VITAMIN K (Systemic)

Introduction

This monograph includes information on the following:1) Menadiol a, b; 2) Phytonadione.

INN:

Phytonadione¾Phytomenadione 3

JAN:

Phytonadione¾Phylloquinone 3

VA CLASSIFICATION (Primary/Secondary)
Menadiol¾VT701/BL300
Phytonadione¾VT702/
Commonly used brand name(s):AquaMEPHYTON2; Mephyton2.
Other commonly used names for phytonadione.

are phylloquinone , phytomenadione , and vitamin K 1 .
Another commonly used name for menadiol.

is Vitamin K 4 .

Note: For a listing of dosage forms and brand names by country availability, see Dosage Forms section(s).

a Not commercially available in the U.S.

b Not commercially available in Canada.

Category

Nutritional supplement (vitamin), prothrombogenic¾Menadiol sodium diphosphate; Phytonadione.

Antidote (to drug-induced hypoprothrombinemia)¾Menadiol sodium diphosphate; Phytonadione.

Antihemorrhagic¾Phytonadione.

Note: Vitamin K is a fat-soluble vitamin.

Indications

Accepted

Hypoprothrombinemia (prophylaxis and treatment) 1, 2, 4¾Vitamin K is indicated for the treatment and prevention of various coagulation disorders involving impaired formation of factors II,

VII, IX, and X resulting from vitamin K deficiency or impairment of vitamin K activity, including hypoprothrombinemia due to coumarin- or indanedione-derivative (oral) anticoagulants, salicylates, and some antibiotics. 1, 2, 4 Vitamin K does not return abnormal platelet function to normal. Vitamin K does not counteract the anticoagulant activity of heparin. Vitamin K may not be effective in hepatic function impairment since prothrombin synthesis occurs in the liver. Hypoprothrombinemia secondary to vitamin K deficiency may occur in the following persons or conditions: Patients with hepatic or biliary tract disease, including obstructive jaundice 1, 4, 5 or biliary fistula; 1, 2, 4, 5 in malabsorption syndromes 1, 2, 4, 5 or diseases affecting the small intestine or pancreas, such as celiac disease, 1, 2 cystic fibrosis, 1, 2, 4 intestinal resection, 1, 2, 4 persistent diarrhea or dysentery, 4 regional enteritis, 1, 2, 4 sprue, 1, 2, 4 or ulcerative colitis 1, 2 ; prolonged T-tube drainage; abetalipoproteinemia; patients receiving total parenteral nutrition (TPN); 2, 4, 5 or in infants receiving unfortified milk substitute formulas or those who are exclusively breast-fed. 2, 4, 5 Also, Vitamin K deficiency may occur when vitamin K activity is impaired by sulfonamides, 2 quinine, 2 quinidine, 2 or dactinomycin, or when absorption is decreased by concurrent administration of cholestyramine, colestipol, mineral oil, or sucralfate.

Hemorrhagic disease of the newborn (prophylaxis and treatment) 1, 2, 4¾The American Academy of Pediatrics recommends routine vitamin K 1 administration at birth to prevent hemorrhagic disease of the newborn 1, 4 , since vitamin K from the mother may be inadequate because of poor passage through the placenta and because intestinal bacteria responsible for natural synthesis of vitamin K are not present for 5 to 8 days following birth. In addition, the risk of hemorrhagic disease of the newborn is increased in infants of mothers who received anticonvulsants (e.g., phenobarbital, phenytoin) during pregnancy. Phytonadione is preferred over menadiol in the prophylaxis and treatment of hemorrhagic disease of the newborn, because phytonadione is less likely to cause hyperbilirubinemia and hemolytic anemia, especially in premature infants. 1, 4

Unaccepted

Menadiol sodium diphosphate may be used as a liver function test, although it has generally been replaced by newer methods.

Pharmacology/Pharmacokinetics

Physicochemical characteristics:

Source¾Phytonadione (vitamin K 1) occurs naturally in plants as phylloquinone 1, 2, 4, 5 , and also is produced synthetically 1, 2.

Another naturally occurring form of vitamin K is synthesized by human intestinal flora 2, 4, 5.

Menadiol sodium diphosphate (vitamin K 4) is a water-soluble derivative converted in the body to menadione (vitamin K 3) 4.

