



- The only Phytonadione Inj. available in Prefilled Syringe with safety device (Saf-T-Jet™)
- Complies with Needlestick Safety and Prevention Act
- Preservative free formulation (does not contain benzyl alcohol or phenol)
- Eliminates handling of ampules and filter needles

PHYTONADIONE Injection, USP

Safety Prefilled Syringe (Saf-T-Jet™)

PRODUCT	DELIVERY SYSTEM	UNIT SIZE	UNITS / BOX	NDC#
Phytonadione Injection, USP	Saf-T-Jet™	1 mg/0.5 mL	10	76329-1240-1

NDC#	WHOLESALE ITEM NUMBERS			
	AMERISOURCE BERGEN	CARDINAL	MCKESSON	MORRIS & DICKSON
76329-1240-1	10129722	4933784	2046712	768556

TO PLACE AN ORDER, PLEASE CALL 1-800-423-4136

INTERNATIONAL MEDICATION SYSTEMS, LTD.
 1886 Santa Anita Avenue, South El Monte, CA 91733
 An Amphastar Pharmaceuticals Company | www.ims-limited.com

Please see reverse for important safety information for Phytonadione Injection, USP.



Rx Only
 02/18
 01-019-09

PHYTONADIONE

Injection, USP

Rx Only

INDICATIONS AND USAGE

Phytonadione is indicated in the following coagulation disorders which are due to faulty formation of factors II, VII, IX and X when caused by vitamin K deficiency or interference with vitamin K activity.

Phytonadione Injectable Emulsion, USP is indicated in:

- anticoagulant-induced prothrombin deficiency caused by coumarin or indanedione derivatives;
- prophylaxis and therapy of hemorrhagic disease of the newborn;
- hypoprothrombinemia due to antibacterial therapy;
- hypoprothrombinemia secondary to factors limiting absorption or synthesis of vitamin K, e.g., obstructive jaundice, biliary fistula, sprue, ulcerative colitis, celiac disease, intestinal resection, cystic fibrosis of the pancreas, and regional enteritis;
- other drug-induced hypoprothrombinemia where it is definitely shown that the result is due to interference with vitamin K metabolism, e.g., salicylates.

CONTRAINDICATION

Hypersensitivity to any component of this medication.

WARNINGS

Use benzyl alcohol-free formulations in neonates and infants, if available. Serious and fatal adverse reactions including “gaspings syndrome” can occur in neonates and infants treated with benzyl alcohol-preserved drugs, including Phytonadione. The “gaspings syndrome” is characterized by central nervous system depression, metabolic acidosis, and gasping respirations.

When prescribing Phytonadione in infants, consider the combined daily metabolic load of benzyl alcohol from all sources including Phytonadione and other drugs containing benzyl alcohol. The minimum amount of benzyl alcohol at which serious adverse reactions may occur is not known.

An immediate coagulant effect should not be expected after administration of phytonadione. It takes a minimum of 1 to 2 hours for measurable improvement in the prothrombin time. Whole blood or component therapy may also be necessary if bleeding is severe.

Phytonadione will not counteract the anticoagulant action of heparin.

When vitamin K₁ is used to correct excessive anticoagulant-induced hypoprothrombinemia, anticoagulant therapy still being indicated, the patient is again faced with the clotting hazards existing prior to starting the anticoagulant therapy. Phytonadione is not a clotting agent, but overzealous therapy with vitamin K₁ may restore conditions which originally permitted thromboembolic phenomena. Dosage should be kept as low as possible, and prothrombin time should be checked regularly as clinical conditions indicate.

Repeated large doses of vitamin K are not warranted in liver disease if the response to initial use of the vitamin is unsatisfactory. Failure to respond to vitamin K may indicate that the condition being treated is inherently unresponsive to vitamin K.

PRECAUTIONS

General

Vitamin K₁ is fairly rapidly degraded by light; therefore, always protect Phytonadione from light. Store Phytonadione Injectable Emulsion USP in closed original carton until contents have been used. (See also HOW SUPPLIED, Storage.)

Drug Interactions

Temporary resistance to prothrombin-depressing anticoagulants may result, especially when larger doses of phytonadione are used. If relatively large doses have been employed, it may be necessary when reinstating anticoagulant therapy to use somewhat larger doses of the prothrombin-depressing anticoagulant, or to use one which acts on a different principle, such as heparin sodium.

Laboratory Tests

Prothrombin time should be checked regularly as clinical conditions indicate.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Studies of carcinogenicity, mutagenesis or impairment of fertility have not been conducted with Phytonadione.

Pregnancy

Pregnancy Category C: Animal reproduction studies have not been conducted with Phytonadione. It is also not known whether Phytonadione can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Phytonadione should be given to a pregnant woman only if clearly needed.

Nursing Mothers

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Phytonadione is administered to a nursing woman.

Pediatric Use

Hemolysis, jaundice, and hyperbilirubinemia in newborns, particularly in premature infants, may be related to the dose of Phytonadione. Therefore, the recommended dose should not be exceeded (see ADVERSE REACTIONS and DOSAGE AND ADMINISTRATION).

