Chemical Research and Development

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revision B date: December 4, 2012
origination date: July 29, 2004

MATERIAL SAFETY DATA SHEET

[CAUTION: The identity of this substance may be proprietary to Starks Associates, Inc. and to National Institute of Allergy and Infectious Diseases]

----------IDENTIFICATION----------

Chemical Name: 2,4,6,8-Tetraoxa-5-phosphanonanedioic acid, 5-[[(1R)-2-(6-amino-9H-purin-9-yl)-1-methylethoxy]-methyl]-, 1,9-bis(1-methylethyl) ester, 5-oxide, (2E)-2-butenedioate (1:1)

Other Name: Tenofovir disoproxil fumarate

Starks Reference No: NG41-110-2

Chemical Formula: $C_{19}H_{30}N_5O_{10}P \cdot C_4H_4O_4$

----------CAS REGISTRY NUMBER(S)----------

CAS #: 202138-50-9

----------HEALTH HAZARD DATA----------

This compound is an approved drug. See attached pages from FDA-approved drug product package insert for warning and side effects. This compound also has RTECS number SZ6563700. See attached RTECS file data.

----------PRIMARY ROUTE(S) OF ENTRY (Accidental Exposure)--------

No applicable information was found; prevent all accidental exposure to skin, eyes, or lungs.

----------PHYSICAL AND CHEMICAL CHARACTERISTICS----------

White solid; melting point 114-116°C (uncorrected); soluble in H_2O or methanol.

----------PHYSICAL HAZARDS----------

No applicable information was found; as with most organic powders, dust explosion may be possible when powder is suspended in air.

----------EXPOSURE LIMIT----------

No specifically applicable information was found; advisable to avoid exposure to skin, eyes or lungs.

----------NTP, IARC, OSHA----------

No entries were found. To the best of our knowledge, the potential carcinogenic properties of this material are not known.

----------PRECAUTIONS FOR SAFE HANDLING----------

This product should be handled only by, or under the close supervision of, those properly qualified in the handling and use of potentially hazardous chemicals. It should be borne in mind that the toxicological and physiological properties of many compounds are not yet well defined.

Appropriate Hygiene Practices

Avoid personal contact through ingestion, inhalation, contact with eyes or skin.

Protective Measures During Repair or Maintenance of Contaminated Equipment

No applicable information was found.

Steps to be taken if material is released or spilled

Wear self-contained breathing apparatus, rubber boots and heavy rubber gloves.

Sweep up, place in a bag and hold for waste disposal.

Avoid raising dust.
Ventilate area and wash spill site after material pickup is complete.

Waste disposal method

Dissolve or mix the material with a combustible solvent and burn in a chemical incinerator equipped with an afterburner and scrubber.

Observe all federal, state & local laws.

CONTROL MEASURES

Engineering Controls

Mechanical exhaust required.

Personal Protective Equipment

Safety glasses or chemical safety goggles. Impermeable gloves and lab coat. NIOSH/MSHA approved respirator may be advisable.

EMERGENCY AND FIRST AID PROCEDURES

In case of contact, immediately flush eyes with copious amounts of water for at least 15 minutes.

In case of contact, immediately wash skin with soap and copious amount of water.

If inhaled, remove to fresh air. If not breathing give artificial respiration. If breathing is difficult, give oxygen.

Call a physician.

Wash contaminated clothing before reuse or discard.

Information contained herein is based upon observations made in the course of isolating this substance and other information available to us. We have undertaken no tests to confirm the accuracy or completeness of this information and assume no responsibility in this regard.

What should I do if I miss a dose of VIREAD?

It is important that you do not miss any doses. If you miss a dose of VIREAD, take it as soon as possible and then take your next scheduled dose at its regular time. If it is almost time for your next dose, do not take the missed dose. Wait and take the next dose at the regular time. Do not double the next dose.

What happens if I take too much VIREAD?

If you suspect that you took more than the prescribed dose of VIREAD, contact your local poison control center or emergency room right away.