Chemical group¾All vitamin K compounds are 2-methyl-1,4-naphthoquinones 1, 2, 4, 5.

Molecular weight¾Menadiol sodium diphosphate: 530.18 3

Phytonadione: 450.71 3

Solubility¾Vitamin K is a fat-soluble vitamin. Phytonadione 1, 2, 4 and menadione 4 are lipid-soluble. Menadiol sodium diphosphate 4 is a water-soluble salt.

Mechanism of action/Effect:

Vitamin K promotes the hepatic formation of active prothrombin (factor II), proconvertin (factor VII), plasma thromboplastin component or Christmas factor (factor IX), and Stuart factor (factor X) 1, 2, 4, 5, 6 , which are required for normal blood clotting. Vitamin K is an essential cofactor for a hepatic microsomal enzyme that catalyzes the post-translational carboxylation of multiple, specific, peptide-bound glutamic acid residues in inactive hepatic precursor proteins of factors II, VII, IX, and X. The resulting gamma-carboxyglutamic acid residues convert the precursor proteins to active coagulation factors that subsequently are secreted by liver cells into the blood. 1

In healthy individuals, supplemental vitamin K is virtually devoid of pharmacodynamic activity. However, in the presence of vitamin K deficiency, or in the presence of coumarin- or indanedione-derivative anticoagulants, the pharmacologic activity of vitamin K is related to its normal physiological function, which is to promote the hepatic formation of vitamin K-dependent clotting factors 1.

Vitamin K does not return abnormal platelet function to normal. Vitamin K does not counteract the anticoagulant activity of heparin.

Absorption:

Oral¾Vitamin K is readily absorbed from healthy gastrointestinal tract (duodenum); phytonadione requires the presence of bile salts for absorption.
Parenteral¾Following intramuscular administration, phytonadione is readily absorbed 1.

Distribution:

Phytonadione is concentrated in the liver initially, but the concentration declines rapidly 1, 4.

Very little vitamin K accumulates in tissues 1, 2, 4, 5.

Biotransformation:

Hepatic (rapid).

Onset of action:

Menadiol sodium diphosphate¾
Parenteral: 8 to 24 hours.

Phytonadione¾
Oral: 6 to 12 hours 1.

Parenteral: 1 to 2 hours [1], with hemorrhage usually controlled in 3 to 6 hours; normal prothrombin concentrations are often obtained in 12 to 14 hours [1].

Elimination:

Renal/biliary. Almost no free, unmetabolized vitamin K appears in bile or urine [1].

Bacterial synthesis of vitamin K in the intestine may result in high fecal concentrations [4].

Precautions to Consider

Carcinogenicity

Studies have not been done [1].

Mutagenicity

Phytonadione, at concentrations of up to 2000 mcg per plate with or without metabolic activation, was negative in the Ames microbial mutagen test [1].

Pregnancy/Reproduction

Pregnancy¾Studies have not been done in humans.
Studies have not been done in animals.
FDA Pregnancy Category C [1].

In general, administration before delivery to prevent hemorrhagic disease of the newborn is not recommended because of possible neonatal toxicity.

Breast-feeding

It is not known whether supplemental vitamin K is distributed into breast milk. However, problems in humans have not been documented. Vitamin K is especially needed in breast-fed infants since there is little [4], [5] vitamin K in breast milk [2].

Pediatrics

Note: Menadiol sodium diphosphate has been shown to cause hepatotoxicity and hemolytic anemia in children, and hemolytic anemia, hyperbilirubinemia, and kernicterus [2], [4], [5] in neonates; administration to newborns (especially premature infants) is not recommended. Also, hemolysis, hyperbilirubinemia, and jaundice have been associated with the administration of high doses of phytonadione in neonates, especially premature infants; therefore, the recommended dose should not be exceeded [1].

The parenteral dosage form of phytonadione contains benzyl alcohol, which is not recommended for use in neonates. However, the small amount of benzyl alcohol contained in these preparations, when used as directed, has not been shown to cause toxicity [1].

Geriatrics

No information is available on the relationship of age to the effects of vitamin K in geriatric patients.

