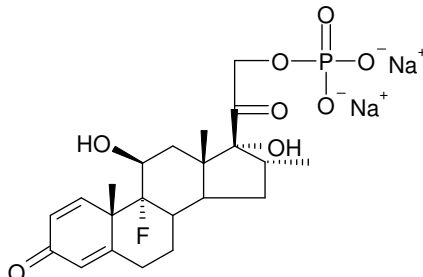


Dexamethasone Sodium Phosphate USP



$C_{22}H_{28}FNa_2O_8P$

MW 516.41

NOMENCLATURE

Pregna-1,4-diene-3,20-dione, 9-fluoro-11,17-dihydroxy-16-methyl-21-(phosphonoxy)-, disodium salt, (11 β ,16 α)-

9-Fluoro-11 β ,17,21-trihydroxy-16 α -methylpregna-1,4-diene-3,20-dione 21-(dihydrogen phosphate) disodium salt

9-Fluoro-11 β ,17-dihydroxy-16 α -methyl-3,20-dioxopregna-1,4-dien-21-yl disodium phosphate

CAS 2392-39-4

Glucocorticoid

Laboratory Code: PNU-33439E

USAN, BAN, JAN: Dexamethasone Sodium Phosphate

DESCRIPTION

Dexamethasone Sodium Phosphate from Pfizer is a white or slightly yellow crystalline powder. It is odorless or has a slight odor of alcohol, and is exceedingly hygroscopic. It is freely soluble in water; slightly soluble in alcohol; very slightly soluble in dioxane; insoluble in chloroform and in ether.

USP SPECIFICATIONS

	<u>Test</u>	<u>Specification</u>
Identification		
	A. Thin-layer Chromatography (as Dexamethasone)	Positive
	B. Residue on Ignition (as Sodium and Phosphate)	Positive
Specific Rotation (Water-free and Alcohol-free Basis)		+74° to +82° (water)
pH		7.5 to 10.5
Water (includes Alcohol)		Not More Than 16.0%

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USP SPECIFICATIONS (continued)

<u>Test</u>	<u>Specification</u>
Phosphate	Not More Than 1.0%
Free Dexamethasone	Not More Than 0.4%
Chromatographic Purity	
Any Individual Impurity	Not More Than 1.0%
Total Impurities	Not More Than 2.0%
Organic Volatile Impurities	Meets Test
Alcohol	Not More Than 8.0%
Assay (Water-free and Alcohol-free Basis)	97.0% to 102.0%

In addition to the US Registration Specifications, the following apply to Dexamethasone Sodium Phosphate from Pfizer labeled “EP”.

CHARACTERS

Dexamethasone Sodium Phosphate from Pfizer is a white or almost white powder. It is very hygroscopic. It is freely soluble in water; slightly soluble in alcohol; practically insoluble in ether and in methylene chloride.

Regarding the EP monograph statement that Dexamethasone Sodium Phosphate shows polymorphism, refer to the Pfizer “Polymorphism” statement.

EP SPECIFICATIONS

<u>Test</u>	<u>Specification</u>
Identification	
B. Infrared	Positive
C. Thin-Layer Chromatography	Positive
Appearance of Solution	Meets Test
pH	7.6 to 9.5
Specific Optical Rotation (Anhydrous)	+75° to +83° (water)
Related Substances	Meets Test
Any Individual Impurity	Not More Than 0.5%
Total Impurities	Not More Than 1.0%
Inorganic Phosphate	Meets Test (Not More Than 1.0%)
Ethanol	Not More Than 3.0%
Ethanol and Water	Not More Than 13.0%
Assay (Anhydrous, Ethanol-free)	97.0% to 103.0%

Regulatory Filings:

See Dexamethasone sodium phosphate under Regulatory

Organic Volatile Impurities

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Of the solvents targeted in USP 26 General Chapter <467>, only methylene chloride may appear in bulk pharmaceutical products manufactured by Pfizer at the Kalamazoo plant. For those products where OVI testing is required, our material will meet the compendial limits for methylene chloride and other solvents that may be added to the target list in the future.

Dexamethasone Sodium Phosphate from Pfizer meets the requirements of USP 26 General Chapter <467>.

ICH Residual Solvents

As of 01 July 2000, Pfizer's laboratories began to internally report all solvents that are present above the assay detection limit. During the review of the batch data, it is verified that no solvents are present above the ICH limits. Therefore, all lots of Dexamethasone Sodium Phosphate released after 01 July 2000 will meet the ICH residual solvent guidance, except for the solvent Ethanol.

