SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of drug product:

Name of the medicinal product

INJEK- 10

Phytomenadione Injection B.P

Strength

10 mg/mL

Pharmaceutical dosage form:

Solution for Injection.

2. Qualitative and quantitative composition

Sr. No.	Particulars	Grade	Qty. / ml	Function
1.	Phytomenadione	B.P.	10 mg	Active

For excipients, refer 6.1

3. Pharmaceutical form

A Clear to Slightly Opalescent liquid

4. Clinical Particulars

4.1 Therapeutic indications

Phytomenadione 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.

Phytomenadione injection is indicated in:

i anticoagulant-induced prothrombin deficiency caused by coumarin or indanedione derivatives;

ii Prophylaxis and therapy of hemorrhagic disease of the newborn;

iii Hypoprothrombinemia due to antibacterial therapy;

iv 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;

v. other drug-induced hypoprothrombinemia where it is definitely shown that the result is due to interference with vitamin K metabolism, e.g., salicylates.

4.2 Posology and method of administration

Route of administration: Intramuscular/ Intravenous

Whenever possible, Phytomenadione should be given by the subcutaneous. 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.

Do not use if separation has occurred or oil droplets have appeared. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

Directions for Dilution:

Phytomenadione may be diluted with 0.9% w/v Sodium Chloride Injection, 5% w/v Dextrose Injection, or 5% w/v 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. 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 ampoule.

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 Phytomenadione 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.

Phytomenadione 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 Phytomenadione 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 rare instances 50 mg may be required. Frequency and amount of subsequent doses should be determined by prothrombin time response or clinical condition. If in 6 to 8 hours after parenteral administration the prothrombin time has not been shortened satisfactorily, the dose should be repeated.
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 (rarely 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 interferingwith coagulation mechanisms (such as salicylates, antibiotics) is suggested as an alternative to administering concurrent Phytomenadione. The severity of the coagulation disorder should determine whether the immediate administration of Phytomenadione is required in addition to discontinuation or reduction of interfering drugs.

Phytomenadione Summary of Dosage Guidelines	
Newborns	
Hemorrhagic Disease of the Newborn	
Prophylaxis	0.5 - 1 mg IM within 1 hour of birth
Treatment	1 mg SC or IM (Higher doses may be necessary if the mother has been receiving oral anti-coagulants)
Adults	Initial Dosage

Anticoagulant - induced Prothrombin Deficiency – (caused by coumarin or indanedione derivatives)	2.5mg - 10 mg or up to 25 mg (rarely 50 mg)
Hypoprothrombinemia due to other causes (Antibiotics; Salicylates or other drugs; Factors limiting absorption or synthesis)	2.5 mg - 25 mg or more (rarely up to 50mg)

4.3 Contraindications

Hypersensitivity to any component of this medication.

4.4 Special warnings and precautions for use

INTRAVENOUS AND INTRAMUSCULAR USE

Severe reactions, including fatalities, have occurred during and immediately after the parenteral administration of Phytomenadione. Typically these severe reactions have resembled hypersensitivity or anaphylaxis, including shock and cardiac and/or respiratory arrest. Some patients have exhibited these severe reactions on receiving Phytomenadione for the first time. The majority of these reported events occurred following intravenous administration, even when precautions have been taken to dilute the Phytomenadione and to avoid rapid infusion. Therefore, the INTRAVENOUS route should be restricted to those situations where another route is not feasible and the increased risk involved is considered justified.

PRECAUTIONS

Drug Interactions:

Temporary resistance to prothrombin-depressing anticoagulants may result, especially when larger doses of Phytomenadione are used. If relatively large doses have been employed, it may be necessary when reinstituting anticoagulant therapy to use somewhat larger doses of the prothrombindepressing 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 Phytomenadione.

4.5 Interaction with other medicinal products and other forms of interaction

No significant interactions are known other than antagonism of coumarin anticoagulants.

4.6 Pregnancy and lactation

Pregnancy Category C:

Animal reproduction studies have not been conducted with Phytomenadione. It is also not known whether Phytomenadione can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Phytomenadione 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 Phytomenadione 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 Phytomenadione. Therefore, the recommended dose should not be exceeded.

