Vitamin K_1 (phytomenadione) 2016

Alert	Check ampoule carefully as an adult 10 mg ampoule (Konakion MM Adult) is also available.
Indication	Prophylaxis and treatment of vitamin K deficiency bleeding (VKDB) including haemorrhagic disease of the newborn.
Action	Fat soluble vitamin which promotes the activation of blood coagulation Factors II, VII, IX and X in the liver.
Drug Type	Vitamin.
Trade Name	Konakion MM Paediatric.
Presentation	2 mg/0.2 mL ampoule.
Dosage / Interval	**IM prophylaxis** < 1500 g administer 0.5 mg (0.05 mL) as a single dose at birth. ≥ 1500 g administer 1 mg (0.1 mL) as a single dose at birth. **Oral prophylaxis** Administer 2 mg orally for 3 doses: First dose: At birth. Second dose: 3–5 days of age (at time of newborn screening) or at one week of age Third dose: 4 weeks of age. **IV prophylaxis** Administer 0.3 mg/kg as a single dose. Administer slowly, not exceeding 1 mg/minute. IV prophylaxis may be given in sick infants if unable to give by IM injection. **IV treatment of haemorrhagic disease of the newborn** Administer 1 mg IV as a slow bolus (maximum 1 mg per minute). If required, dilute with glucose 5% or sodium chloride 0.9% as described below. Dose can be repeated in 4–6 hours if required. Must be administered in the presence of a medical officer. May be given subcutaneously if venous access not available.
Route	IM, Oral, IV, subcutaneous
Preparation/Dilution	IM and oral: Administer injection undiluted. IV: If required draw up one ampoule (0.2 mL) and dilute up to 2 mL (to make a 1 mg/mL solution) with glucose 5% or sodium chloride 0.9%.
Administration	IV: Administer as a slow IV bolus. Maximum rate 1mg per minute. Administer undiluted or dilute with sodium chloride 0.9% or glucose 5% as above. May be injected into the lower part of an infusion set running sodium chloride 0.9% or glucose 5%. IM: Administer undiluted. Do not use the solution if it is turbid or separated. Solution must be clear. Oral: Injection solution can be administered orally. Break ampoule, place dispenser vertically into ampoule; withdraw solution from ampoule into dispenser until solution reaches marking on dispenser (2 mg); administer contents directly into mouth.
Monitoring	Monitor prothrombin time when treating clotting abnormalities (a minimum of 2 to 4 hours is needed for measurable improvement). Efficacy of treatment with Vitamin K_1 is decreased in patients with liver disease. The risk of childhood cancer is not increased by IM administration of vitamin K_1. Repeated doses are advised if infant vomits within an hour of an oral dose or if diarrhoea occurs within 24 hours of administration. Check with medical officer for advice.
Contraindications	Oral prophylaxis is contraindicated in infants who are: Premature; unwell; on antibiotics; have cholestasis; have diarrhoea.

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	Oral prophylaxis is contraindicated in infants of mothers who are on anticonvulsants including phenytoin, barbiturates and carbamazepine; rifampicin and the vitamin K antagonists including warfarin and phenindione.
Precautions	IV administration is associated with a possible risk of kernicterus in premature infants weighing less than 2.5 kg.
Drug Interactions	Co-administration of anticonvulsants can impair the action of vitamin K_1.
Adverse Reactions	Pain, swelling and erythema at IM injection site. Severe hypersensitivity reactions, including death have been reported with rapid IV administration – administer IV doses slowly and only on recommendation by a consultant.
Compatibility	Fluids: Glucose 5%, glucose 10%, sodium chloride 0.9%. Y site: Alfentanil, amikacin, aminophylline, ascorbic acid, atracurium, atropine sulfate, aztreonam, calcium chloride, calcium gluconate, cefazolin, cefotaxime, ceftriaxone, dexamethasone, dopamine, adrenaline (epinephrine), fentanyl, furosemide (frusemide), gentamicin, heparin sodium, hydrocortisone, indomethacin, magnesium sulfate, midazolam, morphine, phenobarbital (phenobarbitone), sodium bicarbonate, vancomycin.
Incompatibility	Fluids: Fat emulsion (intravenous) Y-site: Amphotericin (conventional), ampicillin, dantrolene sodium, diazepam, diazoxide, dobutamine, haloperidol lactate, hydralazine, magnesium sulfate, methylprednisolone, phenytoin, promethazine, sulfamethoxazole-trimethoprim.
Stability	Use immediately.
Storage	Store below 25^{O}C. Protect from light.
Special comments	Check ampoule carefully as an adult 10 mg ampoule (Konakion MM Adult) is also available.
Evidence summary	**Australian NH&MRC Guideline:** All newborn infants should receive vitamin K prophylaxis. Healthy newborn infants should receive vitamin K_1 either: • By intramuscular injection of 1 mg (0.1 mL) of Konakion® MM Paediatric at birth. This is the preferred route for reliability of administration and level of compliance. Or • As three 2 mg (0.2 mL) oral doses of Konakion® MM Paediatric, given at birth, at the time of newborn screening (usually at three to five days of age) and in the fourth week. [1] Newborns who are too unwell and are unable to take oral vitamin K_1 (or whose mothers have taken medications that interfere with vitamin K metabolism) should be given 1 mg of Konakion® MM Paediatric by intramuscular injection at birth. A smaller intramuscular dose of 0.5 mg (0.05 mL) should be given to infants with a birth weight of less than 1.5 kg.[1] **Efficacy:** A single dose (1.0 mg) of intramuscular vitamin K_1 after birth is effective in the prevention of classic HDN. Either intramuscular or oral (1.0 mg) vitamin K prophylaxis improves biochemical indices of coagulation status at 1–7 days. Neither intramuscular nor oral vitamin K_1 has been tested in randomised trials with respect to effect on late HDN. When three doses of oral vitamin K_1 are compared to a single dose of intramuscular vitamin K_1, the plasma vitamin K_1 concentrations are higher in the oral group at two weeks and two months, but, again, there is no evidence of a difference in coagulation status. (LOE II, GOR B)[2] Continuous oral prophylaxis with weekly doses of 1 mg or daily doses of 25 microgram for 3 months appears to be the most effective dosing strategy. Studies using 3 x 2 mg (days 1, 4–10, and 28–42) reported an incidence of late VKDB at 0.4–0.87 per 10^5 infants. (LOE III-2, GOR B).[3, 4] Failure of prophylaxis occurs principally with parental refusal of infant vitamin K_1 and in infants with cholestasis (prolonged jaundice). (LOE III-2, GOR B) [4, 5] **Management of vitamin K deficiency bleeding:** Administer Vitamin K_1 (phytomenadione) 1 mg intravenously slowly (LOE IV, GOR B). Give subcutaneously if venous access not