As with all medicines, VIREAD should be kept out of reach of children.

What should I avoid while taking VIREAD?

- Do not breast-feed. See "What should I tell my healthcare provider before taking VIREAD?"

What are the possible side effects of VIREAD?

- Clinical studies: The most common side effects of VIREAD are: diarrhea, nausea, vomiting, and flatulence (intestinal gas).
- Marketing experience: Other side effects reported since VIREAD has been marketed include: weakness, inflammation of the pancreas, low blood phosphate, dizziness, shortness of breath, and rash.
- Some patients treated with VIREAD have had kidney problems. If you have had kidney problems in the past or need to take another drug that can cause kidney problems, your healthcare provider may need to perform additional blood tests.
- Laboratory tests show changes in the bones of patients treated with VIREAD. It is not known whether long-term use of VIREAD will cause damage to your bones. If you have had bone problems in the past, your healthcare provider may need to perform additional tests or may suggest additional medication.
- Some patients taking antiviral drugs like VIREAD have developed a condition called lactic acidosis (a buildup in the blood of lactic acid, the same substance that causes your muscles to burn during heavy exercise). Symptoms of lactic acidosis include nausea, vomiting, unusual or unexpected stomach discomfort, and weakness. If you notice these symptoms or if your medical condition changes suddenly, call your healthcare provider right away.
- Changes in body fat have been seen in some patients taking anti-HIV medicine. These changes may include increased amount of fat in the upper back and neck ("buffalo hump"), breast, and around the main part of your body (trunk). Loss of fat from the legs, arms and face may also happen. The cause and long term health effects of these conditions are not known at this time.
- If you have hepatitis B virus (HBV) infection, you may have a "flare-up" of hepatitis B, in which the disease suddenly returns in a worse way than before if you stop taking VIREAD. VIREAD is not for the treatment of hepatitis B virus infection.
- There have been other side effects in patients taking VIREAD. However, these side effects may have been due to other medicines that patients were taking or to the illness itself. Some of these side effects can be serious.

VIREAD®

(tenofovir disoproxil fumarate) Tablets

℞ Only

WARNING

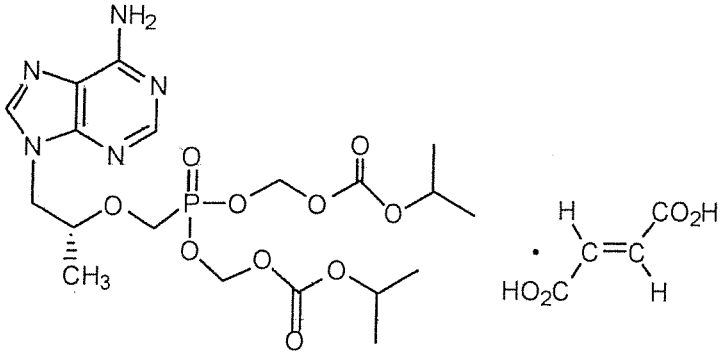
LACTIC ACIDOSIS AND SEVERE HEPATOMEGALY WITH STEATOSIS, INCLUDING FATAL CASES, HAVE BEEN REPORTED WITH THE USE OF NUCLEOSIDE ANALOGS ALONE OR IN COMBINATION WITH OTHER ANTIRETROVIRALS (SEE WARNINGS).

VIREAD IS NOT INDICATED FOR THE TREATMENT OF CHRONIC HEPATITIS B VIRUS (HBV) INFECTION AND THE SAFETY AND EFFICACY OF VIREAD HAVE NOT BEEN ESTABLISHED IN PATIENTS COINFECTED WITH HBV AND HIV. SEVERE ACUTE EXACERBATIONS OF HEPATITIS B HAVE BEEN REPORTED IN PATIENTS WHO ARE COINFECTED WITH HBV AND HIV AND HAVE DISCONTINUED VIREAD. HEPATIC FUNCTION SHOULD BE MONITORED CLOSELY WITH BOTH CLINICAL AND LABORATORY FOLLOW-UP FOR AT LEAST SEVERAL MONTHS IN PATIENTS WHO DISCONTINUE VIREAD AND ARE COINFECTED WITH HIV AND HBV. IF APPROPRIATE, INITIATION OF ANTI-HEPATITIS B THERAPY MAY BE WARRANTED (SEE WARNINGS).

