
Technical Information

January 2004
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Isotretinoin

® = Registered trademark of
BASF Aktiengesellschaft

crystalline
Product No. 018933

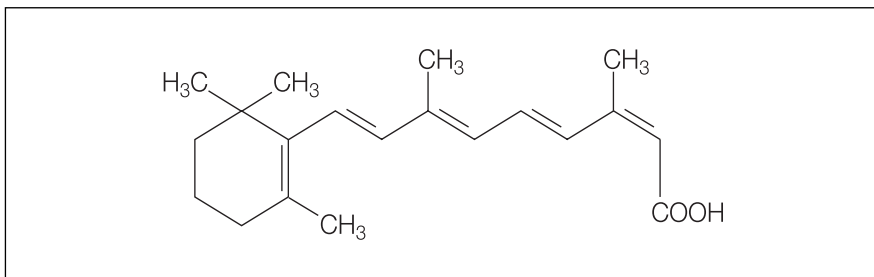
Ph. Eur./USP

Isotretinoin

Synonyms

13-Z-Retinoic acid, 13-cis-retinoic acid

Structural formula



Relative molecular mass 300.4 (C₂₀H₂₈O₂)

Description

Pure crystalline isotretinoin is a yellow-orange powder whose faint odour resembles that of vitamin A. It melts at around 175 °C.

Solubility

The crystalline product is soluble in chloroform and methylene chloride; it is sparingly soluble in ethanol, 2-propanol and polyethylene glycol (e. g. Lutrol® E 400) and very sparingly soluble in water. Its solubility in soy bean oil is less than 1 mg/100 ml.

Specifications

Assay	98.0 – 102.0%
Identification	conforms
Sulphated ash	≤ 0.1%
Heavy metals	≤ 10 ppm
Loss on drying	≤ 0.5% (USP/Ph. Eur.)
Tretinoin	≤ 1% (USP)
Tretinoin	≤ 2% (Ph. Eur.)
Related substances (as Isotretinoin)	≤ 0.5% (Ph. Eur.)

Single related substances:

4-oxo-Isotretinoin	}	each substance below 0.1% (BASF method M 99/0033/01e)
4-oxo Tretinoin		
5,8-Epoxy-Tretinoin		
5,8-Epoxy-Isotretinoin		
9 Z-Isotretinoin		

5,6-Epoxy-Tretinoin	}	in sum below 0.1%
5,6-Epoxy-Isotretinoin		

Residual solvents:

Dioxan	≤ 50 ppm	}	(BASF method 0443/03)
Acetone	≤ 100 ppm		
Ethanol	≤ 100 ppm		
Ethylacetate	≤ 100 ppm		
Methanol	≤ 100 ppm		
Heptane	≤ 2500 ppm		
Isopropanol	≤ 2500 ppm		

OVLs conform (USP/NF)

Unless otherwise stated, the analytical methods have been taken from the USP/Ph. Eur. monographs "Isotretinoin". The crystalline product meets the requirements of these monographs. In case of BASF methods, they are validated.

Drug Master File (DMFs) has been submitted to the Food and Drug Administration (FDA) of the United States of America for Isotretinoin (DMF-No. 4676).

A Drug Master File has also been submitted to the Canadian Health Protection Branch for Isotretinoin (DMF-No. 9669) for corresponding product registrations. A European DMF has been submitted, too.

Stability

The product is not stabilized. It is stable for 36 months if the original containers are unopened. In common with vitamin A and its esters, Isotretinoin has a limited stability, so that it must be processed in the absence of light and air.

Particle size distribution

D 0.1	not larger than 40 micron
D 0.5	75–150 micron
D 0.9	not larger than 450 micron

The applied technique is laser light diffraction method (Malvern Master Sizer) in an aqueous suspension.

Application

As an active ingredient in preparations for oral and topical use in dermatology, especially in acne therapy. Only peroxide-free auxiliaries should be used for processing. No adjuvant that tends to form peroxide can be considered. The addition of an antioxidant, e. g. butylhydroxytoluene is recommended.

Packaging

Aluminium cans with PE-inner bag of 10 g, 100 g, 500 g and 5 kg capacity. Larger containers on request.

The product is filled under argon.

Storage

Should be kept below 25 °C. Opened packages should be flushed with nitrogen, tightly closed again and used up as quickly as possible.

Important note

Sale of dangerous substances.

“It is unlawful to sell or offer for sale a dangerous substance without indicating in accordance with § 3 a Section 1 the danger relating to the substance”.

Isotretinoin is affected and is marked with number [13].

Isotretinoin [13] is described in the literature as teratogenic. Manufacturers of isotretinoin preparations must therefore inform the user and the physician that such preparations must not be taken during pregnancy. Consideration should be given to combining the product with a contraceptive.

In view of the high therapeutic efficacy, certain care must be exercised in processing. Contact with and inhalation of dusts must be avoided.

Product number

Isotretinoin, crystalline (13-cis-retinoic acid, crystalline):
18933/1/81

Note

The information submitted in this publication is based on our current knowledge and experience. In view of the many factors that may affect processing and application, these data do not relieve processors of the responsibility of carrying out their own tests and experiments; neither do they imply any legally binding assurance of certain properties or of suitability for a specific purpose. It is the responsibility of those to whom we supply our products to ensure that any proprietary rights and existing laws and legislation are observed.