Drug interactions and/or related problems

The following drug interactions and/or related problems have been selected on the basis of their potential clinical significance (possible mechanism in parentheses where appropriate)¾not necessarily inclusive (>> = major clinical significance):

Note: Combinations containing any of the following medications, depending on the amount present, may also interact with this medication.
Antacids

(large amounts of aluminum hydroxide may precipitate bile acids in the upper small intestine, thereby decreasing absorption of fat-soluble vitamins)

Antibiotics, broad-spectrum 2, 4, 5 , or

Quinidine 2 or

Quinine 2 or

Salicylates, high doses 2 , or

Sulfonamides 2 , antibacterial

(requirements for vitamin K may be increased in patients receiving these medications)

>> Anticoagulants, coumarin- or indanedione-derivative 1, 2, 5

(concurrent use with vitamin K may decrease the effects of these anticoagulants as a result of increased hepatic synthesis of procoagulant factors. When reinstituting oral anticoagulant therapy after the administration of large doses of vitamin K, it may be necessary to temporarily increase the dose of the oral anticoagulant, or to use one such as heparin that acts on a different principle 1, 2 .)

Cholestyramine or

Colestipol or

Mineral oil or

Sucralfate

(concurrent use may decrease absorption of vitamin K; requirements for vitamin K may be increased in patients receiving these medications)

Dactinomycin

(concurrent use may decrease the effects of vitamin K; evidence is inconclusive; observation of patients is recommended and a higher dose of vitamin K may be required)

>> Hemolytics, other (see Appendix II)

(concurrent use with vitamin K, especially menadiol, may increase the potential for toxic side effects)

Medical considerations/Contraindications

The medical considerations/contraindications included have been selected on the basis of their potential clinical significance (reasons given in parentheses where appropriate)¾ not necessarily inclusive (>> = major clinical significance).
Risk-benefit should be considered when the following medical problems exist

Glucose-6-phosphate dehydrogenase (G6PD) deficiency 4, 9

(menadiol sodium diphosphate may induce erythrocyte hemolysis)

>> Hepatic function impairment 1, 2, 4

(vitamin K administration may not be effective in the treatment of hypoprothrombinemia in these patients 1, 2, 4 ; large doses of vitamin K may further impair liver function in the presence of severe hepatic disease 2, 4)

Sensitivity to the vitamin K analog considered for use, or history of

Patient monitoring

The following may be especially important in patient monitoring (other tests may be warranted in some patients, depending on condition; >> = major clinical significance):
>> Prothrombin time (PT) determinations

(The prothrombin test is sensitive to the levels of three of the vitamin K-dependent clotting factors (II, VII, and X); 1 regular prothrombin level determinations are recommended to determine responsiveness to and need for additional vitamin K therapy 1 .)

Side/Adverse Effects

Note: A rare hypersensitivity-like reaction, which has occasionally resulted in death, has been reported after intravenous administration of phytonadione, especially when administration was rapid. Typically this severe reaction has resembled hypersensitivity or anaphylaxis, including shock and cardiac and/or respiratory arrest. This reaction has occurred in some patients after receiving phytonadione for the first time, even when precautions have been taken to dilute the drug and to avoid rapid infusion. Therefore, the intravenous route of administration should be restricted to those situations in which other routes are not feasible, and the potential benefits have been determined to justify the serious risks. 1, 2, 4

In newborns, especially premature infants, menadiol sodium diphosphate has been associated with hemolytic anemia 2, 4, 5 , hyperbilirubinemia 2, 4, 5 , and kernicterus 2, 4, 5 because of immature hepatic function in these infants. There is less risk with phytonadione, unless high doses are given 1, 2.

The following side/adverse effects have been selected on the basis of their potential clinical significance (possible signs and symptoms in parentheses where appropriate)¾not necessarily inclusive:
Those indicating need for medical attention

Incidence less frequent

Hemolytic anemia 1, 2, 4 (difficulty in breathing; enlarged liver; general body swelling; paleness)¾in children or neonates, with menadiol or large doses of phytonadione; hyperbilirubinemia 1, 2, 4 (yellow eyes or skin)¾in children or neonates, with menadiol or large doses of phytonadione; may be clinically asymptomatic; jaundice 1 (yellow eyes or skin)¾in neonates, with menadiol or large doses of phytonadione; kernicterus 2, 4, 5 (decreased appetite; decreased movement or activity; difficulty in breathing; muscle stiffness)¾in neonates, with menadiol
Incidence rare