4.7 Effects on ability to drive and operate machines
None

4.8 Undesirable effects
Severe hypersensitivity reactions, including anaphylactoid reactions and deaths have been reported following parenteral administration. The majority of these reported events occurred following intravenous administration. The possibility of allergic sensitivity, including an anaphylactoid reaction, should be kept in mind following parenteral administration.
Transient ―flushing sensations‖ and ―peculiar‖ sensations of taste have been observed, as well as rare instances of dizziness, rapid and weak pulse, profuse sweating, brief hypotension dyspnea and cyanosis.
Pain, swelling, and tenderness at the injection site may occur.
Infrequently, usually after repeated injection, erythematous, indurated, pruritic plaques have occurred; rarely, 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 Phytomenadione. This has occurred rarely and primarily with doses above those recommended.

4.9 Overdosage
With Reference to literature the intravenous LD50 of Phytomenadione Injection in the mouse is 41.5 and 52 mL/kg for the 0.2% and 1.0% concentrations, respectively.

5. Pharmacological properties

5.1 Pharmacodynamic properties
Pharmacotherapeutic group (ATC code): B02BA01
Phytomenadione aqueous colloidal solution of vitamin K1 for parenteral injection, possesses the same type and degree of activity as does naturally occurring vitamin K, which is necessary for the production via the liver of active prothrombin (factor II), proconvertin (factor VII), plasma thromboplastin component (factor IX), and Stuart factor (factor X). The prothrombin test is sensitive to the levels of three of these four factors—II, VII, and X. Vitamin K is an essential cofactor for a microsomal enzyme that catalyzes the posttranslational carboxylation of multiple, specific, peptide bound glutamic acid residues in inactive hepatic precursors of factors II, VII, IX, and X. The resulting gamma-carboxyglutamic acid residues convert the precursors into active coagulation factors that are subsequently secreted by liver cells into the blood.
Phytomenadione is readily absorbed following intramuscular administration. After absorption, Phytomenadione is initially concentrated in the liver, but the concentration declines rapidly. Very little vitamin K accumulates in tissues. Little is known about the metabolic fate of vitamin K. Almost no free unmetabolized vitamin K appears in bile or urine.
In normal animals and humans, Phytomenadione is virtually devoid of pharmacodynamic activity. However, in animals and humans deficient in vitamin

K, the pharmacological action of vitamin K is related to its normal physiological function, that is, to promote the hepatic biosynthesis of vitamin K dependent clotting factors.
The action of the aqueous colloidal solution, when administered intravenously, is generally detectable within an hour or two and hemorrhage is usually controlled within 3 to 6 hours. A normal prothrombin level may often be obtained in 12 to 14 hours.
In the prophylaxis and treatment of hemorrhagic disease of the newborn, Phytomenadione has demonstrated a greater margin of safety than that of the water-soluble vitamin K analogues.

5.2 Pharmacokinetic properties

In blood plasma, 90% of vitamin K1 is bound to lipoproteins. Following an intramuscular dose of 10mg vitamin K, plasma concentrations of 10 - 20mcg/l are produced (normal range 0.4 - 1.2mcg/l). Systemic availability following intramuscular administration is about 50% and elimination half-life in plasma is approximately 1.5 - 3 hours.

5.3 Pre-clinical Safety Data

None applicable

6. Pharmaceutical particulars

6.1 List of excipients

1. Tween 80 BP
2. Dextrose BP (Anhydrous).
3. Sodium Acetate BP (trihydrate)
4. Water for injection BP (Bulk)

6.2 Incompatibilities

None

6.3 Shelf life

18 months

6.4 Special precautions for storage

Store below 25°C., protected from light. Do not freeze.

6.5 Nature and contents of container

1 mL amber double band snap off ampoule (green above and yellow band on constriction) Such 5 ampoules are packed in a blister pack and such two blisters are then pack in a carton along with package insert.

6.6 Special Precautions for Handling and Disposal

Whenever possible, Phytomenadione should be given by the subcutaneous. 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. Do not use if separation has occurred or oil droplets have appeared. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

7. Marketing authorization holder:

M/s. NEON LABORATORIES LIMITED

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8. Marketing Authorization Number (s):
06517/07597/NMR/2019

9. Date of first authorization/ Renewal of the authorisation :
13-5-2022

10. Date of revision of the text:
July,2023