# VITAMIN K1

Cite this Record

STRUCTURE VENDORS DRUG INFO PHARMACOLOGY LITERATURE PATENTS BIOACTIV

| | |
|---|---|
| **PubChem CID:** | 5284607 |
| **Chemical Names:** | VITAMIN K1; Phytonadione; Phylloquinone; 84-80-0; Phytylmenadione; Phyllochinon More... |
| **Molecular Formula:** | $C_{31}H_{46}O_2$ |
| **Molecular Weight:** | 450.707 g/mol |
| **InChI Key:** | MBWXNTAXLNYFJB-NKFFZRIASA-N |
| **Drug Information:** | Drug Indication Therapeutic Uses Clinical Trials FDA Orange Book FDA UNII |
| **Safety Summary:** | Laboratory Chemical Safety Summary (LCSS) |

VITAMIN K1 is a family of phylloquinones that contains a ring of 2-methyl-1,4-naphthoquinone and an isoprenoid side chain. Members of this group of vitamin K 1 have only one double bond on the proximal isoprene unit. Rich sources of vitamin K 1 include green plants, algae, and photosynthetic bacteria. Vitamin K1 has antihemorrhagic and prothrombogenic activity.

*from MeSH*

Vitamin K is a family of fat-soluble compounds with a common chemical structure based on 2-methyl-1, 4-naphthoquinone

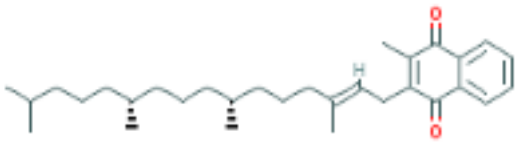
*Metabolite Description from Human Metabolome Database (HMDB)*

PUBCHEM › COMPOUND › VITAMIN K1 *Modify Date: 2018-01-06; Create Date: 2004-09-16*

# Contents

## 1 2D Structure

Search Download Get Image

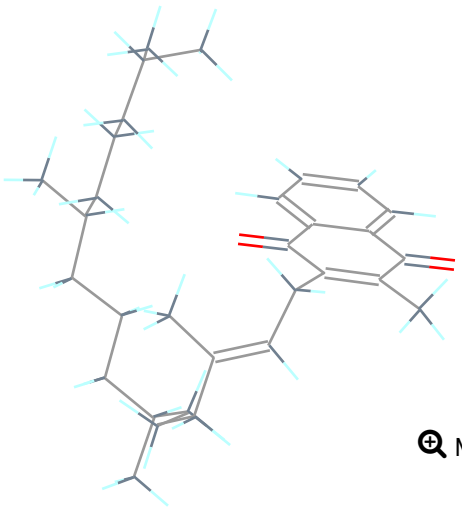


Magnify

*from PubChem*

## 2 3D Conformer

Search Download Get Image



Magnify

Show Hydrogens Show Atoms Animate

*from PubChem*

# 3 Names and Identifiers

## 3.1 Computed Descriptors

### 3.1.1 IUPAC Name

2-methyl-3-[(E,7R,11R)-3,7,11,15-tetramethylhexadec-2-enyl]naphthalene-1,4-dione

*from PubChem*

### 3.1.2 InChI

InChI=1S/C31H46O2
/c1-22(2)12-9-13-23(3)14-10-15-24(4)16-11-17-25(5)20-21-27-26(6)30(32)28-18-7-8-19-29(28)31(27)33/h7-8,18-20,22-24H,9-17,21H2,1-6H3/b25-20+/t23-,24-/m1/s1

*from PubChem*

### 3.1.3 InChI Key

MBWXNTAXLNYFJB-NKFFZRIASA-N

*from PubChem*

### 3.1.4 Canonical SMILES

CC1=C(C(=O)C2=CC=CC=C2C1=O)CC=C(C)CCCC(C)CCCC(C)CCCC(C)C

*from PubChem*

### 3.1.5 Isomeric SMILES

CC1=C(C(=O)C2=CC=CC=C2C1=O)C/C=C(\C)/CCC[C@H](C)CCC[C@H](C)CCCC(C)C

*from PubChem*

## 3.2 Molecular Formula

$C_{31}H_{46}O_2$

*from PubChem*

## 3.3 Other Identifiers

### 3.3.1 CAS

84-80-0

*from ChemIDplus, DTP/NCI, DrugBank, EPA DSStox, European Chemicals Agency - ECHA, H...*

11104-38-4

*from ChemIDplus, European Chemicals Agency - ECHA*

79083-00-4

*from ChemIDplus, European Chemicals Agency - ECHA*

12001-79-5

*from European Chemicals Agency - ECHA*

81382-12-9

*from Human Metabolome Database (HMDB)*

### 3.3.2 EC Number

201-564-2

*from European Chemicals Agency - ECHA*

234-330-3

*from European Chemicals Agency - ECHA*

234-408-7

*from European Chemicals Agency - ECHA*

279-052-3

*from European Chemicals Agency - ECHA*

### 3.3.3 NSC Number

760373

*from DTP/NCI*

### 3.3.4 UNII

S5Z3U87QHF

*from DrugBank, FDA/SPL Indexing Data*

### 3.3.5 Wikipedia

| | |
|---|---|
| Title | (E)-phytonadione |
| Description | chemical compound |

*from Wikipedia*

## 3.4 Synonyms

### 3.4.1 MeSH Entry Terms

1. Aquamephyton
2. Konakion
3. Phyllohydroquinone
4. Phylloquinone
5. Phytomenadione
6. Phytonadione
7. Vitamin K 1
8. Vitamin K1

*from MeSH*

### 3.4.2 Depositor-Supplied Synonyms

1. VITAMIN K1
2. phytonadione
3. Phylloquinone
4. 84-80-0
5. Phytylmenadione
6. Phyllochinon
7. Phytomenadione
8. alpha-Phylloquinone
9. 3-Phytylmenadione
10. 2-Methyl-3-phytyl-1,4-naphthoquinone
11. Kinadion
12. Konakion
13. Mephyton
14. Monodion
15. Kephton
16. Antihemorrhagic vitamin
17. Synthex P
18. VITAMIN K
19. Mono-Kay
20. Combinal K1
21. Kativ N
22. trans-Phylloquinone
23. VitaminK1
24. K-Ject
25. UNII-S5Z3U87QHF
26. Aquamephyton
27. Fitomenadiona
28. Phyllochinonum
29. Phytomenadionum
30. Phytonadionum

*from PubChem*

# 4 Chemical and Physical Properties

## 4.1 Computed Properties

| Property Name | Property Value |
|---|---|
| Molecular Weight | 450.707 g/mol |
| Hydrogen Bond Donor Count | 0 |
| Hydrogen Bond Acceptor Count | 2 |
| Rotatable Bond Count | 14 |
| Complexity | 696 |
| CACTVS Substructure Key Fingerprint | AAADcfB4MAAAAAAAAAAAAAAAAAAAAAAA wQAAAAAAAAACBAAAAGgAAAAADQSAmAAyAI AAAACIAqBSAAACAAAkAAAIiAEAAMgIIDKAFRCA IQAggAAIiYcJiMCOgAAAAAAQAAAAAAAACAAA AAAAAAAAA== |
| Topological Polar Surface Area | 34.1 A^2 |
| Monoisotopic Mass | 450.35 g/mol |
| Exact Mass | 450.35 g/mol |
| XLogP3-AA | 10.9 |
| Compound Is Canonicalized | true |
| Formal Charge | 0 |
| Heavy Atom Count | 33 |
| Defined Atom Stereocenter Count | 2 |
| Undefined Atom Stereocenter Count | 0 |
| Defined Bond Stereocenter Count | 1 |
| Undefined Bond Stereocenter Count | 0 |
| Isotope Atom Count | 0 |
| Covalently-Bonded Unit Count | 1 |

*from PubChem*

## 4.2 Experimental Properties

### 4.2.1 Physical Description

Solid

*from Human Metabolome Database (HMDB)*

Liquid

▸ *from Human Metabolome Database (HMDB)*

### 4.2.2 Color

Yellow viscous oil

*O'Neil, M.J. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. 13th Edition, Whitehouse Station, NJ: Merck and Co., Inc., 2001., p. 1532*

▸ *from HSDB*

LIGHT-YELLOW SOLIDS OR OILS

*Osol, A. and J.E. Hoover, et al. (eds.). Remington's Pharmaceutical Sciences. 15th ed. Easton, Pennsylvania: Mack Publishing Co., 1975., p. 942*

▸ *from HSDB*

Pale yellow oil or yellow crystals

*Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 10th ed. Volumes 1-3 New York, NY: John Wiley & Sons Inc., 1999., p. V2 3690*

▸ *from HSDB*

Clear, yellow to amber, viscous, odourless liquid

*IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). Available at: http://monographs.iarc.fr/ENG/Classification/index.php , p. V76 422 (2000)*

▸ *from HSDB*

### 4.2.3 Odor

Odorless

*Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 13th ed. New York, NY: John Wiley & Sons, Inc. 1997., p. 880*

▸ *from HSDB*

### 4.2.4 Boiling Point

142.5 °C at 1.00E-03 mm Hg

*PhysProp*

▸ *from DrugBank*

140-145 deg C @ 0.001 mm Hg

*Lide, DR (ed.). CRC Handbook of Chemistry and Physics. 81st Edition. CRC Press LLC, Boca Raton: FL 2000, p. 3-216*

▸ *from HSDB*

### 4.2.5 Melting Point

-20 °C

*PhysProp*

*from DrugBank*

-20 deg C

*Lide, DR (ed.). CRC Handbook of Chemistry and Physics. 81st Edition. CRC Press LLC, Boca Raton: FL 2000, p. 3-216*

*from HSDB*

-20 °C

*from Human Metabolome Database (HMDB)*

### 4.2.6 Solubility

**Water Solubility**

Insoluble in water

*from DrugBank*

Insoluble in water; sparingly soluble in methanol; sol in ethanol; sol in acetone, benzene, petroleum ether, hexane, and dioxane; sol in chloroform, and other fat solvents; sol in vegetable oils

*O'Neil, M.J. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. 13th Edition, Whitehouse Station, NJ: Merck and Co., Inc., 2001., p. 1322*

*from HSDB*

SOL IN FATS

*Goodman, L.S., and A. Gilman. (eds.) The Pharmacological Basis of Therapeutics. 5th ed. New York: Macmillan Publishing Co., Inc., 1975., p. 1592*

*from HSDB*

5.92e-05 g/L

*from Human Metabolome Database (HMDB)*

### 4.2.7 Density

0.964 @ 25 deg C/25 deg C

*O'Neil, M.J. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. 13th Edition, Whitehouse Station, NJ: Merck and Co., Inc., 2001., p. 1322*

*from HSDB*

### 4.2.8 LogP

9.3

*from DrugBank, Human Metabolome Database (HMDB)*

### 4.2.9 Stability

STABLE TO AIR & MOISTURE, BUT DECOMP IN SUNLIGHT

*The Merck Index. 9th ed. Rahway, New Jersey: Merck & Co., Inc., 1976., p. 1291*

▸ *from HSDB*

STABLE IN QUINONE FORM

*Osol, A. and J.E. Hoover, et al. (eds.). Remington's Pharmaceutical Sciences. 15th ed. Easton, Pennsylvania: Mack Publishing Co., 1975., p. 943*

▸ *from HSDB*

UNAFFECTED BY DIL ACIDS, DESTROYED BY ALKALI HYDROXIDES & REDUCING AGENTS

*The Merck Index. 9th ed. Rahway, New Jersey: Merck & Co., Inc., 1976., p. 1291*

▸ *from HSDB*

Phytonadione is stable to heat and moisture and may be autoclaved.

*McEvoy, G.K. (ed.). American Hospital Formulary Service- Drug Information 2002. Bethesda, MD: American Society of Health-System Pharmacists, Inc. 2002 (Plus Supplements)., p. 3566*

▸ *from HSDB*

### 4.2.10 Decomposition

When heated to decomposition it emits acrid smoke and irritating fumes.

*Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996., p. 3391*

▸ *from HSDB*

### 4.2.11 pH

SOLN OF 1 PART VIT K1 & 20 PARTS ALC IS NEUTRAL TO LITMUS

*Budavari, S. (ed.). The Merck Index - Encyclopedia of Chemicals, Drugs and Biologicals. Rahway, NJ: Merck and Co., Inc., 1989., p. 1580*

▸ *from HSDB*

### 4.2.12 Kovats Retention Index

| | |
|---|---|
| Standard non-polar | 3287 |

▸ *from NIST*

## 4.3 Spectral Properties

Index of refraction: 1.5263 @ 20 deg C/D; specific optical rotation (dioxane): -0.28 @ 589 nm

*O'Neil, M.J. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. 13th Edition, Whitehouse Station, NJ: Merck and Co., Inc., 2001., p. 1322*

▸ *from HSDB*

UV max absorption (petroleum ether): 242, 248, 260, 269, 325 nm (E= 396, 419, 383, 387, 68, 1%, 1 cm)

*O'Neil, M.J. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. 13th Edition, Whitehouse Station, NJ: Merck and Co., Inc., 2001., p. 1332*

▸ *from HSDB*

SADTLER REF NUMBER: 16104 (IR, PRISM)

*Weast, R.C. (ed.). Handbook of Chemistry and Physics. 60th ed. Boca Raton, Florida: CRC Press Inc., 1979., p. C-543*

▸ *from HSDB*

IR: 5231 (Coblentz Society Spectral Collection)

*Lide, D.R., G.W.A. Milne (eds.). Handbook of Data on Organic Compounds. Volume I. 3rd ed. CRC Press, Inc. Boca Raton ,FL. 1994., p. V4 3535*

▸ *from HSDB*

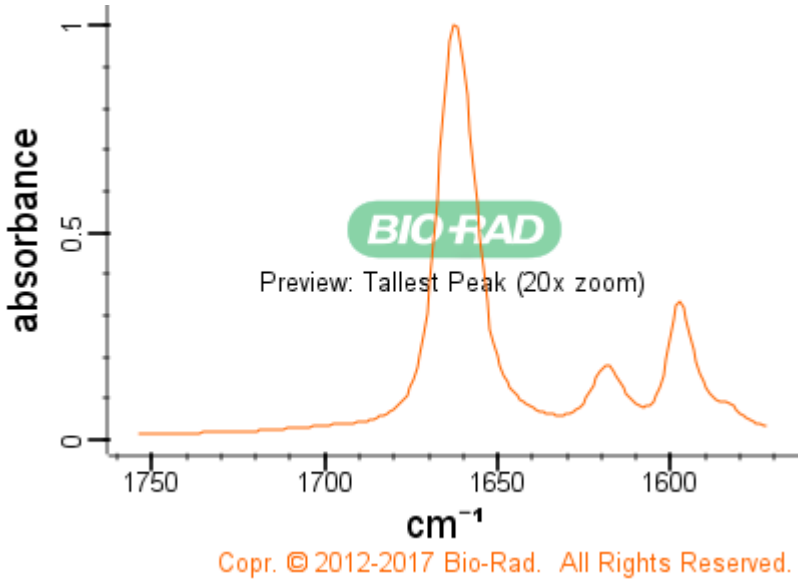
UV: 2-826 (Organic Electronic Spectral Data, Phillips et al, John Wiley & Sons, NY)

*Lide, D.R., G.W.A. Milne (eds.). Handbook of Data on Organic Compounds. Volume I. 3rd ed. CRC Press, Inc. Boca Raton ,FL. 1994., p. V4 3535*

▸ *from HSDB*

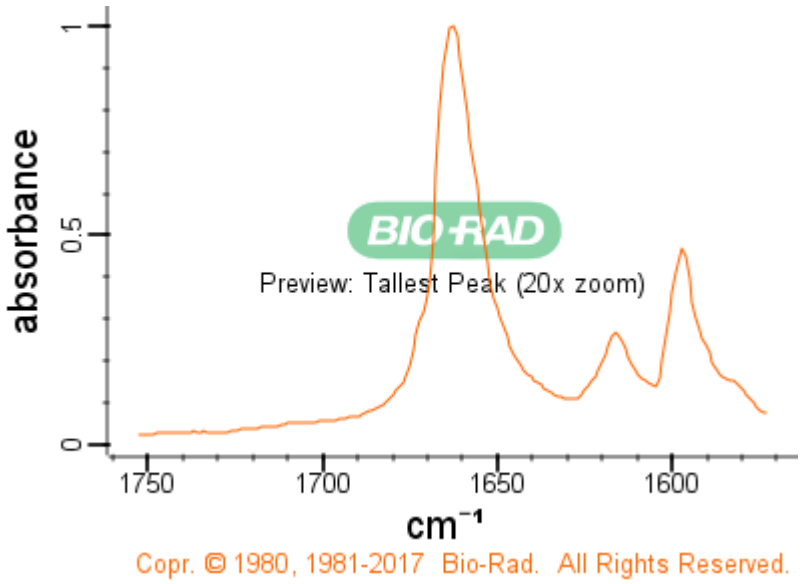
### 4.3.1 Infrared Spectra

| **Infrared Spectra: 1 of 2 (FTIR Spectra)** | |
|---|---|
| Instrument Name | Bio-Rad FTS |
| Technique | Neat (KBr) |
| Source of Spectrum | Forensic Spectral Research |
| Source of Sample | Spectrum Chemical Manufacturing Corp. |
| Catalog Number | PH195 |
| Lot Number | WG0878 |
| Copyright | Copyright © 2012-2017 Bio-Rad Laboratories, Inc. All Rights Reserved. |

| Infrared Spectra: 1 of 2 (FTIR Spectra) | |
|---|---|
| Thumbnail |  |



*from SpectraBase*

| Infrared Spectra: 2 of 2 (FTIR Spectra) | |
|---|---|
| Technique | BETWEEN SALTS |
| Source of Sample | Merck & Company, Inc. |
| Copyright | Copyright © 1980, 1981-2017 Bio-Rad Laboratories, Inc. All Rights Reserved. |
| Thumbnail |  |



*from SpectraBase*

### 4.3.2 Mass Spectrometry

#### 4.3.2.1 GC-MS

1. GC-MS Spectrum 2301 - GC-MS
11. GC-MS Spectrum 31506
21. GC-MS Spectrum 31

2. GC-MS Spectrum 2304 - GC-MS (1 TMS)
3. GC-MS Spectrum 2313 - GC-MS (2 TMS)
4. GC-MS Spectrum 2318 - GC-MS (2 TMS)
5. GC-MS Spectrum 2321 - GC-MS (2 TMS)
6. GC-MS Spectrum 2329 - GC-MS (2 TMS)
7. GC-MS Spectrum 2332 - GC-MS (2 TMS)
8. GC-MS Spectrum 11862
9. GC-MS Spectrum 28236
10. GC-MS Spectrum 28237
12. GC-MS Spectrum 31507
13. GC-MS Spectrum 31508
14. GC-MS Spectrum 31509
15. GC-MS Spectrum 31510
16. GC-MS Spectrum 31511
17. GC-MS Spectrum 31512
18. GC-MS Spectrum 31587
19. GC-MS Spectrum 31588
20. GC-MS Spectrum 31589
22. GC-MS Spectrum 315
23. GC-MS Spectrum 315
24. GC-MS Spectrum 315

*from Human Metabolome Database (HMDB)*

#### 4.3.2.2 MS-MS

1. MS-MS Spectrum 89529
2. MS-MS Spectrum 89530
3. MS-MS Spectrum 89531
4. MS-MS Spectrum 152475
5. MS-MS Spectrum 152476
6. MS-MS Spectrum 152477

*from Human Metabolome Database (HMDB)*

# 5 Related Records

CLICK TO LOAD...

*from NCBI*

## 5.1 Related Compounds with Annotation

CLICK TO LOAD...

*from PubChem*

## 5.2 Related Compounds

| | |
|---|---|
| Same Tautomer | 25 records |
| Same Connectivity | 23 records |
| Same Stereo | 5 records |
| Same Isotope | 13 records |
| Same Parent, Tautomer | 30 records |
| Same Parent, Connectivity | 28 records |
| Same Parent, Stereo | 10 records |
| Same Parent, Isotope | 18 records |
| Same Parent, Exact | 6 records |
| Mixtures, Components, and Neutralized Forms | 14 records |

| | |
|---|---|
| Similar Compounds | 4007 records |
| Similar Conformers | 12 records |

*from PubChem*

## 5.3 Substances

### 5.3.1 Related Substances

| | |
|---|---|
| All | 114 records |
| Same | 96 records |
| Mixture | 18 records |

*from PubChem*

### 5.3.2 Substances by Category

CLICK TO LOAD...

*from PubChem*

## 5.4 Entrez Crosslinks

| | |
|---|---|
| PubMed | 1 record |
| Protein Structures | 1 record |

*from PubChem*

## 6 Chemical Vendors

CLICK TO LOAD...

*from PubChem*

# 7 Drug and Medication Information

## 7.1 Drug Indication

For the treatment of haemorrhagic conditions in infants, antidote for coumarin anticoagulants in hypoprothrombinaemia.

*from DrugBank*

## 7.2 FDA Orange Book

### 7.2.1 Prescription Drug Products

| **Prescription Drug Products: 1 of 9 (RX Drug Ingredient)** | |
|---|---|
| Drug Ingredient | PHYTONADIONE |
| Proprietary Name | VITAMIN K1 |
| Applicant | 1. HOSPIRA (Application Number: A087954)<br>2. HOSPIRA (Application Number: A087955) |

*from FDA Orange Book*

| **Prescription Drug Products: 2 of 9 (RX Drug Ingredient)** | |
|---|---|
| Drug Ingredient | PHYTONADIONE |
| Proprietary Name | MEPHYTON |
| Applicant | VALEANT PHARMS (Application Number: N010104) |

*from FDA Orange Book*

| **Prescription Drug Products: 3 of 9 (RX Drug Ingredient)** | |
|---|---|
| Drug Ingredient | PHYTONADIONE |
| Proprietary Name | PHYTONADIONE |
| Applicant | INTL MEDICATION (Application Number: A083722) |

*from FDA Orange Book*

View All 9 Prescription Drug Products

### 7.2.2 Discontinued Drug Products

| **Discontinued Drug Products: 1 of 5 (DISCN Drug Ingredient)** | |
|---|---|
| Drug Ingredient | ASCORBIC ACID; BIOTIN; CYANOCOBALAMIN; ERGOCALCIFEROL; |

| Discontinued Drug Products: 1 of 5 (DISCN Drug Ingredient) | |
|---|---|
| | FOLIC ACID; NIACINAMIDE; PANTOTHENIC ACID; PHYTONADIONE; PYRIDOXINE; RIBOFLAVIN; THIAMINE; VITAMIN A PALMITATE; VITAMIN E |
| Proprietary Name | VITAPED |
| Applicant | HOSPIRA (Application Number: N020176) |

▸ *from FDA Orange Book*

| Discontinued Drug Products: 2 of 5 (DISCN Drug Ingredient) | |
|---|---|
| Drug Ingredient | PHYTONADIONE |
| Proprietary Name | PHYTONADIONE |
| Applicant | GLAXOSMITHKLINE (Application Number: A084060) |

▸ *from FDA Orange Book*

| Discontinued Drug Products: 3 of 5 (DISCN Drug Ingredient) | |
|---|---|
| Drug Ingredient | PHYTONADIONE |
| Proprietary Name | VITAMIN K1 |
| Applicant | HOSPIRA (Application Number: A087956) |

▸ *from FDA Orange Book*

View All 5 Discontinued Drug Products

## 7.3 Drug Labels for Ingredients

| Drug Labels for Ingredients: 1 of 6 (Label Title) | |
|---|---|
| Label Information | Total 34 labels |
| Drug Ingredient | PHYTONADIONE |
| NDC Code(s) | **NDC Code(s)**<br>0005-4365-56, 0179-0133-70, 0187-1704-05, 0409-9157-01, 0409-9157-25, 0409-9158-01, 0409-9158-25, 11695-4014-1, 21695-168-10, 46066-915-01 ... total 55. |
| Packagers | Aspen Veterinary Resources; Avera McKennan Hospital; Bimeda Inc., Division of Cross Vetpharm Group; Butler Animal Health; Cardinal Health; Carilion Materials Management; General Injectables & Vaccines, Inc; Hospira, Inc.; International Medication Systems, Limited; KAISER FOUNDATION HOSPITALS; Neogen Corporation - Nandino; Physicians Total Care, Inc.; Rebel Distributors Corp; Sandoz Canada Inc; Teligent Pharma, Inc.; Ultimate Formulations Inc. dba Best Formulations; Valeant Pharmaceuticals North America LLC; |

| Drug Labels for Ingredients: 1 of 6 (Label Title) | |
|---|---|
| | Wyeth Pharmaceutical Division of Wyeth Holdings LLC, a subsidiary of Pfizer Inc. |

*from DailyMed*

| Drug Labels for Ingredients: 2 of 6 (Label Title) | |
|---|---|
| Label Information | Total 143 labels |
| Drug Ingredient | VITAMIN K |
| NDC Code(s) | **NDC Code(s)**<br>0005-4365-56, 0056-0168-01, 0056-0168-70, 0056-0168-75, 0056-0169-01, 0056-0169-10, 0056-0169-70, 0056-0169-75, 0056-0169-90, 0056-0170-01 ... total 724. |
| Packagers | A-S Medication Solutions; Aidarex Pharmaceuticals LLC; American Health Packaging; Amneal Pharmaceuticals LLC; Aphena Pharma Solutions - Tennessee, Inc.; Aphena Pharma Solutions - Tennessee, LLC; Aspen Veterinary Resources; Avera McKennan Hospital; Bimeda Inc., Division of Cross Vetpharm Group; Bristol-Myers Squibb Pharma Company ... total 53. |

*from DailyMed*

| Drug Labels for Ingredients: 3 of 6 (Label Title) | |
|---|---|
| Label Title | INFUVITE ADULT MULTIPLE VITAMINS- ascorbic acid, vitamin a palmitate, cholecalciferol, thiamine hydrochloride, riboflavin-5 phosphate sodium, pyridoxine hydrochloride, niacinamide, dexpanthenol, alpha-tocopherol acetate, vitamin k1, folic acid, biotin, cyanocobalamin injection, solution<br>More information... |
| Drug Ingredient | ALPHA-TOCOPHEROL ACETATE; ASCORBIC ACID; BIOTIN; CHOLECALCIFEROL; CYANOCOBALAMIN; DEXPANTHENOL; FOLIC ACID; NIACINAMIDE; PYRIDOXINE HYDROCHLORIDE; RIBOFLAVIN 5'-PHOSPHATE SODIUM; THIAMINE HYDROCHLORIDE; VITAMIN A PALMITATE; VITAMIN K |
| Label Image | CLICK TO LOAD... |
| Label Download | PDF Label |

| Drug Labels for Ingredients: 3 of 6 (Label Title) | |
|---|---|
| NDC Code(s) | **NDC Code(s)**<br>54643-5649-1, 54643-5650-2 |
| Packager | Sandoz Canada Inc |

*from DailyMed*

View All 6 Drug Labels for Ingredients

## 7.4 Drugs at PubMed Health

| Drugs at PubMed Health: 1 of 7 (PubMed Health Drug Name) | |
|---|---|
| Drug Name | Vitamin K (Class) (Oral route, Parenteral route) |
| Description | Vitamins are compounds that you must have for growth and health. They are needed in only small amounts and usually are available in the foods that you eat. Vitamin K is necessary for normal clotting of the blood. |

*from PubMed Health*

| Drugs at PubMed Health: 2 of 7 (PubMed Health Drug Name) | |
|---|---|
| Drug Name | Mephyton |
| Notes | See Phytonadione |

*from PubMed Health*

| Drugs at PubMed Health: 3 of 7 (PubMed Health Drug Name) | |
|---|---|
| Drug Name | Phytonadione |
| Drug Classes | Antidote, Nutriceutical, Nutritive Agent |