Anaphylaxis 1, 2, 4 (difficult, fast, or irregular breathing; difficulty in swallowing; flushing or redness of skin; shortness of breath; skin rash, hives and/or itching; sudden, severe decrease in blood pressure; swelling of the eyelids, face or lips; tightness in chest; wheezing)¾with injection only; cyanosis 1 (bluish discoloration of skin); dizziness 1; hypotension 1¾transient; profuse sweating 1; rapid and weak pulse 1
Those indicating need for medical attention only if they continue or are bothersome

Incidence less frequent

Flushing of face 1, 2, 4; redness, pain, or swelling at injection site 1, 2¾with parenteral administration; skin lesions (plaques)¾very rare, with repeated injection at one site; unusual taste 1, 2

Patient Consultation

As an aid to patient consultation, refer to Advice for the Patient, Vitamin K (Systemic) .
In providing consultation, consider emphasizing the following selected information (>> = major clinical significance):
Description of use

For use as a nutritional supplement (vitamin)¾Description should include function of vitamin K in the body, dietary sources, and signs of deficiency

For use as an antidote to hypoprothrombinemia¾Description should include the role of vitamin K in blood clotting, its effect on oral anticoagulants, and the importance of not varying the level of intake of foods rich in vitamin K while taking oral anticoagulants
Before using this medication

>> Conditions affecting use, especially:

Sensitivity to vitamin K analog considered for use, or history of
Use in children¾Menadiol may cause hepatotoxicity, hemolytic anemia, and kernicterus, and is not recommended for use in newborns, especially premature infants. The risk of side effects is lower with phytonadione
Other medications, especially coumarin- or indanedione-derivative anticoagulants and hemolytics
Other medical problems, especially hepatic function impairment
Proper use of this medication

>> Importance of not taking more medication than the amount prescribed

>> Proper dosing
Missed dose: Taking as soon as remembered; not taking if almost time for next dose; not doubling doses; telling physician about any missed doses
>> Proper storage
Precautions while using this medication

>> Need for patient to inform all physicians and dentists that this medication is being used

>> Not taking any other medications unless discussed with physician since they may alter the effect

>> Regular visits to physician to check progress and to perform regular prothrombin time tests

Side/adverse effects

Signs of potential side effects, especially anaphylaxis, cyanosis, dizziness, hypotension (transient), profuse sweating, rapid and weak pulse, and, in newborns, hemolytic anemia and liver toxicity, which may progress to kernicterus

General Dosing Information

Note: Severe reactions, including fatalities, have occurred with the intravenous administration of phytonadione. The intravenous administration of vitamin K is not recommended; however, when it is considered necessary, intravenous injection should be conducted very slowly at a rate not exceeding 1 mg per minute 1, 2.

Dosage of vitamin K should be based on laboratory tests of clotting function, specifically, determinations of the prothrombin time (PT) 1, 2, 4, 6.

Also, intake of vitamin K from dietary and other sources should be evaluated in determining the therapeutic dosage.
For treatment of hypoprothrombinemia secondary to coumarin- or indanedione-derivative anticoagulants, use of the smallest effective dose of vitamin K is recommended, since excessive dosage may result in temporary refractoriness to subsequent oral anticoagulant therapy 1, 2.

Depending on the severity of the hemorrhagic condition, withdrawal of or reduction in the dose of oral anticoagulant may be sufficient to correct the prothrombin deficiency [1, 2].

The use of vitamin K to correct excessive anticoagulation may restore underlying conditions that originally permitted a hypercoagulable or thromboembolic state [1].

Therefore, dosage should be kept as low as possible and the PT should be monitored regularly [1].

In the event of severe hemorrhage, administration of fresh whole blood, plasma, or component therapy may be required because of the delay in onset of vitamin K activity. [1, 2]

For treatment of hemorrhagic disease of the newborn, empiric administration of vitamin K 1 should not replace proper laboratory evaluation and clinical assessment. A prompt response to vitamin K 1 therapy consists of shortening of the PT within 2 to 4 hours, and is usually diagnostic of hemorrhagic disease of the newborn. Failure to respond to vitamin K 1 suggests a different condition or a coagulation disorder unrelated to vitamin K status [1].