<u>Solvent</u>	<u>Pfizer Specification</u>	<u>ICH Class and Specification</u>
Residual Solvents (Total) *	Not More Than 0.5% **	
Methanol	Not More Than 3000 ppm	2: Not More Than 3000 ppm
Methyl <i>t</i> -Butyl Ether	Not More Than 5000 ppm	3: Not More Than 0.5%
Methylene Chloride	Not More Than 500 ppm **	2: Not More Than 600 ppm

* Residual Solvents (Total) does not include Ethanol for Dexamethasone Sodium Phosphate.

** Pfizer does not have Registered Specifications for Residual Solvents (Total) and Methylene Chloride, only quality control Targets.

Other solvents used: tetrahydrofuran

ICH Residual Metals

Pfizer is currently developing a strategy to assess the detection and quantitation of ICH residual metals in Pfizer's active pharmaceutical ingredients. Currently, no residual metals are known to be present in Dexamethasone Sodium Phosphate from Pfizer.

Chemical and TSE Certificate of Suitability

Certificate No. R0-CEP 1998-154-Rev 00 was granted to Pfizer by the European Directorate for the Quality of Medicines on 25 June 2002 for five years, for the product Dexamethasone Sodium Phosphate. A copy of the certificate is available upon request.

Viral Safety Statement for Active Pharmaceutical Ingredients (APIs)

Dexamethasone Sodium Phosphate USP

Pfizer has reviewed the viral safety risks of its manufacturing practices for production of non-biological active pharmaceutical ingredients (APIs). The API Dexamethasone Sodium Phosphate presents no viral safety concerns. Pfizer APIs produced by bacterial or fungal fermentation and/or bioconversion processes are not considered to present viral safety risks. The raw materials used in the stages of production are sterilized prior to inoculation with a monoculture of the desired microorganisms. Only Pfizer's bioconversion reactions that employ purified enzymes (e.g. introduction of a double bond at the 1,2-position of the steroid ring system) use animal-derived materials that are not sterilized prior to introduction to the process. To support the safety of these enzymes, suppliers are required to provide documentation to Pfizer that these materials are in compliance with the CPMP and CVMP guidances on minimization of the risk of transmitting animal spongiform encephalopathy (TSE) agents via medicinal or veterinary products. Pfizer requires suppliers to provide similar certification for all TSE-risk animal-derived materials.

Based upon the nature of our manufacturing processes and the control of animal-derived materials used in the manufacture of APIs, Pfizer is in compliance with applicable regulatory requirements for viral safety.

Statement Regarding Genetically Modified Materials in the Production of Active Pharmaceutical Ingredients (APIs)

The organism(s) currently used in the fermentation/bioconversion of plant sterols to produce intermediates that are chemically transformed into Dexamethasone Sodium Phosphate are not genetically engineered. However, Pfizer does not make any commitment that would preclude using genetically modified (recombinant) strains at some future date.

There are a number of ingredients used in the fermentation/bioconversion process that are derived from plants that are major agricultural products in the United States. It is well known that the U.S. agriculture industry has a growing reliance upon genetically modified (recombinant) plants such as corn and soybeans. Although some grain handlers and processors have contacted farmers about needing to segregate genetically modified seeds from non-genetically modified seeds, this concept has only recently been introduced and lacks effective enforcement and monitoring components. Pfizer has not evaluated the sources of ingredients for fermentation/bioconversion-derived intermediates and APIs relative to ingredients having been derived in part from genetically engineered varieties of plants or other organisms.

Vegetable Origin of Raw Materials

Pfizer produces steroid active pharmaceutical ingredients (APIs) by what is best described as a semi-synthetic process using a crude mixture of vegetable sterols that are isolated from various oilseeds as the starting material. These vegetable sterols, stigmasterol and sitosterol, are processed through several fermentation and chemical steps to yield Dexamethasone Sodium Phosphate.

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Gluten

The raw materials used in the manufacture of Dexamethasone Sodium Phosphate are not derived from the gluten-containing grains wheat, rye, barley, or oats. Therefore, although Pfizer does not specifically assay for the presence of gluten, it is unlikely that any gluten proteins are present.

Polymorphism

Evaluation of infrared (IR) spectra indicates that Dexamethasone Sodium Phosphate from Pfizer has an amorphous physical form. An IR assay has been implemented to assure detection of any occurrence of undesired polymorphs.

Chirality

Dexamethasone Sodium Phosphate has eight chiral carbons: C8, C9, C10, C11, C13, C14, C16, and C17. Pfizer's manufacturing process can modify the chirality of four of them: C9, C11, C16, and C17.

Stereoisomer Content

Please note that none of the known impurities of Dexamethasone Sodium Phosphate are stereoisomers of Dexamethasone Sodium Phosphate. Therefore, the stereoisomer content is LT 0.1%.