*from PubMed Health*

View All 7 Drugs at PubMed Health

## 7.5 Clinical Trials

Download

1 to 5 of 21 View More

| Record ID | Title | Status | Phase |
|---|---|---|---|
| NCT03358706 | A Study to Evaluate the Effect of Ustekinumab on Cytochrome P450 Enzyme Activities Following Induction | Not yet recruiting | 1 |

| Record ID | Title | Status | Phase |
|---|---|---|---|
| | and Maintenance Dosing in Participants With Moderate to Severe Crohn's Disease | | |
| NCT02740712 | Pharmacokinetic Drug-Drug Interaction Study of Rucaparib | Active, not recruiting | 1 |
| NCT02324686 | Vitamin K Supplementation in Patients on Hemodialysis | Recruiting | 2 |
| NCT02256813 | Study to Evaluate the Effect of Multiple Doses of BIRT 2584 XX Tablets on the Pharmacokinetic Parameters of Warfarin, Omeprazole, Caffeine, and Dextromethorphan in Healthy Male Volunteers | Completed | 1 |
| NCT02243553 | Effects of Tipranavir (With Ritonavir) Capsule and Liquid Formulation on Cytochrome P450 and P-glycoprotein Activity in Healthy Volunteers | Completed | 1 |

*from ClinicalTrials.gov*

## 7.6 Therapeutic Uses

Antifibrinolytic Agents

*National Library of Medicine's Medical Subject Headings online file (MeSH, 1999)*

*from HSDB*

THE RATIONAL THERAPEUTIC USE OF VITAMIN K IS BASED ON ITS ABILITY TO CORRECT BLEEDING TENDENCY OR HEMORRHAGE ASSOC WITH ITS DEFICIENCY. A DEFICIENCY OF VITAMIN K & ITS ATTENDANT DEFICIENCY OF PROTHROMBIN & RELATED CLOTTING FACTORS CAN RESULT FROM INADEQUATE INTAKE, ABSORPTION, OR UTILIZATION OF VITAMIN, OR AS A CONSEQUENCE OF ACTION OF THE ACTION OF A VITAMIN K ANTAGONIST. /VITAMIN K/

*Hardman, J.G., L.E. Limbird, P.B., A.G. Gilman. Goodman and Gilman's The Pharmacological Basis of Therapeutics. 10th ed. New York, NY: McGraw-Hill, 2001., p. 1785*

*from HSDB*

BLEEDING THAT ACCOMPANIES OBSTRUCTIVE JAUNDICE OR BILIARY FISTULA RESPONDS PROMPTLY TO ADMINISTRATION OF VITAMIN K. ORAL PHYTONADIONE ADMIN WITH BILE SALTS IS BOTH SAFE AND EFFECTIVE AND SHOULD BE USED IN THE CARE OF THE JAUNDICED PATIENT, BOTH PREOPERATIVELY & POSTOPERATIVELY.

*Hardman, J.G., L.E. Limbird, P.B., A.G. Gilman. Goodman and Gilman's The Pharmacological Basis of Therapeutics. 10th ed. New York, NY: McGraw-Hill, 2001., p. 1785*

*from HSDB*

IF FOR SOME REASON ORAL ADMIN IS NOT FEASIBLE /IN TREATMENT OF OBSTRUCTIVE JAUNDICE OR BILIARY FISTULA/, A PARENTERAL PREPN SHOULD BE USED.

*Hardman, J.G., L.E. Limbird, P.B., A.G. Gilman. Goodman and Gilman's The Pharmacological Basis of Therapeutics. 10th ed. New York, NY: McGraw-Hill, 2001., p. 1785*

*from HSDB*

VIT K MAY BE OF HELP IN COMBATING BLEEDING AND HYPOPROTHROMBINEMIA THAT FOLLOW THE BITE OF THE TROPICAL AMERICAN PIT VIPER OR OTHER SPECIES WHOSE VENOM DESTROYS OR INACTIVATES PROTHROMBIN. /VITAMIN K/

*Hardman, J.G., L.E. Limbird, P.B., A.G. Gilman. Goodman and Gilman's The Pharmacological Basis of*

*Therapeutics. 10th ed. New York, NY: McGraw-Hill, 2001., p. 1786*

*from HSDB*

VARIOUS DISORDERS THAT RESULT IN INADEQUATE ABSORPTION FROM THE INTESTINAL TRACT MAY LEAD TO A DEFICIENCY OF VITAMIN K AND HYPOPROTHROMBINEMIA. THESE INCLUDE MUCOVISCIDOSIS, SPRUE, REGIONAL ENTERITIS AND ENTEROCOLITIS, ULCERATIVE COLITIS, DYSENTERY, AND EXTENSIVE RESECTION OF BOWEL. SINCE DRUGS THAT GREATLY REDUCE THE BACTERIAL POPULATION OF THE BOWEL ARE FREQUENTLY USED IN MANY OF THESE DISORDERS, THE AVAILABILITY OF THE VITAMIN MAY BE FURTHER REDUCED. MOREOVER, DIETARY RESTRICTIONS MAY ALSO LIMIT THE AVAILABILITY OF THE VITAMIN. FOR IMMEDIATE CORRECTION OF DEFICIENCY, PARENTERAL /VITAMIN K/ THERAPY SHOULD BE GIVEN. /VITAMIN K/

*Hardman, J.G., L.E. Limbird, P.B., A.G. Gilman. Goodman and Gilman's The Pharmacological Basis of Therapeutics. 10th ed. New York, NY: McGraw-Hill, 2001., p. 1785*

*from HSDB*

MEDICATION (VET): PARENTERAL THERAPY IS INDICATED IN SWEET CLOVER DISEASES & POSSIBLY IN SOME MYCOTOXICOSES & HEMATURIAS OF CATTLE. ... IT MAY HAVE VALUE IN PROPHYLAXIC AS WELL AS IN TREATMENT OF EPISTAXIS IN RACE HORSES. FED TO SOWS IT HELPS PREVENT HEMORRHAGING NAVELS IN NEW BORN PIGS... /VIT K/

*Rossoff, I.S. Handbook of Veterinary Drugs. New York: Springer Publishing Company, 1974., p. 659*

*from HSDB*

MEDICATION (VET): TO PREVENT & TREAT BLOOD COAGULATION PROBLEMS (HEMORRHAGIC SYNDROME) ASSOC WITH HYPOPROTHROMBINEMIA. IT IS REQUIRED FOR LIVER PROTHROMBIN SYNTHESIS. ... PRESURGICAL USE OF VIT K IS ESSENTIAL IN ANIMALS WITH INADEQUATE SECRETION OF BILE & IN NEWBORN (LITTLE OR NO INTESTINAL BACTERIAL SYNTHESIS OF VIT K). /VIT K/

*Rossoff, I.S. Handbook of Veterinary Drugs. New York: Springer Publishing Company, 1974., p. 659*

*from HSDB*

MEDICATION (VET): IN HYPOPROTHROMBINEMIAS; ANTIDOTE FOR DICOUMAROL POISONING

*The Merck Index. 9th ed. Rahway, New Jersey: Merck & Co., Inc., 1976., p. 1291*

*from HSDB*

Vitamin K is indicated for 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 oral anticoagulants, salicylates, and some antibiotics. 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. /Vitamin K; Included in US product labeling/

*MICROMEDEX Thomson Health Care. USPDI - Drug Information for the Health Care Professional. 22nd ed. Volume 1. MICROMEDEX Thomson Health Care, Greenwood Village, CO. 2002. Content Reviewed and Approved by the U.S. Pharmacopeial Convention, Inc., p. 2956*

*from HSDB*

The American Academy of Pediatrics recommends routine phytonadione administration at birth to prevent hemorrhagic disease of the newborn, 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 (eg, phenobarbital, phenytoin) during pregnancy. Phytonadione is preferred over menadiol because the risk of causing hyperbilirubinemia and hemolytic anemia is less, especially in premature infants. /Vitamin K;

Included in US product labeling/

*MICROMEDEX Thomson Health Care. USPDI - Drug Information for the Health Care Professional. 22nd ed. Volume 1. MICROMEDEX Thomson Health Care, Greenwood Village, CO. 2002. Content Reviewed and Approved by the U.S. Pharmacopeial Convention, Inc., p. 5956*

▸ *from HSDB*

Phytonadione is useful in restoring the prothrombin time to normal levels and in decreasing or stopping bleeding episodes.

*Ellenhorn, M.J., S. Schonwald, G. Ordog, J. Wasserberger. Ellenhorn's Medical Toxicology: Diagnosis and Treatment of Human Poisoning. 2nd ed. Baltimore, MD: Williams and Wilkins, 1997., p. 459*

▸ *from HSDB*

Phytonadione and other Vitamin K preparations do not combat hemorrhage caused by overdosage of heparin.

*American Medical Association, Council on Drugs. AMA Drug Evaluations Annual 1994. Chicago, IL: American Medical Association, 1994., p. 794*

▸ *from HSDB*

Phytonadione has a more prompt, potent, and prolonged effect than the other vitamin K analogues and is generally preferred when large doses or long-term therapy is indicated. ...

*American Medical Association, Council on Drugs. AMA Drug Evaluations Annual 1994. Chicago, IL: American Medical Association, 1994., p. 795*

▸ *from HSDB*

Anticoagulants are indicated for prophylaxis and/or treatment of venous (or arterial /Not included in US product labeling/) thrombosis (and its extension) and pulmonary embolism. Deep vein thrombosis (DVP) or pulmonary embolism (treatment). Oral anticoagulatns are used during and following initial heparin therapy to decrease the risk of extension, recurrence, or death. /Anticoagulants; Included in US product labeling/

*MICROMEDEX Thomson Health Care. USPDI - Drug Information for the Health Care Professional. 22nd ed. Volume 1. MICROMEDEX Thomson Health Care, Greenwood Village, CO. 2002. Content Reviewed and Approved by the U.S. Pharmacopeial Convention, Inc., p. 265*

▸ *from HSDB*

Oral anticoagulants are used to prevent thromboembolic complications after surgery, although low-dose subcutaneous heparin is used more commonly. /Anticoagulants; Included in US product labeling/

*MICROMEDEX Thomson Health Care. USPDI - Drug Information for the Health Care Professional. 22nd ed. Volume 1. MICROMEDEX Thomson Health Care, Greenwood Village, CO. 2002. Content Reviewed and Approved by the U.S. Pharmacopeial Convention, Inc., p. 265*

▸ *from HSDB*

Anticoagulants are indicated for prophylaxis and/or treatment of thromboembolic complications (ischemic stroke) associated with atrial fibrillation. They are strongly recommended in patients at high risk of stroke (including patients with recent stroke, transient ischemic attack, or systemic embolism; poor left ventricular function; age over 75 years; hypertension; rheumatic mitral valve disease; mechanical or tissue prosthetic heart valves.) /Anticoagulants; Included in US product labeling/

*MICROMEDEX Thomson Health Care. USPDI - Drug Information for the Health Care Professional. 22nd ed. Volume 1. MICROMEDEX Thomson Health Care, Greenwood Village, CO. 2002. Content Reviewed and Approved by the U.S. Pharmacopeial Convention, Inc., p. 265*

▸ *from HSDB*

Anticoagulants are indicated after myocardial infarction to reduce the risk of death, recurrent

myocardial infarction, and thromboembolic events such as stroke or systemic embolization. /Anticoagulants; Included on U.S. product labeling/

*MICROMEDEX Thomson Health Care. USPDI - Drug Information for the Health Care Professional. 22nd ed. Volume 1. MICROMEDEX Thomson Health Care, Greenwood Village, CO. 2002. Content Reviewed and Approved by the U.S. Pharmacopeial Convention, Inc., p. 265*

▸ *from HSDB*

Oral anticoagulants are indicated, alone or in combination with aspirin, for primary prevention of thrombotic complications of coronary artery disease in patients without history of myocardial infarction, stroke, or transient ischemic attacks but with increasing levels of risk. /Anticoagulants, Included in US product labeling/

*MICROMEDEX Thomson Health Care. USPDI - Drug Information for the Health Care Professional. 22nd ed. Volume 1. MICROMEDEX Thomson Health Care, Greenwood Village, CO. 2002. Content Reviewed and Approved by the U.S. Pharmacopeial Convention, Inc., p. 265*

▸ *from HSDB*

Anticoagulants are indicated for prophylaxis and/or treatment of thromboembolic complications associated with tissue and mechanical cardiac valve replacement. /Anticoagulants; Included in US product labeling/

*MICROMEDEX Thomson Health Care. USPDI - Drug Information for the Health Care Professional. 22nd ed. Volume 1. MICROMEDEX Thomson Health Care, Greenwood Village, CO. 2002. Content Reviewed and Approved by the U.S. Pharmacopeial Convention, Inc., p. 265*

▸ *from HSDB*

Anticoagulants are used in certain patients with valvular heart disease to prevent systemic embolization. /NOT included in US product labeling/

*MICROMEDEX Thomson Health Care. USPDI - Drug Information for the Health Care Professional. 22nd ed. Volume 1. MICROMEDEX Thomson Health Care, Greenwood Village, CO. 2002. Content Reviewed and Approved by the U.S. Pharmacopeial Convention, Inc., p. 265*

▸ *from HSDB*

Oral anticoagulants are used, following initial heparinization, to prevent recurrent thromboembolism in peripheral arterial occlusive disease. They are not indicated for routine prophylaxis after intrainguinal bypass and other vascular reconstructions but are indicated, usually in combination with aspirin, in patients at high risk of graft thrombosis. /NOT included in US product labeling/

*MICROMEDEX Thomson Health Care. USPDI - Drug Information for the Health Care Professional. 22nd ed. Volume 1. MICROMEDEX Thomson Health Care, Greenwood Village, CO. 2002. Content Reviewed and Approved by the U.S. Pharmacopeial Convention, Inc., p. 266*

▸ *from HSDB*

## 7.7 Drug Warning

IN PT WHO HAVE SEVERE HEPATIC DISEASE, ADMIN OF LARGE DOSES OF MENADIONE OR PHYLLOQUINONE MAY FURTHER DEPRESS FUNCTION OF LIVER.