Note: In neonates, particularly in premature infants, toxicity has been associated with the administration of menadiol sodium diphosphate, or high doses of phytonadione. When the administration of vitamin K 1 is considered necessary in this age group, the recommended dose of phytonadione should not be exceeded. The use of menadiol in newborns is not recommended. Hypoprothrombinemia due to hepatocellular damage is not corrected by administration of vitamin K [2, 4].

Repeated large doses of vitamin K should not be used in the presence of liver disease if the initial response is unsatisfactory [1], as it may further depress liver function [2, 4].

Failure to respond to vitamin K therapy may indicate a coagulation defect or a condition unresponsive to vitamin K [1, 2, 7].

For oral dosage forms only

The oral route of administration should be avoided when the clinical condition may prevent proper absorption of vitamin K. Bile salts must be given concurrently with the oral dosage form of vitamin K when the endogenous supply of bile to the gastrointestinal tract is deficient [1, 7].

For parenteral dosage forms only

The intramuscular or subcutaneous route of administration is preferred whenever possible, especially when oral administration is not possible because of malabsorption problems.
Because of the risk of severe hypersensitivity-like or anaphylactic reactions, the intravenous administration of vitamin K is not recommended; however, when intravenous administration is considered necessary, intravenous injection should be conducted very slowly at a rate not exceeding 1 mg per minute [1, 2].

Diet/Nutrition

Recommended Dietary Allowances (RDAs) for vitamin K usually are met or exceeded by a normal diet and intestinal bacterial synthesis 2, 5.

The minimum daily requirement for vitamin K is estimated to be .03 mcg per kilogram of body weight for adults, and 1 to 5 mcg of vitamin K per kilogram of body weight for infants.
The best dietary sources of vitamin K include green, leafy vegetables, meats, and dairy products 5, 8.

There is little loss of vitamin K from foods with ordinary cooking.

MENADIOL

Oral Dosage Forms

MENADIOL SODIUM DIPHOSPHATE TABLETS USP

Usual adult and adolescent dose

Hypoprothrombinemia secondary to obstructive jaundice and biliary fistulas 9¾
Oral, 5 mg per day.
Hypoprothrombinemia secondary to the administration of antibacterials or salicylates¾
Oral, 5 to 10 mg per day.

Usual pediatric dose

Vitamin (prothrombogenic); or
Antidote (to drug-induced hypoprothrombinemia)¾
Oral, 5 to 10 mg per day.

Strength(s) usually available

U.S.¾Not commercially available.
Canada¾Not commercially available.

Packaging and storage:

Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Store in a well-closed, light-resistant container.

Parenteral Dosage Forms

MENADIOL SODIUM DIPHOSPHATE INJECTION USP

Usual adult and adolescent dose

Nutritional supplement (vitamin), prothrombogenic 9 ; or
Antidote (to drug-induced hypoprothrombinemia)¾
Intramuscular or subcutaneous, 5 to 15 mg one or two times a day.

Usual pediatric dose

Vitamin (prothrombogenic); or
Antidote (to drug-induced hypoprothrombinemia)¾
Intramuscular or subcutaneous, 5 to 10 mg one or two times a day.

Strength(s) usually available

U.S.¾Not commercially available.
Canada¾Not commercially available.

Packaging and storage:

Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Store in a light-resistant container. Protect from freezing.

Incompatibilities:

Incompatible with protein hydrolysate.

PHYTONADIONE

Oral Dosage Forms

PHYTONADIONE TABLETS USP

Usual adult and adolescent dose

Hypoprothrombinemia, anticoagulant-induced (coumarin- or indanedione-derivative)¾
Oral, 2.5 to 10 mg, or up to 25 mg (rarely up to 50 mg) 1 ; subsequent doses should be determined by prothrombin time (PT) response and/or clinical condition 1.

Hypoprothrombinemia due to other causes¾
Oral, 2.5 to 25 mg or more (rarely up to 50 mg); the amount administered depends on the severity of the condition and the clinical and/or PT response obtained 1.

Usual pediatric dose

Safety and efficacy have not been established.

Strength(s) usually available

U.S.¾5 mg (Rx)[Mephyton 1 (scored) (acacia) (calcium phosphate) (colloidal silicon dioxide) (lactose) (magnesium stearate) (starch) (talc)]

Canada¾Not commercially available.

