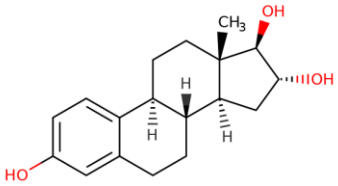
THE CONNECTING LINK TRANSO-PHARM

Revision No. 1.1 08/03/2021

Estriol

Synonym	Oestriol / Hormomed / Trihydroxyestrin / 3,16α,17β-Trihydroxy-1,3,5(10)-estratriene 16α-Hydroxyestradiol / 1,3,5(10)-Estratriene-3,16α,17β-triol
CAS. No.	50-27-1
Quality	EP
CMO / Manufacturer	Hapila GmbH, Otto-Schott-Straße 9, 07552 Gera, Germany
Pharmacological Group	Estrogen
Application	tocpical (cream / ointment), vaginal (suppositories, rings), oral



Manufacturing / Extraction	*Synthetic*	*Semi-Synthetic*	*Fermentation*	*Extractive*
	■	–	–	–

Project status	*Lab*	*Up-Scale*	*Validation*	*Commercial*
	–	–	–	–

Regulatory documentation	*CEP*	*EU-AP (Open Part)*	*US-TDP*	*J-DMF*	*Other*
	■	–	–	–	–

Technical product specification	*Samples*	*Batch size*	*Retest Period*	*Stability Data*	*Packaging*
	■	10-12 kg	3 years	■	1 kg / 5 kg

Lead Time	*Shipping & Storage Conditions*	*Other*
to be agreed	below 30°C	–

GMP status / Audit	• EU-GMP • US-FDA approved
Other information	• customized primary pack-size possible
Contact / Productmanager	Timo Krabiell krabiell@transopharm.de fon: +49 (0) 4107 8778 131

Estriol micro (CAS No.: 50-27-1)
Manufacturer: HAPILA GmbH, Gera

Frequently asked questions:

With our newsletter of 12/01/2022 we informed you about the production expansion at HAPILA to cover the additional demand for Estriol micro.

In the following we would like to answer frequently asked questions:

Will the manufacturer's address remain the same?

- Yes, the manufacturer's address will not change and the production site will remain the same:

  HAPILA GmbH
  Otto-Schott-Str. 9
  D-07552 Gera

Will the batch size change?

- No, the batch size will not change.

Will the manufacturing process change?

- No, no changes to the manufacturing process.

Regulatory changes?

- There are no regulatory changes intended.
  CEP No. R1-CEP 2013-277 (latest version in each case) will remain in effect.
  ASMF updates, ASMF based variations or submissions will be supported as usual.

What is the production capacity after the expansion?

- The production capacity will be in the range of 200 kg/year.

What will the production intervals be and how will delivery times change after the expansion?

- Estriol micro will be produced in campaigns on a mono line dedicated exclusively to Estriol.
  It is envisaged that there will be a steady build-up of stock from the campaigns, so that "just-in-time" deliveries will be possible for marketing authorization holders.

Price impact?

- A price increase is not foreseen due to the investment and transfer to the new facility. Fundamental influencing factors for price adjustments include rising energy and raw material prices, as well as costs for environmentally compatible disposal of special production waste. These main cost drivers must be evaluated regularly, but also independently of the place of production.

Estriol micro (CAS No.: 50-27-1)
Manufacturer: HAPILA GmbH, Gera, Germany

When will the new plant be put into operation?

- IQ/OQ is planned for the 2nd half of the year and we currently assume PQ at the end of 2022. We will continue to provide information on this separately via newsletters and communicate updates accordingly. Please follow our updates.

When can we expect first quantities after the production expansion?

- We expect additional volumes to be available at the end of quarter I or beginning of quarter II 2023. We will continue to inform you separately via newsletters and provide updates accordingly. Please follow our updates.

Is there a shared audit for the new production facility and who can we contact?

- In order to meet all audit requests, we propose a shared audit program in which as many customers as possible should participate.
  Contact details and date will be shared with you accordingly in due time.

When can an audit take place?

- After successful production of the first batches. Dates will be coordinated. Preference is given to participation in the "Shared Audit" program

GMP certificate?

- The TLV authority responsible for the site is involved in the project and will carry out an acceptance inspection.

When and how will we know about the commissioning?

- We will keep you informed at regular intervals about the progress of construction including commissioning.

Who can I contact if I have any questions?

Transo-Pharm Handels-GmbH

Contact: Timo Krabiell (Product Development)
E-Mail: krabiell@transopharm.de