*Hardman, J.G., L.E. Limbird, P.B., A.G. Gilman. Goodman and Gilman's The Pharmacological Basis of Therapeutics. 10th ed. New York, NY: McGraw-Hill, 2001., p. 1784*

▸ *from HSDB*

Maternal Medication usually Compatible with Breast-Feeding: K1 (vitamin): Reported Sign or Symptom in Infant or Effect on Lactation: None. /from Table 6/

*Report of the American Academy of Pediatrics Committee on Drugs in Pediatrics 93 (1): 141 (1994)*

▸ *from HSDB*

A rare hypersensitivity-like reaction, which has occasionally resulted in death, has been reported after intravenous administration of phytonadione, especially when administration is rapid.

*MICROMEDEX Thomson Health Care. USPDI - Drug Information for the Health Care Professional. 22nd ed. Volume 1. MICROMEDEX Thomson Health Care, Greenwood Village, CO. 2002. Content Reviewed and Approved by the U.S. Pharmacopeial Convention, Inc., p. 2957*

▸ *from HSDB*

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

*MICROMEDEX Thomson Health Care. USPDI - Drug Information for the Health Care Professional. 22nd ed. Volume 1. MICROMEDEX Thomson Health Care, Greenwood Village, CO. 2002. Content Reviewed and Approved by the U.S. Pharmacopeial Convention, Inc., p. 2957*

▸ *from HSDB*

Side/Adverse Effects: Flushing of face; redness, pain, or swelling at injection site (with parenteral administration); skin lesions (plaques) -- very rare, wtih repeated injection at one site; unusual taste. /Vitamin K/

*MICROMEDEX Thomson Health Care. USPDI - Drug Information for the Health Care Professional. 22nd ed. Volume 1. MICROMEDEX Thomson Health Care, Greenwood Village, CO. 2002. Content Reviewed and Approved by the U.S. Pharmacopeial Convention, Inc., p. 2796*

▸ *from HSDB*

Phytonadione is relatively nontoxic; however, severe reactions have occurred rarely during or immediately following IV administration. These severe reactions, which may occur in patients receiving phytonadione for the first time, resemble hypersensitiviey or anaphylaxis. Symptoms include cramp-like pains, convulsive movements, cardiac irregularities, chest pains, cyanosis, dulled consciousness, flushing of the face, a sense of chest constriction, circulatory collapse, bronchospasm, hyperhidrosis, dyspnea, alteration of taste, dizziness, rapid and weak pulse, brief hypotension, shock, cardiac and/or respiratory arrest, and death.

*McEvoy, G.K. (ed.). American Hospital Formulary Service- Drug Information 2002. Bethesda, MD: American Society of Health-System Pharmacists, Inc. 2002 (Plus Supplements)., p. 3565*

▸ *from HSDB*

Spontaneous abortion and stillbirth have occurred, as well as low birth weight and growth retardation. In addition, fetal or neonatal hemorrhage, fetal death from hemorrhage in utero, and increased risk of maternal hemorrhage during the second and third trimesters have been reported. There is some evidence that embryopathy occurs only with oral anticoagulant administration between the 6th and 12th weeks of gestation. /Anticoagulants/

*MICROMEDEX Thomson Health Care. USPDI - Drug Information for the Health Care Professional. 22nd ed. Volume 1. MICROMEDEX Thomson Health Care, Greenwood Village, CO. 2002. Content Reviewed and Approved by the U.S. Pharmacopeial Convention, Inc., p. 267*

▸ *from HSDB*

If a coumarin or indandione derivative is used during the third trimester, it should be discontinued after the 37th week of gestation, and heparin substituted if maternal anticoagulation is required, to reduce the risk of fetal hemorrhage during labor and of neonatal hemorrhage following delivery. Anticoagulants also increase the risk of maternal hemorrhage during or following delivery. /Anticoagulants/

*MICROMEDEX Thomson Health Care. USPDI - Drug Information for the Health Care Professional. 22nd ed. Volume 1. MICROMEDEX Thomson Health Care, Greenwood Village, CO. 2002. Content Reviewed and Approved by the U.S. Pharmacopeial Convention, Inc., p. 267*

▸ *from HSDB*

Administration of anticoagulants in the immediate postpartum period may increase the risk of maternal hemorrhage. /Anticoagulants/

*MICROMEDEX Thomson Health Care. USPDI - Drug Information for the Health Care Professional. 22nd ed. Volume 1. MICROMEDEX Thomson Health Care, Greenwood Village, CO. 2002. Content Reviewed and Approved by the U.S. Pharmacopeial Convention, Inc., p. 267*

▸ *from HSDB*

Infants, especially neonates, may be more susceptible to the effects of anticoagulants because of vitamin K deficiency. /Anticoagulants/

*MICROMEDEX Thomson Health Care. USPDI - Drug Information for the Health Care Professional. 22nd ed. Volume 1. MICROMEDEX Thomson Health Care, Greenwood Village, CO. 2002. Content Reviewed and Approved by the U.S. Pharmacopeial Convention, Inc., p. 267*

▸ *from HSDB*

Geriatric patients may be more susceptible to the effects of anticoagulants, increasing the risk of hemorrhage. Geriatric patients may have advanced vascular disease that alters hemostatic mechanisms, hepatic function impairment that decreases procoagulant factor synthesis or anticoagulant metabolism, or they may have renal function impairment. Lower maintenance doses than those usually recommended for adults may be required for these patients. /Anticoagulants/

*MICROMEDEX Thomson Health Care. USPDI - Drug Information for the Health Care Professional. 22nd ed. Volume 1. MICROMEDEX Thomson Health Care, Greenwood Village, CO. 2002. Content Reviewed and Approved by the U.S. Pharmacopeial Convention, Inc., p. 267*

▸ *from HSDB*

Anticoagulant therapy increases the risk of localized hemorrhage during and following oral surgical procedures. Consultation with the prescribing physician may be advisable prior to oral surgery, to determine whether a temporary dosage reduction or withdrawal of anticoagulant therapy is feasible. Also, local measures to minimize bleeding should be used at the time of surgery. /Anticoagulants/

*MICROMEDEX Thomson Health Care. USPDI - Drug Information for the Health Care Professional. 22nd ed. Volume 1. MICROMEDEX Thomson Health Care, Greenwood Village, CO. 2002. Content Reviewed and Approved by the U.S. Pharmacopeial Convention, Inc., p. 267-8*

▸ *from HSDB*

The occurrence of gastrointestinal or genitourinary hemorrhage during anticoagulant therapy, especially if the prothrombin time is within the therapeutic range, may indicate the presence of an underlying occult lesion such as a tumor or ulcer. /Anticoagulants/

*MICROMEDEX Thomson Health Care. USPDI - Drug Information for the Health Care Professional. 22nd ed. Volume 1. MICROMEDEX Thomson Health Care, Greenwood Village, CO. 2002. Content Reviewed and Approved by the U.S. Pharmacopeial Convention, Inc., p. 273*

▸ *from HSDB*

Necrosis is caused by thrombosis of the venules and capillaries within the subcutaneous fat. It usually occurs on the 3rd to 8th day of therapy and may be more frequent in patients with protein C deficiency. Initial lesions, which are painful, are erythematous or ecchymotic with a sharply demarcated border, subsequently developing bullae with full-thickness skin necrosis. It is important to determine whether necrosis is caused by the anticoagulant or by an underlying disease. In severe cases, debridement or even amputation of affected tissue, limb, breast, or penis may be necessary. Fatalities have occurred. /Anticoagulants/

*MICROMEDEX Thomson Health Care. USPDI - Drug Information for the Health Care Professional. 22nd ed. Volume 1. MICROMEDEX Thomson Health Care, Greenwood Village, CO. 2002. Content Reviewed and Approved by the U.S. Pharmacopeial Convention, Inc., p. 273*

▸ *from HSDB*

Constipation may be a symptom of hemorrhage-induced paralytic ileus or intestinal obstuction caused by submucosal or intramural hemorrhage. /Anticoagulants/

*MICROMEDEX Thomson Health Care. USPDI - Drug Information for the Health Care Professional. 22nd ed. Volume 1. MICROMEDEX Thomson Health Care, Greenwood Village, CO. 2002. Content Reviewed and Approved by the U.S. Pharmacopeial Convention, Inc., p. 273*

▸ *from HSDB*

Fatal or nonfatal bleeding or hemorrhage can occur from any tissue or organ. Signs, symptoms, and severity vary depending on the site and extent of bleeding. Therefore, bleeding should be considered as a potential cause of any sign or symptom not otherwise explainable. /Anticoagulants/

*MICROMEDEX Thomson Health Care. USPDI - Drug Information for the Health Care Professional. 22nd ed. Volume 1. MICROMEDEX Thomson Health Care, Greenwood Village, CO. 2002. Content Reviewed and Approved by the U.S. Pharmacopeial Convention, Inc., p. 273*

▸ *from HSDB*

Purple toes syndrome may develop 3 to 20 weeks after initiation of anticoagulant therapy; it results from systemic cholesterol microembolization. Anticoagulant therapy may enhance the release of atheromatous plaque emboli, which may increase the risk of purple toes syndrome and other complications of systemic cholesterol embolization. Purple spots may blanch with pressure or elevation on the leg. The syndrome is usually reversible but in some cases may progress to gangrene or necrosis. /Anticoagulants/

*MICROMEDEX Thomson Health Care. USPDI - Drug Information for the Health Care Professional. 22nd ed. Volume 1. MICROMEDEX Thomson Health Care, Greenwood Village, CO. 2002. Content Reviewed and Approved by the U.S. Pharmacopeial Convention, Inc., p. 273*

▸ *from HSDB*

Adrenal hemorrhage may result in acute adrenal insufficiency. Diagnosis may be difficult because the initial symptoms (abdominal pain, apprehension, diarrhea, dizziness or fainting, headache, loss of appetite, nausea or vomiting, and weakness) are nonspecific and variable. /Anticoagulants/

*MICROMEDEX Thomson Health Care. USPDI - Drug Information for the Health Care Professional. 22nd ed. Volume 1. MICROMEDEX Thomson Health Care, Greenwood Village, CO. 2002. Content Reviewed and Approved by the U.S. Pharmacopeial Convention, Inc., p. 273*

▸ *from HSDB*

Large amounts of aluminum hydroxide may precipitate bile acids in the upper small intestine, thereby decreasing absorption of fat-soluble vitamins. /Vitamin K/

*MICROMEDEX Thomson Health Care. USPDI - Drug Information for the Health Care Professional. 22nd ed. Volume 1. MICROMEDEX Thomson Health Care, Greenwood Village, CO. 2002. Content Reviewed and Approved by the U.S. Pharmacopeial Convention, Inc., p. 2957*

▸ *from HSDB*

Concurrent use /with cholestyramine, colestipol, mineral oil, or sucralfate/ may decrease absorption of vitamin K; requirements for vitamin K may be increased in patients receiving these medications. /Vitamin K/

*MICROMEDEX Thomson Health Care. USPDI - Drug Information for the Health Care Professional. 22nd ed. Volume 1. MICROMEDEX Thomson Health Care, Greenwood Village, CO. 2002. Content Reviewed and Approved by the U.S. Pharmacopeial Convention, Inc., p. 2957*

▸ *from HSDB*

Oral and intramuscular phytomenadione (vitamin K1) prophylaxis became an issue following the report of a potential carcinogenic effect of intramuscular but not oral phytomenadione prophylaxis. There is

increasing evidence, however, that oral phytomenadione prophylaxis is less effective for the prevention of late vitamin K deficiency bleeding (VKDB) than intramuscular prophylaxis. Following a report of an increased cancer risk after intramuscular phytomenadione, a series of papers on this issue appeared. Although an increased risk for solid tumours could almost certainly be excluded, a potential risk for acute lymphatic leukaemia in childhood could not be ruled out definitively. Almost all cases of late VKDB are preventable with intramuscular phytomenadione prophylaxis administered once at birth, whereas a single oral dose given at birth is much less effective. Repeated oral phytomenadione doses given to breast-fed infants either weekly (1 mg) or daily (25 microg) seem to be as effective as intramuscular phytomenadione prophylaxis. The efficacy of 3 oral 2mg doses with the new mixed micellar preparation ('Konakion MM') remains to be established. Although a number of studies have failed to confirm a cancer risk with phytomenadione, these studies have been unable to rule out a risk definitely because absence of evidence is not evidence of absence. A meta-analysis of the available studies might provide 95% confidence intervals narrow enough to exclude even a small cancer risk with some certainty. Oral prophylaxis will probably be as safe as the intramuscular prophylaxis if given daily (25 microg) or weekly (1 mg).

*von Kries R.; Drug Saf 21(1): p 1-6 (1999)*

▸ *from HSDB*

## 7.8 Drug Tolerance

/HEREDITARY/ RESISTANT INDIVIDUALS /TO COUMARIN/ WERE FOUND TO SHOW ANOTHER CHARACTERISTIC, UNUSUAL SENSITIVITY TO ANTIDOTAL EFFECTS OF VIT K. ... SENSITIVITY WAS...CALCULATED TO BE ABOUT 20 TIMES THAT OBSERVED IN OTHER PATIENTS. ...SYNTHESIS OF CLOTTING FACTOR II, VII, IX & X HAS BEEN MODIFIED BY GENETIC MUTATION... /VIT K/

*LaDu, B.N., H.G. Mandel, and E.L. Way. Fundamentals of Drug Metabolism and Disposition. Baltimore: Williams and Wilkins, 1971., p. 323*

▸ *from HSDB*

# 8 Pharmacology and Biochemistry

## 8.1 Pharmacology

Phylloquinone is a vitamin, indicated in the treatment of 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. Phylloquinone 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).

*from DrugBank*

## 8.2 MeSH Pharmacological Classification

**Vitamins**

Organic substances that are required in small amounts for maintenance and growth, but which cannot be manufactured by the human body.
See a list of PubChem compounds matching this category.

