by coadministration of Konakion.

Use of the oral formulations: The chewable dragées should be chewed thoroughly before swallowing or allowed to dissolve slowly in the mouth.