Packaging and storage:

Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Store in a well-closed container. Protect from light.

Parenteral Dosage Forms

PHYTONADIONE INJECTION USP

Note: Some preparations are for intramuscular use only.

Usual adult and adolescent dose

Hypoprothrombinemia, anticoagulant-induced (coumarin- or indanedione-derivative)¾
Intramuscular or subcutaneous, 2.5 to 10 mg, or up to 25 mg (rarely up to 50 mg) 1 ; may be repeated after six to eight hours if necessary; subsequent doses should be determined by prothrombin time (PT) response and/or clinical condition 1.

Hypoprothrombinemia due to other causes¾
Intramuscular or subcutaneous, 2.5 to 25 mg or more (rarely up to 50 mg) 1 ; the amount administered depends on the severity of the condition and the clinical and/or PT response obtained 1.

Prevention of hypoprothrombinemia during prolonged total parenteral nutrition¾
Intramuscular, 5 to 10 mg once a week 2.

Usual pediatric dose

Infants receiving unfortified milk substitutes or who are exclusively breast-fed¾
Intramuscular or subcutaneous, 1 mg per month if vitamin K content of diet is less than 0.1 mg per L. 10

Prevention of hypoprothrombinemia during prolonged total parenteral nutrition¾
Intramuscular, 2 to 5 mg once a week 2.

Treatment of hypoprothrombinemia, anticoagulant-induced (coumarin- or indanedione-derivative)¾
Infants¾Intramuscular or subcutaneous, 1 to 2 mg; may be repeated in four to eight hours 2.

Children¾Intramuscular or subcutaneous, 2.5 to 10 mg; may be repeated in six to eight hours 2.

Treatment of hypoprothrombinemia due to other causes¾
Infants¾Intramuscular or subcutaneous, 2 mg 2.

Children¾Intramuscular or subcutaneous, 5 to 10 mg 2.

Hemorrhagic disease of the newborn¾
Prophylaxis¾Intramuscular, 0.5 to 1 mg within one hour of birth 1 ; may be repeated after six to eight hours if necessary (e.g., if mothers received anticonvulsants during pregnancy).

Treatment¾Intramuscular or subcutaneous, 1 mg 1 ; higher doses may be required for infants whose mothers received oral anticoagulants or anticonvulsants during pregnancy 1, 2, 4.

Note: The parenteral dosage form of phytonadione contains benzyl alcohol, which is not recommended for use in neonates. However, the small amount of benzyl alcohol contained in these preparations, when used as directed, has not been shown to cause toxicity 1.

Strength(s) usually available

U.S.¾2 mg per mL (1 mg per 0.5-mL ampul) (Rx)[AquaMEPHYTON 1 (benzyl alcohol 0.9%) (dextrose 18.75 mg) (polyoxyethylated fatty acid derivative 35 mg)] [Generic]

10 mg per mL (Rx)[AquaMEPHYTON 1 (benzyl alcohol 0.9%) (dextrose 37.5 mg) (polyoxyethylated fatty acid derivative 70 mg)] [Generic]

Canada¾2 mg per mL (1 mg per 0.5-mL ampul) (Rx) [Generic]

10 mg per mL (Rx) [Generic]

Packaging and storage:

Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Protect from light. Protect from freezing.

Preparation of dosage form:

Phytonadione injection may be diluted with 0.9% sodium chloride injection, 5% dextrose injection, or 5% dextrose and sodium chloride injection 1.

All diluents should be preservative-free 1.

Other diluents should not be used 1.

Stability:

Solutions should be prepared immediately prior to use and any unused portion discarded.

Incompatibilities:

Phytonadione injection is physically incompatible with phenytoin injection.

Additional information:

The administration of large amounts of benzyl alcohol in newborns has been associated with a fatal toxic syndrome consisting of metabolic acidosis, central nervous system depression, respiratory problems, renal failure, hypotension, and possibly seizures and intracranial hemorrhage. Therefore, products containing benzyl alcohol should be used with caution in newborns, especially those who are receiving other benzyl alcohol-containing medications 2.

However, the small amount of benzyl alcohol contained in the parenteral dosage form of commercial preparations of vitamin K 1, when used as directed, has not been shown to cause toxicity in neonates 1.