DESCRIPTION

VIREAD® is the brand name for tenofovir disoproxil fumarate (a prodrug of tenofovir) which is a fumaric acid salt of bis-isopropoxycarbonyloxymethyl ester derivative of tenofovir. In vivo tenofovir disoproxil fumarate is converted to tenofovir, an acyclic nucleoside phosphonate (nucleotide) analog of adenosine 5'-monophosphate. Tenofovir exhibits activity against HIV-1 reverse transcriptase.

The chemical name of tenofovir disoproxil fumarate is 9-[(*R*)-2-[[bis[[(isopropoxycarbonyl)oxy]methoxy]phosphinyl]methoxy]propyl]adenine fumarate (1:1). It has a molecular formula of $C_{19}H_{30}N_5O_{10}P \bullet C_4H_4O_4$ and a molecular weight of 635.52. It has the following structural formula:



Tenofovir disoproxil fumarate is a white to off-white crystalline powder with a solubility of 13.4 mg/mL in distilled water at 25 °C. It has an octanol/phosphate buffer (pH 6.5) partition coefficient (log p) of 1.25 at 25 °C.

FILE 'RTECS' ENTERED AT 08:47:32 ON 04 DEC 2012

CHARGED TO COST=NG

Registry of Toxic Effects of Chemical Substances (RTECS). This National Institute of Occupational Safety and Health (NIOSH) file is a compendium of toxicity data extracted from the scientific literature. File Last Reloaded: OCTOBER 2012

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l1
L2 1 L1

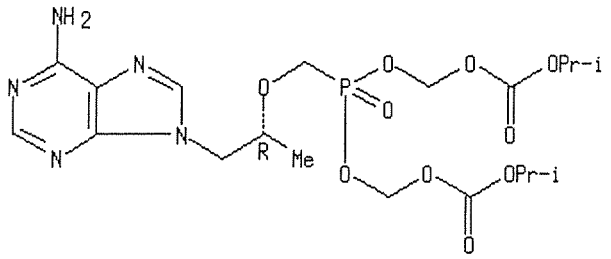
=> d l2 all

L2 ANSWER 1 of 1 RTECS
CAS Registry Number (RN): **202138-50-9** RTECS
RTECS Number (RTN): SZ6563700
Molecular Formula (MF): C19 H30 N5 O10 P . C4 H4 O4
Formula Weight (FW): 635.52
Chemical Name (CN): Phosphonic acid,

(((1R)-2-(6-amino-9H-purin-9-yl)-1-methylethoxy)methyl)-,bis(1-methylethoxycarbonyloxymethyl) ester, (2E)-2-butenedioate (1:1);
Tenofovir disoproxil fumarate; Viread
Entry/Update Date (DATE): Dec 2010
Character Count: 660

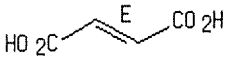
CM 1

Absolute stereochemistry.



CM 2

Double bond geometry as shown.



TOXICOLOGY REVIEW (TREV):
TOXICOLOGY REVIEW APHRER 37,849,2003
TOXICOLOGY REVIEW TPHSDY 23,381,2002
TOXICOLOGY REVIEW TXAPA9 243,167,2010

TOXICOLOGY REVIEW REFERENCES:
APHRER Annals of Pharmacotherpy (Harvey Whitney Books Co., POB 42696, Cincinnati, OH 45242) V. 26- 1992-

TPHSDY Trends in Pharmacological Sciences (Elsevier Science Pub. Co., Inc., 52 Vanderbilt Ave., New York, NY 10017) V.1- 1979-
TXAPA9 Toxicology and Applied Pharmacology (Academic Press, Inc., 1 E. First St., Duluth, MN 55802) V.1- 1959-