	available.[6] **Pharmacokinetics:** In healthy, fully breast-fed, newborn babies, significantly higher plasma vitamin K_1 concentrations were reported several weeks after IM as compared to oral vitamin K_1. Half-life of oral and intramuscular vitamin K_1 were considerably longer in newborn infants (median 76 hours; range 26 to 193 hours) [7, 8] compared to adults (6 hours; range 2–26 hours)[9]. Re-dosing of oral vitamin K_1 is recommended by 1 month in breast fed infants.[8] (LOE II GOR B) In preterm infants and sick infants unable to receive intramuscular vitamin K_1, 0.3 mg/kg intravenously resulted in similar serum concentrations as oral administration of 3 mg vitamin K_1 and after intramuscular administration of 1.5 mg vitamin K_1. Supports recommendation for intravenous 0.4 mg/kg phytomenadione - vitamin K_1 - Konakion MM Paediatric in infants unable to receive oral or intramuscular vitamin K_1.[7] (LOE IV, GOR B).
References	1. NHMRC. Joint statement and recommendations on vitamin K administration to newborn infants to prevent vitamin K deficiency bleeding in infancy. National Health and Medical Research Council; 2010. 2. Puckett RM, Offringa M. Prophylactic vitamin K for vitamin K deficiency bleeding in neonates. The Cochrane Database of Systematic Reviews. 2000:CD002776. 3. Ipema HJ. Use of oral vitamin K for prevention of late vitamin k deficiency bleeding in neonates when injectable vitamin K is not available. The Annals of Pharmacotherapy. 2012;46:879-83. 4. Laubscher B, Banziger O, Schubiger G, Swiss Paediatric Surveillance U. Prevention of vitamin K deficiency bleeding with three oral mixed micellar phylloquinone doses: results of a 6-year (2005-2011) surveillance in Switzerland. European Journal of Pediatrics. 2013;172:357-60. 5. Busfield A, Samuel R, McNinch A, Tripp JH. Vitamin K deficiency bleeding after NICE guidance and withdrawal of Konakion Neonatal: British Paediatric Surveillance Unit study, 2006-2008. Archives of Disease in Childhood. 2013;98:41-7. 6. Williams MD, Chalmers EA, Gibson BE, Haemostasis, Thrombosis Task Force BCfSiH. The investigation and management of neonatal haemostasis and thrombosis. British Journal of Haematology. 2002;119:295-309. 7. Raith W, Fauler G, Pichler G, Muntean W. Plasma concentrations after intravenous administration of phylloquinone (vitamin K(1)) in preterm and sick neonates. Thrombosis Research. 2000;99:467-72. 8. Stoeckel K, Joubert PH, Gruter J. Elimination half-life of vitamin K1 in neonates is longer than is generally assumed: implications for the prophylaxis of haemorrhaghic disease of the newborn. European Journal of Clinical Pharmacology. 1996;49:421-3. 9. Marinova M, Lutjohann D, Breuer O, Kolsch H, Westhofen P, Watzka M, Mengel M, Stoffel-Wagner B, Hartmann G, Coch C, Oldenburg J. VKORC1-dependent pharmacokinetics of intravenous and oral phylloquinone (vitamin K1) mixed micelles formulation. European Journal of Clinical Pharmacology. 2013;69:467-75. 9. MIMS Online August 2015. 10. Australian Injectable Drugs Handbook, 6th Edition, Society of Hospital Pharmacists of Australia 2014 11. Thomson Reuters (2011). Neofax. Twenty fourth Edition. 12.Trissel's online via Micromedex

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