*from MeSH*

**Antifibrinolytic Agents**

Agents that prevent fibrinolysis or lysis of a blood clot or thrombus. Several endogenous antiplasmins are known. The drugs are used to control massive hemorrhage and in other coagulation disorders.
See a list of PubChem compounds matching this category.

*from MeSH*

## 8.3 ATC Code

B02BA01 - Phytomenadione < B02BA - Vitamin k < B02B - Vitamin k and other hemostatics < B02 - Antihemorrhagics < B - Blood and blood forming organs

*from WHO ATC*

## 8.4 Bionecessity

The discovery of a vitamin K dependent protein in bone suggests that the fetal bone abnormalities associated with the administration of oral anticoagulants during the first trimester of pregnancy "fetal warfarin syndrome" may be related to a deficiency of the vitamin. /Vitamin K/

*Hardman, J.G., L.E. Limbird, P.B., A.G. Gilman. Goodman and Gilman's The Pharmacological Basis of Therapeutics. 10th ed. New York, NY: McGraw-Hill, 2001., p. 1784*

*from HSDB*

State of deficiency: chief clinical manifestation of vitamin k deficiency is increased tendency to bleed, and postoperative hemorrhage are common; intracranial hemorrhage may occur. /vit k/

*Hardman, J.G., L.E. Limbird, P.B., A.G. Gilman. Goodman and Gilman's The Pharmacological Basis of Therapeutics. 10th ed. New York, NY: McGraw-Hill, 2001., p. 1784*

from HSDB

Hypoprothrombinemia secondary to vitamin K deficiency may occur in the following persons or conditions: Patients with hepatic or biliary tract disease, including obstructive jaundice or biliary fistula; in malabsorption syndromes or diseases affecting the small intestine or pancreas, such as celiac disease, cystic fibrosis, intestinal resuction, persistent diarrhea or dysentery, regional enteritis, sprue, or ulcerative colitis; prolonged T-tube drainage; abetalipoproteinemia; patients receiving total parenteral nutrition (TPN); or in infants receiving unfortified milk substitute formulas or those who are exclusively breast-fed. Also vitamin K deficiency may occur when vitamin K activity is impaired by sulfonamides, quinine, quinidine, or dactinomycin, or when absorption is decreased by concurrent administration of cholestyramine, colestipol, mineral oil, or sucralfate. /Vitamin K/

*MICROMEDEX Thomson Health Care. USPDI - Drug Information for the Health Care Professional. 22nd ed. Volume 1. MICROMEDEX Thomson Health Care, Greenwood Village, CO. 2002. Content Reviewed and Approved by the U.S. Pharmacopeial Convention, Inc., p. 2956*

from HSDB

## 8.5 Absorption, Distribution and Excretion

Oral phylloquinone is adequately absorbed from the gastrointestinal tract only if bile salts are present. After absorption, phylloquinone is initially concentrated in the liver, but the concentration declines rapidly. Very little vitamin K accumulates in tissues.

from DrugBank

**Route of Elimination**

Almost no free unmetabolized vitamin K appears in bile or urine.

from DrugBank

Little is known about the excretion of vitamin K. High fecal concentrations of vitamin K probably result from bacterial synthesis in the intestine.

*McEvoy, G.K. (ed.). American Hospital Formulary Service- Drug Information 2002. Bethesda, MD: American Society of Health-System Pharmacists, Inc. 2002 (Plus Supplements)., p. 3566*

from HSDB

Although the drug may be concentrated in the liver for a short time after absorption, only small amounts of phytonadione are stored in body tissues.

*McEvoy, G.K. (ed.). American Hospital Formulary Service- Drug Information 2002. Bethesda, MD: American Society of Health-System Pharmacists, Inc. 2002 (Plus Supplements)., p. 3566*

from HSDB

Phytonadione is absorbed from the GI tract only in the presence of bile salts. Radioisotope studies show that absorption occurs via intestinal lymph. There is some evidence that absorption of phytonadione across the GI mucosa is a saturable, energy-dependent process that occurs in the proximal small intestine.

*McEvoy, G.K. (ed.). American Hospital Formulary Service- Drug Information 2002. Bethesda, MD: American Society of Health-System Pharmacists, Inc. 2002 (Plus Supplements)., p. 3566*

from HSDB

Fat-soluble vit...k...absorbed from skin... /vit k/

*Hayes, W.J., Jr., E.R. Laws Jr., (eds.). Handbook of Pesticide Toxicology Volume 1. General Principles. New York, NY: Academic Press, Inc., 1991., p. 139*

▸ *from HSDB*

Vit k accum in liver, spleen, & lungs, but significant amt are not stored in body for long periods.

*American Medical Association, Council on Drugs. AMA Drug Evaluations Annual 1994. Chicago, IL: American Medical Association, 1994., p. 783*

▸ *from HSDB*

Phytonadione is absorbed rapidly by the subcutaneous route. The subcutaneous rote is preferable to the intravenous route unless problems are anticipatedwith subcutaneous absorption.

*Ellenhorn, M.J., S. Schonwald, G. Ordog, J. Wasserberger. Ellenhorn's Medical Toxicology: Diagnosis and Treatment of Human Poisoning. 2nd ed. Baltimore, MD: Williams and Wilkins, 1997., p. 459*

▸ *from HSDB*

/Phylloquinone/ ... is absorbed chemically unchanged from the proximal intestine after solubilization into mixed micelles composed of bile salts and the products of pancreatic lipolysis. In healthy adults, the efficiency of absorption of phylloquinone in its free form is about 80%, but the efficiency of absorption from green leafy vegetables such as spinach is < 10%.

*IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). Available at: http://monographs.iarc.fr/ENG/Classification/index.php , p. V76 455 (2000)*

▸ *from HSDB*

## 8.6 Metabolism/Metabolites

...In experimental animals...phylloquinone...can be converted to more potent menaquinone series. Whether this can occur in man and of what significance these transformations are to action of phylloquinone...are still unknown.

*Goodman, L.S., and A. Gilman. (eds.) The Pharmacological Basis of Therapeutics. 5th ed. New York: Macmillan Publishing Co., Inc., 1975., p. 1593*

▸ *from HSDB*

In animals treated with warfarin, major fraction of phylloquinone is metabolized to phylloquinone oxide.

*Goodman, L.S., and A. Gilman. (eds.) The Pharmacological Basis of Therapeutics. 5th ed. New York: Macmillan Publishing Co., Inc., 1975., p. 1593*

▸ *from HSDB*

Phytonadione is rapidly metabolized to more polar metabolites, which are excreted in the bile and urine. The major urinary metabolites result from shortening of the side chain to five or seven carbon atoms, yielding carboxylic acids that are conjugated with glucuronate prior to excretion. Treatment with a coumarin-type anticoagulant results in a marked increase in the amount of phytonadione-2,3-epoxide in the liver and blood. Such treatment also increases the urinary excretion of phytonadione metabolites, primarily degradative products of phytonadione-2,3-epoxide. The biliary metabolites of phytonadione have not been identified.

*Hardman, J.G., L.E. Limbird, P.B., A.G. Gilman. Goodman and Gilman's The Pharmacological Basis of Therapeutics. 10th ed. New York, NY: McGraw-Hill, 2001., p. 1784*

▸ *from HSDB*

The liver plays an exclusive role in the metabolic transformations leading to the elimination of vitamin K from the body. After intravenous doses of 45 ug to 1 mg (3)H-phylloquinone, about 20% of the radiolabel was excreted in the urine within three days, and 35-50% was excreted as metabolites in the feces via the bile.

*IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). Available at: http://monographs.iarc.fr/ENG/Classification/index.php , p. V76 461-2 (2000)*

▸ *from HSDB*

## 8.7 Mechanism of Action

Vitamin K is an essential cofactor for the gamma-carboxylase enzymes which catalyze the posttranslational gamma-carboxylation of glutamic acid residues in inactive hepatic precursors of coagulation factors II (prothrombin), VII, IX and X. Gamma-carboxylation converts these inactive precursors into active coagulation factors which are secreted by hepatocytes into the blood. Supplementing with Phylloquinone results in a relief of vitamin K deficiency symptoms which include easy bruisability, epistaxis, gastrointestinal bleeding, menorrhagia and hematuria.

▸ *from DrugBank*

Vit k is necessary for formation of prothrombinogen & other blood clotting factors in liver. During clotting, circulating prothrombin is required for production of thrombin; in turn, thrombin converts fibrinogen to fibrin, network of which constitutes clot. /vit k/

*Osol, A. and J.E. Hoover, et al. (eds.). Remington's Pharmaceutical Sciences. 15th ed. Easton, Pennsylvania: Mack Publishing Co., 1975., p. 943*

▸ *from HSDB*

In normal animals and man, phyltonadione ... /is/ virtually devoid of pharmacodynamic activity. In Animals and man deficient in vitamin k, the pharmacological action of vitamin k is identical to its normal physiological function, that is, to promote hepatic biosynthesis of prothrombin (factor ii), proconvertin (factor vii), plasma thromboplastin component (ptc, christmas factor, factor ix), and Stuart factor (factor x).

*Hardman, J.G., L.E. Limbird, P.B., A.G. Gilman. Goodman and Gilman's The Pharmacological Basis of Therapeutics. 10th ed. New York, NY: McGraw-Hill, 2001., p. 1783*

▸ *from HSDB*

On the basis of studies of microsomal metabolism in vitro and studies in rats and mice in vivo, /it was suggested/ that vitamin K may be mutagenic by affecting the mixed-function oxidase system which metabolizes benzo(a)pyrene. Phylloquinone at a high concentration (200 umol/l) inhibited the conversion of benzo(a)pyrene to its more polar metabolites, ... . Paradoxically, at a lower concentration of phylloquinone (25 umol/l), ... the metabolism of benzo(a)pyrene was increased. In this system, therefore, .... phylloquinone could either potentiate or inhibit it, depending on the concentration. This overall weaker inhibitory effect of phylloquinone could be due to the low solubility of this lipophilic compound, but it is difficult to explain the mechanism of the enhanced metabolism of benzo(a)pyrene at lower concentrations of phylloquinone.

*IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). Available at: http://monographs.iarc.fr/ENG/Classification/index.php , p. V76 472 (2000)*

▸ *from HSDB*

## 8.8 Human Metabolite Information

### 8.8.1 Metabolite Description

Vitamin K is a family of fat-soluble compounds with a common chemical structure based on 2-methyl-1,

4-naphthoquinone

*from Human Metabolome Database (HMDB)*

Phytonadione is often called vitamin K1. It is a fat-soluble vitamin that is stable to air and moisture but decomposes in sunlight. It is found naturally in a wide variety of green plants. Phylloquinone is also an antidote for coumatetralyl. Vitamin K is needed for the posttranslational modification of certain proteins, mostly required for blood coagulation.

*from Human Metabolome Database (HMDB)*

### 8.8.2 Biofluid Locations

1. Blood
2. Urine

*from Human Metabolome Database (HMDB)*

### 8.8.3 Cellular Locations

1. Extracellular
2. Membrane (predicted from logP)

*from Human Metabolome Database (HMDB)*

1. Extracellular
2. Membrane

*from Human Metabolome Database (HMDB)*

### 8.8.4 Metabolite Pathways

1. Acenocoumarol Pathway
2. Alteplase Pathway
3. Aminocaproic Acid Pathway
4. Anistreplase Pathway
5. Aprotinin Pathway
6. Ardeparin Pathway
7. Argatroban Pathway
8. Bivalirudin Pathway
9. Coagulation
10. Dicoumarol Action Pathway
11. Dicumarol Pathway
12. Enoxaparin Pathway
13. Fondaparinux Pathway
14. Heparin Pathway
15. Lepirudin Pathway
16. Phenindione Action Pathway
17. Phenprocoumon Pathway
18. Reteplase Pathway
19. Streptokinase Pathway
20. Tenecteplase Pathway
21. Tranexamic Acid Pathway
22. Urokinase Pathway
23. Vitamin K Metabolism
24. Warfarin Pathway
25. Ximelagatran Pathway

*from Human Metabolome Database (HMDB)*

# 9 Use and Manufacturing

## 9.1 Methods of Manufacturing

Partial syntheses from menadione and phytol ... Synthesis using a pi-allylic nickel(I) complex ... .

*O'Neil, M.J. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. 13th Edition, Whitehouse Station, NJ: Merck and Co., Inc., 2001., p. 1322*

▸ *from HSDB*

Synthetically from 2-methyl-1,4-naphthoquinone and phytol.

*Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 13th ed. New York, NY: John Wiley & Sons, Inc. 1997., p. 880*

▸ *from HSDB*

The first syntheses and structural elucidation of phylloquinone were published in 1939 almost simultaneously by four groups. The starting materials were menadione or menadiol as the aromatic component and natural phytol or one of its derivatives. A breakthrough in commercial synthesis was achieved in the 1950s, when it was found that monoacylated menadiols (e.g. the monoacetate or the monobenzoate) could be used advantageously in the alkylation step and that natural phytol could be replaced by isophytol, which is easy to synthesize.

*IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). Available at: http://monographs.iarc.fr/ENG/Classification/index.php , p. V76 427 (2000)*

▸ *from HSDB*

## 9.2 Impurities

Commercial preparations may contain up to 20% of the cis isomer.

*Budavari, S. (ed.). The Merck Index - Encyclopedia of Chemicals, Drugs and Biologicals. Rahway, NJ: Merck and Co., Inc., 1989., p. 1580*

▸ *from HSDB*

Commercially available phylloquinone (vitamin K1) is prepared synthetically and may contain not only 2',3'-trans-phylloquinone (not less than 75%), but also 2',3'-cis-phylloquinone and trans-epoxyphylloquinone (not more than 4.0 percent). Phylloquinone occurs in nature only as the 2',3'-trans-7R,11R-stereoisomer.

*IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). Available at: http://monographs.iarc.fr/ENG/Classification/index.php , p. V76 424 (2000)*

▸ *from HSDB*

## 9.3 Formulations/Preparations

PHYTONADIONE, USP (VIT K1, AQUAMEPHYTON, KONAKION, MEPHYTON)... MARKETED IN 5-MG TABLETS, & IN AMPULS CONTAINING EMULSION OF 2 OR 10 MG/ML OF PHYTONADIONE DISPERSED IN SOLN OF BUFFERED POLYSORBATE & PROPYLENE GLYCOL (KONAKION) OR POLYETHYLATED FATTY ACID DERIV & DEXTROSE (AQUAMEPHYTON).

*Goodman, L.S., and A. Gilman. (eds.) The Pharmacological Basis of Therapeutics. 5th ed. New York: Macmillan*

*Publishing Co., Inc., 1975., p. 593*

▸ *from HSDB*

KONAKION IS ADMIN ONLY IM; AQUAMEPHYTON MAY BE GIVEN BY ANY PARENTERAL ROUTE.

*Goodman, L.S., and A. Gilman. (eds.) The Pharmacological Basis of Therapeutics. 5th ed. New York: Macmillan Publishing Co., Inc., 1975., p. 1593*

▸ *from HSDB*

COLLOIDAL SOLN IS MARKETED UNDER NAME AQUA-MEPHYTON.

*Budavari, S. (ed.). The Merck Index - Encyclopedia of Chemicals, Drugs and Biologicals. Rahway, NJ: Merck and Co., Inc., 1989., p. 1580*

▸ *from HSDB*

Oral tablets; 5 mg, Mephyton (scored) Merck.

*McEvoy, G.K. (ed.). American Hospital Formulary Service- Drug Information 2002. Bethesda, MD: American Society of Health-System Pharmacists, Inc. 2002 (Plus Supplements)., p. 3566*

▸ *from HSDB*

Phylloquinone is available as a 5 and 10 mg tablet (chewable), a 2 and 10 mg/mL injection solution, a 10 and 20 mg/mL oral solution, and a 20 mg/mL emulsion. ... Phylloquinone is also available as a component (200 ug) of a multivitamin lyophilized, sterile powder intended for reconstitution and dilution in intravenous infusions, as a component (0.075 mg) of and effervescent multivitamin tablet, and as a component (5.5 ug) of a multivitamin infant formula.

*IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). Available at: http://monographs.iarc.fr/ENG/Classification/index.php , p. V76 424 (2000)*

▸ *from HSDB*

Parenteral injection; 2 mg/ml, AquaMEPHYTON (with polyoxyethylated fatty acid derivative, dextrone, and benzyl alcohol 0.9%), Merck. 10 mg/ml, AquaMEPHYTON (with polyoxyethylated fatty acid derivative, dextrose, and benzyl alcohol 0.9%), Merck.

*McEvoy, G.K. (ed.). American Hospital Formulary Service- Drug Information 2002. Bethesda, MD: American Society of Health-System Pharmacists, Inc. 2002 (Plus Supplements)., p. 3566*

▸ *from HSDB*

# 10 Identification

## 10.1 Analytic Laboratory Methods

Several international pharmacopoeias specify infrared (IR) and ultraviolet (UV) absorption spectrophotometry with comparison to standards as the methods to identify phylloquinone; UV absorption spectrophotometry and liquid chromatography are used to assay its purity. Phylloquinone is identified in pharmaceutical preparations by IR and UV absorption spectrophotometry and liquid chromatography; liquid chromatography is used to assay for its content.

*IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). Available at: http://monographs.iarc.fr/ENG/Classification/index.php , p. V76 426 (2000)*

▸ *from HSDB*

AOAC International (1996) has developed a liquid chromatographic method with UV detection for the determination of phylloquinone in ready-to-feed milk-based infant formula.

*IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). Available at: http://monographs.iarc.fr/ENG/Classification/index.php , p. V76 426 (2000)*

▸ *from HSDB*

AOAC Official Method 992.27: trans-Vitamin K1 (phylloquinone) in ready-to-feed milk-based infant formula; liquid chromatographic method.

*Horwitz W, ed.; Official Methods of Analysis of AOAC International 17th ed. (2000). CD-ROM, AOAC International, Gaithersburg, MD*

▸ *from HSDB*

## 10.2 Clinical Laboratory Methods

QUANTITATIVE ANALYSIS OF VITAMIN K1 & VITAMIN K1 2,3-EPOXIDE IN PLASMA BY ELECTRON-CAPTURE GAS-LIQUID CHROMATOGRAPHY.

*BECHTOLD H, JAEHNCHEN E; QUANTITATIVE ANALYSIS OF VITAMIN K1 & VITAMIN K1 2,3-EPOXIDE IN PLASMA BY ELECTRON-CAPTURE GAS-LIQUID CHROMATOGRAPHY; J CHROMATOGR 164(1) 85-90 (1979)*

▸ *from HSDB*

As a result of its high selectivity and sensitivity, high-performance liquid chromatography (HPLC) is the method of choice for the determination of phylloquinone and menaquinones in the blood, tissues, milk, and in foods. Various procedures for extraction and preliminary purification, normal or reversed-phase HPLC, and ultraviolet, electrochemical, and fluorescence detection (both after electrochemical or chemical reduction and after photochemical decomposition) of the vitamin K substances have been described. The detection limits for phylloquinone are in the range 25-500 pg, depending on the detection method used. ... Alternative methods are thin layer chromatography, high- performance thin layer chromatography and gas chromatography. The spectrophotometric, fluorimetric, and colorimetric methods previously used without chromatographic purification of the samples to be analysed are frequently less sensitive and less specific than HPLC, for instance allowing no distinction between phylloquinone and menaquinones.

*IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). Available at: http://monographs.iarc.fr/ENG/Classification/index.php , p. V76 426 (2000)*

*from HSDB*

# 11 Safety and Hazards

## 11.1 Hazards Identification

### 11.1.1 GHS Classification

**GHS Hazard Statements**
Aggregated GHS information provided by 42 companies from 3 notifications to the ECHA C&L Inventory.

Reported as not meeting GHS hazard criteria by 14 of 42 companies. For more detailed information, please visit ECHA C&L website

Of the 2 notification(s) provided by 28 of 42 companies with hazard statement code(s):

H413 (96.43%): May cause long lasting harmful effects to aquatic life [Hazardous to the aquatic environment, long-term hazard]

Information may vary between notifications depending on impurities, additives, and other factors. The percentage value in parenthesis indicates the notified classification ratio from companies that provide hazard codes. Only hazard codes with percentage values above 10% are shown.

**Precautionary Statement Codes**
P273, and P501
(The corresponding statement to each P-code can be found here.)

*from European Chemicals Agency - ECHA*

## 11.2 Accidental Release Measures

### 11.2.1 Disposal Methods

SRP: At the time of review, criteria for land treatment or burial (sanitary landfill) disposal practices are subject to significant revision. Prior to implementing land disposal of waste residue (including waste sludge), consult with environmental regulatory agencies for guidance on acceptable disposal practices.

*from HSDB*

## 11.3 Handling and Storage

### 11.3.1 Storage Conditions

KEEP WELL CLOSED & PROTECTED FROM LIGHT.

*The Merck Index. 9th ed. Rahway, New Jersey: Merck & Co., Inc., 1976., p. 1291*

*from HSDB*

The drug is photosensitive and must be protected from light at all times. Infusion solutions should be protected from light by wrapping the container with aluminum foil or other opaque material. Phytonadione tablets should be stored in well-closed, light-resistant containers.

*McEvoy, G.K. (ed.). American Hospital Formulary Service- Drug Information 2002. Bethesda, MD: American Society of Health-System Pharmacists, Inc. 2002 (Plus Supplements)., p. 3566*

▸ *from HSDB*

## 11.4 Regulatory Information

### 11.4.1 FDA Requirements

The US Food and Drug Administration ... requires that all infant formula sold in the USA contain a minimum of 4 ug/100 kcal (0.2 mg/kg) of vitamin K; and that any vitamin K added shall be in the form of phylloquinone.

*IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). Available at: http://monographs.iarc.fr/ENG/Classification/index.php , p. V76 438 (2000)*

▸ *from HSDB*

The Approved Drug Products with Therapeutic Equivalence Evaluations List identifies currently marketed prescription drug products, incl phytonadione, approved on the basis of safety and effectiveness by FDA under sections 505 of the Federal Food, Drug, and Cosmetic Act.

*DHHS/FDA; Electronic Orange Book-Approved Drug Products with Therapeutic Equivalence Evaluations. Available from, as of February 26, 2003: http://www.fda.gov/cder/ob/*

▸ *from HSDB*

# 12 Toxicity

## 12.1 Toxicological Information

### 12.1.1 Carcinogen

Evaluation: There is inadequate evidence in humans for the carcinogenicity of vitamin K. There is inadequate evidence in experimental animals for the carcinogenicity of vitamin K. Overall evaluation: Vitamin K is not classifiable as to its carcinogenicity to humans (Group 3). /Vitamin K/

*IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). Available at: http://monographs.iarc.fr/ENG/Classification/index.php , p. V76 475 (2000)*

▸ *from HSDB*

### 12.1.2 Interactions

Vit k antagonizes inhibitory effect of /acenocoumarol, phenprocoumon, anisindione, diphenadione, & phenindione/ on hepatic synthesis of vit k-dependent clotting proteins... /vit k/

*Evaluations of Drug Interactions. 2nd ed. and supplements. Washington, DC: American Pharmaceutical Assn., 1976, 1978., p. 303*

▸ *from HSDB*

Requirements for vitamin K may be increased in patients receiving /broad-spectrum antibiotics, moxalactam, quinidine, quinine, high doses of salicylates, or antibacterial sulfonamides/.

*MICROMEDEX Thomson Health Care. USPDI - Drug Information for the Health Care Professional. 22nd ed. Volume 1. MICROMEDEX Thomson Health Care, Greenwood Village, CO. 2002. Content Reviewed and Approved by the U.S. Pharmacopeial Convention, Inc., p. 2957*

▸ *from HSDB*

Concurrent use /with dactinomycin/ 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. /Vitamin K/

*MICROMEDEX Thomson Health Care. USPDI - Drug Information for the Health Care Professional. 22nd ed. Volume 1. MICROMEDEX Thomson Health Care, Greenwood Village, CO. 2002. Content Reviewed and Approved by the U.S. Pharmacopeial Convention, Inc., p. 2957*

▸ *from HSDB*

Concurrent use /of coumarin- or indandione-derivative anticoagulants/ 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. /Vitamin K/

*MICROMEDEX Thomson Health Care. USPDI - Drug Information for the Health Care Professional. 22nd ed. Volume 1. MICROMEDEX Thomson Health Care, Greenwood Village, CO. 2002. Content Reviewed and Approved by the U.S. Pharmacopeial Convention, Inc., p. 2957*

▸ *from HSDB*

Effects of anticoagulants may be increased paradoxically because of decreased hepatic synthesis of procoagulant factors; this effect may depend on antithyroid dosage and subsequent thyroid status of the patient. /Anticoagulants/

*MICROMEDEX Thomson Health Care. USPDI - Drug Information for the Health Care Professional. 22nd ed. Volume 1. MICROMEDEX Thomson Health Care, Greenwood Village, CO. 2002. Content Reviewed and Approved by the U.S. Pharmacopeial Convention, Inc., p. 269*

▸ *from HSDB*

Effects of anticoagulants may be decreased because of increased hepatic synthesis of procoagulant factors by estrogens; however, increased effects have also been reported. Use of estrogen-containing oral contraceptives in patients with thrombophilic disorders tends to increase the risk of thrombosis, especially in patients with activated protein C resistance due to factor V Leiden mutation. /Anticoagulants/

*MICROMEDEX Thomson Health Care. USPDI - Drug Information for the Health Care Professional. 22nd ed. Volume 1. MICROMEDEX Thomson Health Care, Greenwood Village, CO. 2002. Content Reviewed and Approved by the U.S. Pharmacopeial Convention, Inc., p. 269*

▸ *from HSDB*

The effects of anticoagulants may be increased /if used concurrently with diffunisal/, possibly in part because of displacement of anticoagulant from protein binding sites. /Anticoagulants/

*MICROMEDEX Thomson Health Care. USPDI - Drug Information for the Health Care Professional. 22nd ed. Volume 1. MICROMEDEX Thomson Health Care, Greenwood Village, CO. 2002. Content Reviewed and Approved by the U.S. Pharmacopeial Convention, Inc., p. 269*

▸ *from HSDB*

Effects of anticoagulants may be increased /if used concurrently with cinchophen/. /Anticoagulants/

*MICROMEDEX Thomson Health Care. USPDI - Drug Information for the Health Care Professional. 22nd ed. Volume 1. MICROMEDEX Thomson Health Care, Greenwood Village, CO. 2002. Content Reviewed and Approved by the U.S. Pharmacopeial Convention, Inc., p. 269*

▸ *from HSDB*

Effects of anticoagulants may be increased /when used concurrently with clofibrate/, possibly because of alteration of procoagulant factor synthesis or catabolism or displacement of anticoagulant from protein binding sites. /Anticoagulants/

*MICROMEDEX Thomson Health Care. USPDI - Drug Information for the Health Care Professional. 22nd ed. Volume 1. MICROMEDEX Thomson Health Care, Greenwood Village, CO. 2002. Content Reviewed and Approved by the U.S. Pharmacopeial Convention, Inc., p. 269*

▸ *from HSDB*

Effects of anticoagulants may be decreased /when use concurrently with glutethimide/ because of accelerated metabolism of anticoagulant secondary to stimulation of hepatic microsomal enzyme activity. /Anticoagulants/

*MICROMEDEX Thomson Health Care. USPDI - Drug Information for the Health Care Professional. 22nd ed. Volume 1. MICROMEDEX Thomson Health Care, Greenwood Village, CO. 2002. Content Reviewed and Approved by the U.S. Pharmacopeial Convention, Inc., p. 269*

▸ *from HSDB*

Effects of anticoagulants may be increased /when used concurrently with lepirudin/; gradual reduction in dose and/or infusion rate of lepirudin is recommended prior to switching to an oral anticoagulant. /Anticoagulants/

