Vitamin K_1 (Phytomenadione)

Newborn use only

2022

Alert	Check ampoule carefully as an adult 10 mg ampoule (Konakion MM Adult) is also available. USE ONLY Konakion MM Paediatric. Vitamin K Deficiency Bleeding is also known as Haemorrhagic Disease of Newborn (HDN).
Indication	Prophylaxis and treatment of vitamin K deficiency bleeding (VKDB)
Action	Promotes the activation of blood coagulation Factors II, VII, IX and X in the liver
Drug type	Fat soluble vitamin
Trade name	Konakion MM Paediatric
Presentation	2 mg/0.2 mL ampoule
Dose	**IM prophylaxis (Recommended route)[1]** • Birthweight ≥ 1500 g: 1 mg (0.1 mL of Konakion® MM) as a single dose at birth. • Birthweight <1500 g: 0.5 mg (0.05 mL of Konakion® MM) as a single dose at birth. **Oral prophylaxis[1]** 2 mg (0.2 mL of Konakion® MM) for 3 doses: • First dose: At birth • Second dose: 3–5 days of age (at time of newborn screening) • Third dose: During 4th week (day 22-28 of life) • It is imperative that the third dose is given no later than 4 weeks after birth as the effect of earlier doses decreases after this time • Repeat the oral dose if infant vomits within an hour of an oral dose or if diarrhoea occurs within 24 hours of administration **IV Prophylaxis[5]** • May be given in sick infants if unable to give IM or orally. • 0.3 mg/kg (0.2-0.4 mg/kg) as a single dose as a slow bolus (maximum 1 mg/minute). • Dose may be repeated weekly. **IV treatment of Vitamin K deficiency bleeding (VKDB)** • 1 mg IV as a slow bolus (maximum 1 mg/minute). Dose may 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.
Dose adjustment	No information
Maximum dose	
Total cumulative dose	
Route	IM, Oral, IV, Subcutaneous
Preparation	IM and Oral: Administer undiluted. IV: Draw up 0.2 mL (2 mg) of Konakion MM Paediatric and add 1.8 mL of glucose 5% or sodium chloride 0.9% to make a 1 mg/mL solution. (ANMF consensus)
Administration	IM: Administer undiluted. Oral: Injection solution can be administered orally via dispenser provided. Repeated doses are advised if infant spits out or vomits within an hour of an oral dose or if diarrhoea occurs within 24 hours of administration. Check with medical officer for advice. IV: Slow bolus. Maximum rate 1 mg/minute. Must be administered in the presence of a medical officer. May be given subcutaneously if venous access not available.
Monitoring	Prothrombin time when treating clotting abnormalities (a minimum of 2 to 4 hours is needed for measurable improvement).

Contraindications	Oral prophylaxis is contraindicated in infants who are: preterm, unwell, on antibiotics, have cholestasis or have diarrhoea. 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 <2.5 kg. Efficacy of treatment is decreased in patients with liver disease.
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.
Compatibility	**Fluids[8,9]:** Glucose 5% (use immediately), glucose 10%, sodium chloride 0.9%, sodium chloride 0.45%. **Y-site[8]:** Amikacin, aminophylline, ascorbic acid, atracurium, atropine, azathioprine, aztreonam, benzylpenicillin, calcium chloride, calcium gluconate, cefazolin, cefotaxime, ceftazidime, ceftriaxone, cefuroxime, clindamycin, dexamethasone, dopamine, doxycycline, enalaprilat, adrenaline (epinephrine), epoietin alfa, erythromycin lactobionate, fentanyl, furosemide (frusemide), ganciclovir, gentamicin, heparin sodium, hydrocortisone, indomethacin, insulin regular, isoproterenol, labetalol, lidocaine, midazolam, morphine, naloxone, nitroglycerin, nitroprusside sodium, norepinephrine, oxacillin, penicillin G potassium, penicillin G sodium, phenobarbital (phenobarbitone), piperacillin, potassium chloride, propranolol, protamine, pyridoxine, ranitidine, sodium bicarbonate, streptokinase, succinylcholine, thiamine, ticarcillin, ticarcillin-clavulanate, tobramycin, tolazoline, urokinase, vancomycin, vasopressin, verapamil. **Variable compatibility[8]:** Amphotericin B conventional colloidal, ampicillin, dobutamine, hydralazine, methylprednisolone.
Incompatibility	**Fluids:** Fat emulsion (intravenous). **Y-site[8]:** Diazepam, diazoxide, magnesium sulfate, phenytoin, sulfamethoxazole-trimethoprim.
Stability	Use immediately.
Storage	Store below 25°C. Protect from light.
Excipients	Glycocholic acid, lecithin, sodium hydroxide, hydrochloric acid
Special comments	The risk of childhood cancer is not increased by IM administration of vitamin K_1.
Evidence	**Background** All newborn infants have a relative vitamin K deficiency at birth. Vitamin K_1 crosses the placenta poorly resulting in low foetal plasma concentrations of the vitamin, with a 30:1 maternal-infant gradient. Human breast milk contains relatively low concentrations of vitamin K_1 (1 to 2 mg/L). Relative deficiency of vitamin K_1, particularly in exclusively breastfed infants can lead to vitamin K deficiency bleeding (VKDB), previously known as Haemorrhagic Disease of Newborn (HDN).[1] VKDB is classified into early, classical and late, based on the age of presentation: (a) Early VKDB, occurring on the first day of life, is rare and confined to infants born to mothers who have received medications that interfere with vitamin K metabolism; (b) Classical VKDB occurs from one to seven days after birth and (c) Late VKDB occurs from eight days to six months after birth, with most presenting at one to three months. **Efficacy** **Vitamin K prophylaxis for VKDB in neonates:** Cochrane review by Puckett et al. found that a single dose (1 mg) of intramuscular vitamin K_1 after birth is effective in the prevention of classic VKDB. Either intramuscular or oral (1 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 VKDB. When three doses of oral vitamin K_1 are compared to a single dose of IM 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. [2] (LOE II, GOR B) **Vitamin K prophylaxis for VKDB in preterm neonates:** Cochrane review by Ardell et al. found only RCT that compared IV to IM administration of vitamin K and compared various dosages of vitamin K. Three different prophylactic regimes of vitamin K (0.5 mg IM, 0.2 mg IM, or 0.2 mg IV) were given to infants less than 32 weeks' gestation. There was no statistically significant difference in vitamin K levels in the 0.2 mg