Serious adverse reactions including fatal reactions and the “gaspings syndrome” occurred in premature neonates and infants in the intensive care unit who received drugs containing benzyl alcohol as a preservative. In these cases, benzyl alcohol dosages of 99 to 234 mg/kg/day produced high levels of benzyl alcohol and its metabolites in the blood and urine (blood levels of benzyl alcohol were 0.61 to 1.378 mmol/L). Additional adverse reactions included gradual neurological deterioration, seizures, intracranial hemorrhage, hematologic abnormalities, skin breakdown, hepatic and renal failure, hypotension, bradycardia, and cardiovascular collapse. Preterm, low-birth weight infants may be more likely to develop these reactions because they may be less able to metabolize benzyl alcohol.

When prescribing Phytonadione in infants consider the combined daily metabolic load of benzyl alcohol from all sources including other drugs containing benzyl alcohol. The minimum amount of benzyl alcohol at which serious adverse reactions may occur is not known [see Warnings].

ADVERSE REACTIONS

Deaths have occurred after intravenous and intramuscular administration. (See Box Warning.)

Transient “flushing sensations” and “peculiar” sensations of taste have been observed, as well as instances of dizziness, rapid and weak pulse, profuse sweating, brief hypotension, dyspnea, and cyanosis.

Pain, swelling, and tenderness at the injection site may occur.

The possibility of allergic sensitivity, including an anaphylactoid reaction, should be kept in mind following parenteral administration.

Usually after repeated injection, erythematous, indurated, pruritic plaques have occurred; these have progressed to scleroderma-like lesions that have persisted for long periods. In other cases, these lesions have resembled erythema perstans.

Hyperbilirubinemia has been observed in the newborn following administration of phytonadione. This has occurred primarily with doses above those recommended. (See PRECAUTIONS, *Pediatric Use*.)

To report **SUSPECTED ADVERSE REACTIONS**, contact Amphastar Pharmaceuticals, Inc. at 1-800-423-4136, or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

OVERDOSAGE

The intravenous LD₅₀ of Phytonadione Injectable Emulsion, USP in the mouse is 41.5 and 52 mL/kg for the 0.2% and 1% concentrations, respectively.

DOSAGE AND ADMINISTRATION

Whenever possible, phytonadione should be given by the subcutaneous route (see Box Warning). When intravenous administration is considered unavoidable, the drug should be injected very slowly, not exceeding 1 mg per minute.

Protect from light at all times.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

Directions for Dilution

Phytonadione Injectable Emulsion USP may be diluted with 0.9% Sodium Chloride Injection, 5% Dextrose Injection, or 5% Dextrose and Sodium Chloride Injection. Benzyl alcohol as a preservative has been associated with toxicity in newborns. *Therefore, all of the above diluents should be preservative-free (See WARNINGS).* Other diluents should not be used. When dilutions are indicated, administration should be started immediately after mixture with the diluent, and unused portions of the dilution should be discarded, as well as unused contents of the vial.

Prophylaxis of Hemorrhagic Disease of the Newborn

The American Academy of Pediatrics recommends that vitamin K₁ be given to the newborn. A single intramuscular dose of phytonadione 0.5 to 1 mg within one hour of birth is recommended.

Treatment of Hemorrhagic Disease of the Newborn

Empiric administration of vitamin K₁ should not replace proper laboratory evaluation of the coagulation mechanism. A prompt response (shortening of the prothrombin time in 2 to 4 hours) following administration of vitamin K₁ is usually diagnostic of hemorrhagic disease of the newborn, and failure to respond indicates another diagnosis or coagulation disorder.

Phytonadione 1 mg should be given either subcutaneously or intramuscularly. Higher doses may be necessary if the mother has been receiving oral anticoagulants.

Whole blood or component therapy may be indicated if bleeding is excessive. This therapy, however, does not correct the underlying disorder and phytonadione should be given concurrently.

Anticoagulant-Induced Prothrombin Deficiency in Adults

To correct excessively prolonged prothrombin time caused by oral anticoagulant therapy — 2.5 to 10 mg or up to 25 mg initially is recommended. In instances 50 mg may be required. Frequency and amount of subsequent doses should be determined by prothrombin time response or clinical condition (see WARNINGS). If in 6 to 8 hours after parenteral administration the prothrombin time has not been shortened satisfactorily, the dose should be repeated.

Phytonadione
Summary of Dosage Guidelines
(See insert text for guidelines)

Newborns	Dosage
<i>Hemorrhagic Disease of the Newborn Prophylaxis</i>	0.5 to 1 mg Intramuscular within 1 hour of birth
<i>Treatment</i>	1 mg Subcutaneous or Intramuscular (Higher doses may be necessary if the mother has been receiving oral anticoagulants)
Adults	Initial Dosage
<i>Anticoagulant-Induced Prothrombin Deficiency</i> (caused by coumarin or indanedione derivatives)	2.5 mg to 10 mg or more
<i>Hypoprothrombinemia Due to other causes</i> (Antibiotics; Salicylates or other drugs; Factors limiting absorption or synthesis)	2.5 mg to 25 mg or more

In the event of shock or excessive blood loss, the use of whole blood or component therapy is indicated.

Hypoprothrombinemia Due to Other Causes in Adults

A dosage of 2.5 to 25 mg or more (up to 50 mg) is recommended, the amount and route of administration depending upon the severity of the condition and response obtained.

If possible, discontinuation or reduction of the dosage of drugs interfering with coagulation mechanisms (such as salicylates, antibiotics) is suggested as an alternative to administering concurrent phytonadione. The severity of the coagulation disorder should determine whether the immediate administration of phytonadione is required in addition to discontinuation or reduction of interfering drugs.