*MICROMEDEX Thomson Health Care. USPDI - Drug Information for the Health Care Professional. 22nd ed. Volume 1. MICROMEDEX Thomson Health Care, Greenwood Village, CO. 2002. Content Reviewed and Approved by the U.S. Pharmacopeial Convention, Inc., p. 270*

▸ *from HSDB*

Inhibition of the cytochrome p450 enzyme system by omeprazole especially in high doses, may cause a

decrease in hepatic metabolism of anticoagulants, which may result in delayed elimination and increased blood concentration. /Anticoagulants/

*MICROMEDEX Thomson Health Care. USPDI - Drug Information for the Health Care Professional. 22nd ed. Volume 1. MICROMEDEX Thomson Health Care, Greenwood Village, CO. 2002. Content Reviewed and Approved by the U.S. Pharmacopeial Convention, Inc., p. 270*

▸ *from HSDB*

A pharmacodynamic interaction may occur that causes an increased bleeding diathesis despite unaltered PT; since there is little clinical experience, caution is advised when these agents /paroxetine and anticoagulants/ are used concurrently. /Anticoagulants/

*MICROMEDEX Thomson Health Care. USPDI - Drug Information for the Health Care Professional. 22nd ed. Volume 1. MICROMEDEX Thomson Health Care, Greenwood Village, CO. 2002. Content Reviewed and Approved by the U.S. Pharmacopeial Convention, Inc., p. 270*

▸ *from HSDB*

Effects of anticoagulants may be increased /when used concurrently with platelet aggregation inhibitors/; the effect will not be reflected in PT. /Anticoagulants/

*MICROMEDEX Thomson Health Care. USPDI - Drug Information for the Health Care Professional. 22nd ed. Volume 1. MICROMEDEX Thomson Health Care, Greenwood Village, CO. 2002. Content Reviewed and Approved by the U.S. Pharmacopeial Convention, Inc., p. 270*

▸ *from HSDB*

Effects of anticoagulants may be increased because of plicamycin's hypoprothrombinemic effect. Interference with platelet formation by plicamycin may result in increased risk of hemorrhage; this effect cannot be shown by measurement of PT. /Anticoagulants/

*MICROMEDEX Thomson Health Care. USPDI - Drug Information for the Health Care Professional. 22nd ed. Volume 1. MICROMEDEX Thomson Health Care, Greenwood Village, CO. 2002. Content Reviewed and Approved by the U.S. Pharmacopeial Convention, Inc., p. 270*

▸ *from HSDB*

Effects of anticoagulants may be increased /when used concurrently with thyroid hormones/ because of alteration of procoagulant factor synthesis or catabolism and increased receptor affinity for anticoagulant; this effect may depend upon dosage and subsequent thyroid status of the patient. /Anticoagulants/

*MICROMEDEX Thomson Health Care. USPDI - Drug Information for the Health Care Professional. 22nd ed. Volume 1. MICROMEDEX Thomson Health Care, Greenwood Village, CO. 2002. Content Reviewed and Approved by the U.S. Pharmacopeial Convention, Inc., p. 270*

▸ *from HSDB*

Caution in concurrent use /of sertraline/ with anticoagulants is recommended because of possible displacement of either medication from protein-binding sites, leading to increased plasma concentrations of the free (unbound) medications and increased risk of adverse effects. /Anticoagulants/

*MICROMEDEX Thomson Health Care. USPDI - Drug Information for the Health Care Professional. 22nd ed. Volume 1. MICROMEDEX Thomson Health Care, Greenwood Village, CO. 2002. Content Reviewed and Approved by the U.S. Pharmacopeial Convention, Inc., p. 270*

▸ *from HSDB*

The pharmacological response to vitamin K1 (Konakion) in anticoagulated (prothrombin complex activity <30%) New Zealand white rabbits was determined by measuring prothrombin complex activity (P.C.A.) in peripheral plasma. In animals pretreated with ...difenacoum (0.85 mg/kg or 8.5 mg/kg) P.C.A. reached a max 4 hr after admin of vitamin K1 (0.5 mg/kg) and declined at a rate indicating complete inhibition of clotting factor synthesis. ...The duration of action of ...difenacoum was much longer than that of

warfarin. ...Difenacoum /is a/... more potent and persistent antagonist of vitamin K1 than warfarin in vivo. ...
Abstract: PubMed

*Park BK, Leck JB; Biochem Pharmacol 31 (22): 3635-9 (1982)*

▸ *from HSDB*

### 12.1.3 Toxicity Summary

The intravenous $LD_{50}$ of phylloquinone in the mouse is 41.5 and 52 mL/kg for the 0.2% and 1% concentrations, respectively.

▸ *from DrugBank*

### 12.1.4 Human Toxicity Excerpts

/HUMAN EXPOSURE STUDIES/ To determine whether vitamin K administration affects urinary calcium excretion in postmenopausal women. Before- and after-trials with a 2-week treatment period. Healthy postmenopausal women (55 to 75 years old) were recruited from the convents in and around Maastricht. Controls (25 to 40 years old) were healthy premenopausal volunteers. Daily administration of 1 mg of vitamin K for 2 weeks. Serum immunoreactive osteocalcin: hydroxylapatite binding (HAB) capacity of serum immunoreactive osteocalcin; excretion of calcium, hydroxyproline, and creatinine in the urine during the last 2 h of a 16-h fasting period. In premenopausal women, no effect of vitamin K administration was seen. In the postmenopausal group, vitamin K induced increased serum immunoreactive osteocalcin concentration; normalization of the HAB capacity of serum immunoreactive osteocalcin (this marker was less than 50% that of the controls in the pretreatment samples); a decrease in urinary calcium excretion, notably in the "fast losers" of calcium; and a parallel decrease in urinary hydroxyproline excretion in the fast losers of calcium. The serum immunoreactive osteocalcin level may vary with vitamin K status. This variance should be taken into consideration if osteocalcin is used as a marker for osteoblast activity. Vitamin K is one factor that may play a role in the loss of bone mass in postmenopausal osteoporosis.

*Knapen M, et al; Ann Intern Med 111(12): p1001-5 (1989)*

▸ *from HSDB*

/EPIDEMIOLOGY STUDIES/ A retrospective review of anaphylaxis after i.v. phytonadione over a 58-month period at a large academic center was performed. During the period of the study a protocol for the administration of i.v. phytonadione was in place. A review of computerized records and survey of staff identified cases of anaphylaxis meeting predefined inclusion criteria. In addition, a literature review was performed for articles concerning anaphylaxis after i.v. phytonadione. Over the 58 months of the study, a total of 6,572 doses of i.v. phytonadione were administered. Two cases of anaphylaxis after i.v. phytonadione were identified. The incidence of anaphylaxis was 3 per 10,000 doses with 95% confidence intervals of 0.04 to 11 per 10,000 doses. The literature review identified 14 cases meeting inclusion criteria with no reviews of the literature or estimates of incidence. The incidence of anaphylaxis after i.v. phytonadione is overall comparable or slightly less than other drugs known to cause anaphylaxis.

*Riegert-Johnson DL, et al; Ann Allergy Asthma Immunol 89: p 400-6 (2002)*

▸ *from HSDB*

### 12.1.5 Non-Human Toxicity Excerpts

/LABORATORY ANIMALS: Developmental or Reproductive Toxicity/ The offspring of mice treated with

phylloquinone by injection had cleft lip and exencephaly. Six pregnant Sprague-Dawley rats were dosed with 10 mg/kg body weight phylloquinone (Konakion) daily on days 9-20 of gestation, and the fetuses were delivered on day 21 and examined for external malformations and the presence of hemorrhages only. No adverse effects were noted when compared with a group of five untreated controls.

*IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). Available at: http://monographs.iarc.fr/ENG/Classification/index.php , p. V76 468 (2000)*

▸ *from HSDB*

/GENOTOXICITY/ In fetal sheep that received a catheter in the femoral vein 10-15 days before term, phylloquinone significantly increased the frequency of sister chromatid exchange in peripheral blood lymphocytes sampled 24 hours later.

*IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). Available at: http://monographs.iarc.fr/ENG/Classification/index.php , p. V76 469 (2000)*

▸ *from HSDB*

/GENOTOXICITY/ /Phytonadione/ ... at concentrations up to 2,000 mcg/plate with or without metabolic activation, was negative in the Ames microbial mutagen test.

*Medical Economics Co; Physicians Desk Reference 56th ed p.2130 (2002)*

▸ *from HSDB*

/GENOTOXICITY/ /Phylloquinone/ ... enhanced the frequency of sister chromatid exchange in cultured human maternal lymphocytes at concentrations that are relevant in vivo, and a similar increase in sister chromatid exchange frequency was observed in cultured lymphocytes from human placental blood.

*IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). Available at: http://monographs.iarc.fr/ENG/Classification/index.php , p. V76 469 (2000)*

▸ *from HSDB*

### 12.1.6 Non-Human Toxicity Values

LD50 Mouse oral 25 g/kg

*Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996., p. 3391*

▸ *from HSDB*

LD50 Mouse subcutaneous 1000 mg/kg

*Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996., p. 3391*

▸ *from HSDB*

### 12.1.7 Populations at Special Risk

SRP: Persons with bleeding disorders or who are taking anticoagulants should be protected from exposure.

▸ *from HSDB*

## 12.2 Ecological Information

### 12.2.1 Natural Occurring Sources

FAT-SOL VIT OCCURRING NATURALLY AS TRANS ISOMER. ... FIRST ISOLATED FROM ALFALFA; ALSO SHOWS WIDESPREAD DISTRIBUTION IN HIGHER GREEN PLANTS: DAM ET AL, HELV CHIM ACTA 22, 310 (1939).

*Budavari, S. (ed.). The Merck Index - Encyclopedia of Chemicals, Drugs and Biologicals. Rahway, NJ: Merck and Co., Inc., 1989., p. 1580*

▸ *from HSDB*

Phylloquinone is widely distributed in higher plants and in some blue-green algae. It is present in many foods, especially leafy green vegetables and some vegetable oils.

*IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). Available at: http://monographs.iarc.fr/ENG/Classification/index.php , p. V76 436 (2000)*

▸ *from HSDB*

# 13 Literature

## 13.1 Depositor Provided PubMed Citations

CLICK TO LOAD...

*from PubChem*

## 13.2 NLM Curated PubMed Citations

CLICK TO LOAD...

*from PubChem*

## 13.3 Synthesis References

Manfred Dorner, "Method of making vitamin K1." U.S. Patent US5744624, issued June, 1964.

*from DrugBank*

Masaki, Yukio; Hashimoto, Kinji; Kaji, Kenji. Synthetic studies on isoprenoidquinones. II. Syntheses of ubiquinone-10, phylloquinone, and menaquinone-4 by a chain-extending method utilizing terminally functionalized isoprenoidhydroquinones. Chemical & Pharmaceutical Bulletin (1984), 32(10), 3959-67.

*from Human Metabolome Database (HMDB)*

## 13.4 Metabolite References

Download

1 to 1 of 1

| PMID | Reference |
|---|---|
| 16857056 | Tovar A, Ameho CK, Blumberg JB, Peterson JW, Smith D, Booth SL: Extrahepatic tissue concentrations of vitamin K are lower in rats fed a high vitamin E diet. Nutr Metab (Lond). 2006 Jul 20;3:29. |

*from Human Metabolome Database (HMDB)*

Download

1 to 5 of 5

| PMID | Reference |
|---|---|
| 11413487 | Simons K, Toomre D: Lipid rafts and signal transduction. Nat Rev Mol Cell Biol. 2000 Oct;1(1):31-9. |
| 16902246 | Watson AD: Thematic review series: systems biology approaches to metabolic and cardiovascular disorders. Lipidomics: a global approach to lipid analysis in biological systems. J Lipid Res. 2006 Oct;47(10):2101-11. Epub 2006 Aug 10. |
| 17374880 | Sethi JK, Vidal-Puig AJ: Thematic review series: adipocyte biology. Adipose tissue function and plasticity orchestrate nutritional adaptation. J Lipid Res. 2007 Jun;48(6):1253-62. Epub 2007 Mar 20. |
| 20044567 | Lingwood D, Simons K: Lipid rafts as a membrane-organizing principle. Science. 2010 Jan 1;327(5961):46-50. doi: 10.1126/science.1174621. |
| | The lipid handbook with CD-ROM |

*from Human Metabolome Database (HMDB)*

## 13.5 Springer Nature References

CLICK TO LOAD...