	IV group when compared to 0.2 or 0.5 mg IM groups on day 5. By day 25, vitamin K_1 levels had declined in all the groups, but infants who received 0.5 mg IM had higher levels of vitamin K_1 than either the 0.2 mg IV group or the 0.2 mg IM group. Since there is no available evidence that vitamin K is harmful or ineffective and since vitamin K is an inexpensive drug, authors concluded to follow the recommendations of expert bodies and give vitamin K to preterm infants.[3] **Treatment of VKDB:** Any infant suspected of VKDB should receive immediate intravenous vitamin K replacement. It is standard practice to administer a dose of 1 mg which will usually result in correction within a few hours. (LOE IV; GOR C) Intravenous vitamin K can be associated with anaphylactoid reactions and should be administered by slow intravenous injection; if venous access cannot be established it can be given subcutaneously, the intramuscular route being avoided in the presence of a coagulopathy.[4] **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)[5, 6] compared to adults (6 hours; range 2–26 hours)[7]. Re-dosing of oral vitamin K_1 is recommended by 1 month in breast fed infants.[6] (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 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.[5] (LOE IV, GOR B).

Practice points	**<u>Australian NHMRC Guidelines 2010 position statement[1]:</u>**
	• 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**
	  ○ Three 2 mg (0.2 mL) oral doses of Konakion® MM Paediatric, given at birth, at the time of newborn screening (usually at 3-5 days of age) and in the fourth week.
	• 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.

References	1. 2010 NHMRC Joint statement and recommendations on vitamin K administration to newborn infants to prevent vitamin K deficiency bleeding in infancy (Joint Statement). October 2010. Accessed on 4 April 2021. 2. Puckett RM, Offringa M. Prophylactic vitamin K for vitamin K deficiency bleeding in neonates. Cochrane Database of Systematic Reviews. 2000(4):CD002776. 3. Ardell S, Offringa M, Ovelman C, Soll R. Prophylactic vitamin K for the prevention of vitamin K deficiency bleeding in preterm neonates. Cochrane Database of Systematic Reviews. 2018;2:CD008342. 4. Williams MD, Chalmers EA, Gibson BE. The investigation and management of neonatal haemostasis and thrombosis. British journal of haematology. 2002;119(2):295-309. 5. Raith W, Fauler G, Pichler G, Muntean W. Plasma concentrations after intravenous administration of phylloquinone (vitamin K1) in preterm and sick neonates. Thrombosis research. 2000;99(5):467-72. 6. Stoeckel K, Joubert P, Grüter J. Elimination half-life of vitamin K 1 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(5):421-3. 7. Marinova M, Lütjohann D, Breuer O, Kölsch H, Westhofen P, Watzka M, et al. VKORC1-dependent pharmacokinetics of intravenous and oral phylloquinone (vitamin K1) mixed micelles formulation. European journal of clinical pharmacology. 2013;69(3):467-75. 8. Micromedex. Accessed on 4 April 2021. 9. Australian Injectable Drugs Handbook, 8th edition. Accessed on 4 April 2021.

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