

Trientine (triethylenetetramine) formulations available in the UK

(November 2020)

BASL Wilson's Disease Special Interest Group *Zoom* Meeting

Friday, 20th November 2020

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Trientine formulations available in the UK

(as of November 2020)

- **Cufence™** – Trientine dihydrochloride

Univar Solutions B.V. (Rotterdam, The Netherlands)



- **Cuprior™** – Trientine tetrahydrochloride

Orphalan UK (formerly GMP Orphan) (St Albans, UK and Paris, France)



- **Trientine dihydrochloride Tillomed**

Tillomed Laboratories Ltd (Luton, UK) owned by Emcure (India)

[Data from electronic medicines compendium (emc) <https://www.medicines.org.uk/emc/about-the-emc> Other suppliers in USA (<https://www.drugs.com/availability/generic-syprine.html>) and in Europe (<https://ideogen.ch/morbus-wilson-1>)]

UK trientine formulations – SmPC information

- ❑ Cufence 200 mg hard capsules trientine *[as identified in patient leaflet]*

Each size 0 hard capsule contains 300 mg trientine dihydrochloride

– equivalent to 200 mg trientine (free base)

- ❑ Cuprior 150 mg film-coated tablets trientine *[as identified in patient leaflet]*

Each film-coated tablet contains 300 mg trientine tetrahydrochloride

– equivalent to 150 mg trientine (free base)

- ❑ Trientine dihydrochloride Tillomed 250 mg hard capsules trientine dihydrochloride *[as identified in patient leaflet]*

Each hard capsule contains 250 mg trientine dihydrochloride

– equivalent to 167 mg trientine (free base)

Comparison of UK trientine formulations^a

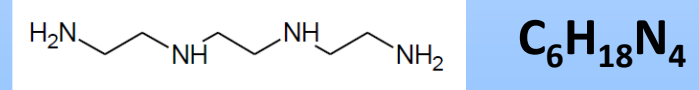
- Size and description of formulation^a
- Dosage form and packaging^a
- Storage conditions^a
- Bioequivalence and dose equivalence data for Cufence and Cuprior^{a,b}
- Licensed dose^a

a. See notes circulated for this meeting for more details of UK trientine formulations.

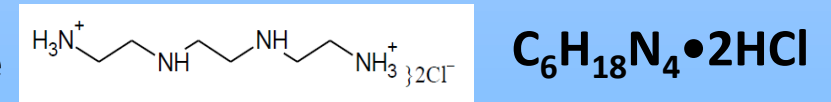
b. Lacking peer-reviewed data in the scientific literature.

Trientine dose equivalents – calculations

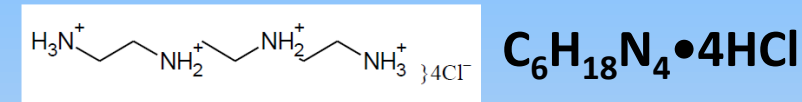
Trientine (free base) – molar mass: **146.2** grams/mole



Trientine dihydrochloride – molar mass: **219.2** grams/mole



Trientine tetrahydrochloride – molar mass: **292.1** grams/mole



i.e. **219.2** g trientine•2HCl \equiv **146.2** g trientine free base \equiv **292.1** g trientine•4HCl

\therefore **ONE** 300 mg trientine•2HCl capsule \equiv 200 mg trientine free base

\therefore **ONE** 300 mg trientine•4HCl tablet \equiv 150 mg trientine free base

Cost of Cuprior in the UK*

- ❑ Reported cost for a one year supply of Cuprior per patient = £40,000
- ❑ For a patient on 4 x 150 mg Cuprior tablets daily, one year's supply = **219 g** trientine base
- ❑ Technical grade (70%) trientine base = £4.2/1000 g*, i.e. **219 g** = £0.92
- ❑ Percentage markup = [(sales price – unit cost) / unit cost] x 100%
- ❑ i.e. [(£40,000 – £0.92) / £0.92] x 100 = 4.4 x 10⁶ per cent; **4.4 million per cent markup**

* Data from Alibaba website, November 2020

https://www.alibaba.com/product-detail/Hot-Sale-Industry-Grade-Triethylenetetramine-With_62300282876.html?spm=a2700.7724857.normalList.48.42831fcbePOtpO

* Similar arithmetic would apply to Cufence.

Comments on Tillomed's trientine dihydrochloride

- ❑ API is manufactured by Emcure, Pune, India.
- ❑ Probably a different manufacturing route than that used for Cufence and Cuprior (patent data).
- ❑ Questionable claim for stability in Tillomed's Summary of Product Characteristics:
“This medicinal product does not require any special temperature storage conditions.”
- ❑ FDA has issued a number of Warning Letters after inspections of Emcure's Pune manufacturing facilities.