*from Springer Nature*

# 14 Patents

## 14.1 Depositor-Supplied Patent Identifiers

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*from PubChem*

# 15 Biomolecular Interactions and Pathways

## 15.1 Protein Bound 3-D Structures

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*from PubChem*

## 15.2 DrugBank Interactions

| | |
|---|---|
| Target | Vitamin K-dependent gamma-carboxylase |
| Action | inducer |
| PubChem Protein Target | P38435 |
| PubChem Gene Target | GGCX |
| General Function | Gamma-glutamyl carboxylase activity |
| Specific Function | Mediates the vitamin K-dependent carboxylation of glutamate residues to calcium-binding gamma-carboxyglutamate (Gla) residues with the concomitant conversion of the reduced hydroquinone form of vitamin K to vitamin K epoxide. |
| Reference | Morris DP, Soute BA, Vermeer C, Stafford DW: Characterization of the purified vitamin K-dependent gamma-glutamyl carboxylase. J Biol Chem. 1993 Apr 25;268(12):8735-42.<br>Abstract: PubMed |
| Reference | Tuan RS: Vitamin K-dependent gamma-glutamyl carboxylase activity in the chick embryonic chorioallantoic membrane. J Biol Chem. 1979 Feb 25;254(4):1356-64.<br>Abstract: PubMed |
| Reference | Reedstrom CK, Suttie JW: Comparative distribution, metabolism, and utilization of phylloquinone and menaquinone-9 in rat liver. Proc Soc Exp Biol Med. 1995 Sep;209(4):403-9.<br>Abstract: PubMed |
| Reference | Tasatargil A, Cadir B, Dalaklioglu S, Yurdakonar E, Caglar S, Turkay C: Effects of vitamin K1 supplementation on vascular responsiveness and oxidative stress in a rat femoral osteotomy model. Cell Biochem Funct. 2007 Sep-Oct;25(5):485-90.<br>Abstract: PubMed |

| | |
|---|---|
| Reference | Olson RE: The function and metabolism of vitamin K. Annu Rev Nutr. 1984;4:281-337.<br>Abstract: PubMed |
| Reference | Chen X, Ji ZL, Chen YZ: TTD: Therapeutic Target Database. Nucleic Acids Res. 2002 Jan 1;30(1):412-5.<br>Abstract: PubMed |

*from DrugBank*

| | |
|---|---|
| Target | Osteocalcin |
| Action | agonist |
| PubChem Gene Target | BGLAP |
| General Function | Structural molecule activity |
| Specific Function | Constitutes 1-2% of the total bone protein. It binds strongly to apatite and calcium. |
| Reference | Sato Y, Tsuru T, Oizumi K, Kaji M: Vitamin K deficiency and osteopenia in disuse-affected limbs of vitamin D-deficient elderly stroke patients. Am J Phys Med Rehabil. 1999 Jul-Aug;78(4):317-22.<br>Abstract: PubMed |
| Reference | Schurgers LJ, Dissel PE, Spronk HM, Soute BA, Dhore CR, Cleutjens JP, Vermeer C: Role of vitamin K and vitamin K-dependent proteins in vascular calcification. Z Kardiol. 2001;90 Suppl 3:57-63.<br>Abstract: PubMed |
| Reference | Vermeer C, Wolf J, Craciun AM, Knapen MH: Bone markers during a 6-month space flight: effects of vitamin K supplementation. J Gravit Physiol. 1998 Oct;5(2):65-9.<br>Abstract: PubMed |
| Reference | Askim M: [Vitamin K in the Norwegian diet and osteoporosis]. Tidsskr Nor Laegeforen. 2001 Sep 20;121(22):2614-6.<br>Abstract: PubMed |
| Reference | Kawana K, Takahashi M, Hoshino H, Kushida K: Circulating levels of vitamin K1, menaquinone-4, and menaquinone-7 in healthy elderly Japanese women and patients with vertebral fractures and patients with hip fractures. Endocr Res. 2001 Aug;27(3):337-43.<br>Abstract: PubMed |

*from DrugBank*

# 16 Biological Test Results

## 16.1 BioAssay Results

CLICK TO LOAD...

*from PubChem*

# 17 Classification

## 17.1 Ontologies

### 17.1.1 MeSH Tree

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*from MeSH*

### 17.1.2 ChEBI Ontology

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*from ChEBI*

### 17.1.3 LIPID MAPS Classification

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*from LIPID MAPS*

### 17.1.4 WHO ATC Classification System

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*from WHO ATC*

### 17.1.5 WIPO IPC

CLICK TO LOAD...

*from WIPO*

### 17.1.6 ChemIDplus

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*from ChemIDplus*

## 18 Information Sources

1. ChemIDplus /source/ChemIDplus

   *Phytonadione [USP:JAN]*
   *https://chem.nlm.nih.gov/chemidplus/sid/0000084800 https://chem.nlm.nih.gov/chemidplus/sid/0000084800*
   *Vitamin K1*
   *https://chem.nlm.nih.gov/chemidplus/sid/0011104384 https://chem.nlm.nih.gov/chemidplus/sid/0011104384*
   *(R*,R*-(E))-(1)-2-Methyl-3-(3,7,11,15-tetramethylhexadec-2-enyl)-1,4-naphthoquinone*
   *https://chem.nlm.nih.gov/chemidplus/sid/0079083004 https://chem.nlm.nih.gov/chemidplus/sid/0079083004*
   *ChemIDplus Chemical Information Classification*
   *https://chem.sis.nlm.nih.gov/chemidplus/chemidheavy.jsp https://chem.sis.nlm.nih.gov/chemidplus/chemidheavy.jsp*

2. DTP/NCI /source/DTP/NCI

   *phytonadione*
   *https://dtp.cancer.gov/dtpstandard/servlet/dwindex?searchtype=NSC&outputformat=html&searchlist=760373 https://dtp.cancer.gov/dtpstandard/servlet/dwindex?searchtype=NSC&outputformat=html&searchlist=760373*

3. DrugBank /source/DrugBank

   *Phylloquinone*
   *http://www.drugbank.ca/drugs/DB01022 http://www.drugbank.ca/drugs/DB01022*
   *http://www.drugbank.ca/drugs/DB01022#targets http://www.drugbank.ca/drugs/DB01022#targets*

4. EPA DSStox /source/EPA DSStox

   *Phytonadione*
   *https://comptox.epa.gov/dashboard/dsstoxdb/results?search=DTXSID8023472 https://comptox.epa.gov/dashboard/dsstoxdb/results?search=DTXSID8023472*

5. European Chemicals Agency - ECHA /source/European Chemicals Agency - ECHA

   *[R*,R*-(E)]-(±)-2-methyl-3-(3,7,11,15-tetramethylhexadec-2-enyl)-1,4-naphthoquinone*
   *https://echa.europa.eu/ https://echa.europa.eu/*
   *Phytomenadione*
   *https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/31318 https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/31318*

6. Human Metabolome Database (HMDB) /source/Human Metabolome Database (HMDB)

   *Reduced Vitamin K (phylloquinone)*
   *http://www.hmdb.ca/metabolites/HMDB0004198 http://www.hmdb.ca/metabolites/HMDB0004198*
   *Phytonadione*
   *http://www.hmdb.ca/metabolites/HMDB0015157 http://www.hmdb.ca/metabolites/HMDB0015157*

7. ClinicalTrials.gov /source/ClinicalTrials.gov

   *phytonadione*
   *https://clinicaltrials.gov/ https://clinicaltrials.gov/*

8. DailyMed /source/DailyMed

   *PHYTONADIONE*
   *https://dailymed.nlm.nih.gov/dailymed/search.cfm?labeltype=all&query=PHYTONADIONE https://dailymed.nlm.nih.gov/dailymed/search.cfm?labeltype=all&query=PHYTONADIONE*
   *VITAMIN K*
   *https://dailymed.nlm.nih.gov/dailymed/search.cfm?labeltype=all&query=VITAMIN+K https://dailymed.nlm.nih.gov/dailymed/search.cfm?labeltype=all&query=VITAMIN+K*
   *ALPHA-TOCOPHEROL ACETATE; ASCORBIC ACID; BIOTIN; CHOLECALCIFEROL; CYANOCOBALAMIN; DEXPANTHENOL; FOLIC ACID; NIACINAMIDE; PYRIDOXINE HYDROCHLORIDE; RIBOFLAVIN 5'-PHOSPHATE SODIUM; THIAMINE HYDROCHLORIDE; VITAMIN A PALMITATE; VITAMIN K*

https://dailymed.nlm.nih.gov/dailymed/search.cfm?labeltype=all&query=INFUVITE+ADULT
https://dailymed.nlm.nih.gov/dailymed/search.cfm?labeltype=all&query=INFUVITE+ADULT
ASCORBIC ACID; BIOTIN; CHOLECALCIFEROL; CYANOCOBALAMIN; DEXPANTHENOL; FOLIC ACID; NIACINAMIDE; PYRIDOXINE; RIBOFLAVIN; THIAMINE; TOCOPHEROL ACETATE; VITAMIN A; VITAMIN K
https://dailymed.nlm.nih.gov/dailymed/search.cfm?labeltype=all&query=INFUVITE+PEDIATRIC
https://dailymed.nlm.nih.gov/dailymed/search.cfm?labeltype=all&query=INFUVITE+PEDIATRIC
ASCORBIC ACID; BIOTIN; CYANOCOBALAMIN; DEXPANTHENOL; ERGOCALCIFEROL; FOLIC ACID; NIACINAMIDE; PHYTONADIONE; PYRIDOXINE HYDROCHLORIDE; RIBOFLAVIN 5'-PHOSPHATE SODIUM; THIAMINE HYDROCHLORIDE; VITAMIN A; VITAMIN E
https://dailymed.nlm.nih.gov/dailymed/search.cfm?labeltype=all&query=M.V.I.+PEDIATRIC
https://dailymed.nlm.nih.gov/dailymed/search.cfm?labeltype=all&query=M.V.I.+PEDIATRIC
ASCORBIC ACID; BIOTIN; CYANOCOBALAMIN; DEXPANTHENOL; ERGOCALCIFEROL; FOLIC ACID; NIACINAMIDE; PYRIDOXINE HYDROCHLORIDE; RIBOFLAVIN 5'-PHOSPHATE SODIUM; THIAMINE HYDROCHLORIDE; VITAMIN A; VITAMIN E; VITAMIN K
https://dailymed.nlm.nih.gov/dailymed/search.cfm?labeltype=all&query=M.V.I.+ADULT
https://dailymed.nlm.nih.gov/dailymed/search.cfm?labeltype=all&query=M.V.I.+ADULT

9. FDA/SPL Indexing Data /source/FDA/SPL Indexing Data

S5Z3U87QHF
https://www.fda.gov/ForIndustry/DataStandards/SubstanceRegistrationSystem-UniqueIngredientIdentifierUNII/
https://www.fda.gov/ForIndustry/DataStandards/SubstanceRegistrationSystem-UniqueIngredientIdentifierUNII/

10. HSDB /source/HSDB

PHYTONADIONE
https://toxnet.nlm.nih.gov/cgi-bin/sis/search/r?dbs+hsdb:@term+@rn+@rel+84-80-0
https://toxnet.nlm.nih.gov/cgi-bin/sis/search/r?dbs+hsdb:@term+@rn+@rel+84-80-0

11. FDA Orange Book /source/FDA Orange Book

ALPHA-TOCOPHEROL ACETATE; ASCORBIC ACID; BIOTIN; CHOLECALCIFEROL; CYANOCOBALAMIN; DEXPANTHENOL; FOLIC ACID; NIACINAMIDE; PYRIDOXINE HYDROCHLORIDE; RIBOFLAVIN 5'-PHOSPHATE SODIUM; THIAMINE HYDROCHLORIDE; VITAMIN A PALMITATE; VITAMIN K
https://www.fda.gov/Drugs/InformationOnDrugs/ucm129662.htm https://www.fda.gov/Drugs/InformationOnDrugs/ucm129662.htm

12. NIST /source/NIST

Phytonadione
http://www.nist.gov/srd/nist1a.cfm http://www.nist.gov/srd/nist1a.cfm

13. PubMed Health /source/PubMed Health

Mephyton
http://www.ncbi.nlm.nih.gov/pubmedhealth/PMHT0024016/ http://www.ncbi.nlm.nih.gov/pubmedhealth/PMHT0024016/
Phytonadione
http://www.ncbi.nlm.nih.gov/pubmedhealth/PMHT0001424/ http://www.ncbi.nlm.nih.gov/pubmedhealth/PMHT0001424/
Phytonadione (By mouth)
http://www.ncbi.nlm.nih.gov/pubmedhealth/PMHT0011730/ http://www.ncbi.nlm.nih.gov/pubmedhealth/PMHT0011730/
Phytonadione (By injection)
http://www.ncbi.nlm.nih.gov/pubmedhealth/PMHT0011731/ http://www.ncbi.nlm.nih.gov/pubmedhealth/PMHT0011731/

14. SpectraBase /source/SpectraBase

https://spectrabase.com/compound/EknsQkjx7Qf#Ama9zoNiU6O https://spectrabase.com/compound/EknsQkjx7Qf#Ama9zoNiU6O
https://spectrabase.com/compound/EknsQkjx7Qf#BjScQ5kbxWj https://spectrabase.com/compound/EknsQkjx7Qf#BjScQ5kbxWj

15. Springer Nature /source/Springer Nature

*vitamin k1*
*https://pubchem.ncbi.nlm.nih.gov/substance/341141027 https://pubchem.ncbi.nlm.nih.gov/substance/341141027*

16. WHO ATC /source/WHO ATC

*https://www.whocc.no/atc/ https://www.whocc.no/atc/*
*ATC Code*
*https://www.whocc.no/atc_ddd_index/ https://www.whocc.no/atc_ddd_index/*

17. Wikipedia /source/Wikipedia

*(E)-phytonadione*
*https://en.wikipedia.org/wiki/Phytomenadione https://en.wikipedia.org/wiki/Phytomenadione*

18. PubChem

*Data deposited in or computed by PubChem*
*https://pubchem.ncbi.nlm.nih.gov https://pubchem.ncbi.nlm.nih.gov*

19. MeSH /source/MeSH

*Vitamin K 1*
*https://www.ncbi.nlm.nih.gov/mesh/68010837 https://www.ncbi.nlm.nih.gov/mesh/68010837*
*MeSH Tree*
*http://www.nlm.nih.gov/mesh/meshhome.html http://www.nlm.nih.gov/mesh/meshhome.html*
*Vitamins*
*https://www.ncbi.nlm.nih.gov/mesh/68014815 https://www.ncbi.nlm.nih.gov/mesh/68014815*
*Antifibrinolytic Agents*
*https://www.ncbi.nlm.nih.gov/mesh/68000933 https://www.ncbi.nlm.nih.gov/mesh/68000933*

20. ChEBI /source/ChEBI

*ChEBI Ontology*
*http://www.ebi.ac.uk/chebi/userManualForward.do#ChEBI%20Ontology http://www.ebi.ac.uk/chebi/userManualForward.do#ChEBI%20Ontology*

21. LIPID MAPS /source/LIPID MAPS

*LIPID MAPS classification system for lipids*
*http://www.lipidmaps.org/data/classification/LM_classification_exp.php http://www.lipidmaps.org/data/classification/LM_classification_exp.php*

22. WIPO /source/WIPO

*International Patent Classification*
*http://www.wipo.int/classifications/ipc/ http://www.wipo.int/classifications/ipc/*

23. NCBI

*LinkOut is a service that allows one to link directly from NCBI databases to a wide range of information and services beyond NCBI systems.*
*https://www.ncbi.nlm.nih.gov/projects/linkout https://www.ncbi.nlm.nih.gov/projects/linkout*