

RISK PROFILE

Tioxolone

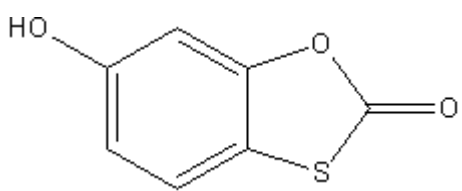
CAS No. 4991-65-5

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1. Identification of substance

Chemical name (IUPAC):	6-Hydroxy-1,3-benzoxathiol-2-one
INCI	Tioxolone
Synonyms	Thioxolone; 6-hydroxy-1,3-benzoxathiol-2-one; 6-hydro-2-oxo-1,3-benzoxathiole; Juvacneine; Tixelone; Acnosan®; Aflosan®
CAS No.	4991-65-5
EINECS No.	225-653-0
Molecular formula	C ₇ H ₄ O ₃ S
Chemical structure	
Molecular weight	168,17
Contents (if relevant)	
Physiochemical properties	Powder, light yellow to beige. Melting point 158-160 °C, boiling point 377,8 °C at 760 mmHg (Chemical Book, Sigma-Aldrich, Guidechem)

2. Uses and origin

Uses	<p>Cosmetic products:</p> <p>Tioxolone is classified as an <i>astringent</i> according to the CosIng database.</p> <p>Codecheck lists a cosmetic product containing tioxolone,</p> <p>No specific products containing tioxolone were found in EWG's Skin Deep database. However, tioxolone as a substance is mentioned in this database. The information is sparse, only indicating that there are data gaps and that the substance has not been assessed for use in cosmetic products.</p> <p>An internet search reveals some shampoos which contain tioxolone. These products are sold as having anti-seborrheic properties. No information indicating concentration of tioxolone in these products has been found.</p> <p>Tioxolone has astringent and keratolytic properties. It has been used topically for many years, in the treatment of various skin and scalp disorders. It is an agent against impure skin. Concentrations of 0.2-0.5% and 1% have been used in anti-acne and rinse-off products respectively. The substance has also been used for seborrheic dermatitis. The maximum suggested concentration of use is 5% (Council of Europe 2008, Martindale).</p> <p>Medicinal products:</p> <p>The ATC code for tioxolone is D10A B03 (“anti-acne preparations for topical use, containing sulphur”). Medicinal products containing tioxolone have earlier been on the market in some countries in Europe (Council of Europe 2008).</p> <p>Currently it seems only to be available in a anti-acne preparation; <i>Stepin® Cosmetique Tinktur</i> (Galderma, Germany).</p> <p>Food: No data available.</p> <p>Other: No data available.</p>
Origin Natural (exo /endo) Synthetic	Tioxolone is a synthetic heterocyclic compound.

3. Regulation

Norway	No current restrictions to tioxolone in Norway. ¹
EU	The substance is not listed in any EU Regulation Annexes.
Rest of the world	Internet searches have not revealed any information about specific

¹ The Norwegian medicinal products agency considered tioxolone a medicinal remedy. Because of that up till 2008 topical products containing the substance were considered a medicines product – meaning a topical product containing it were automatically classified a medicine. This regime has since been lifted.

	regulations for the use of tioxolone in the rest of the world.
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4. Relevant toxicity studies

Absorption Skin GI tractus	No data available
Distribution	No data available
Metabolism	No data available
Excretion	No data available
Local toxic effects Irritation Sensitivity	<p>A previous available medicinal product containing tioxolone was contra-indicated in acute dermatitis and acute seborrheic eczema. It was also recommended to avoid contact with eyes and mucous membranes. This may indicate that the compound has toxic properties which make it unsuitable as an ingredient in cosmetic products (Council of Europe 2008).</p> <p>Tioxolone may cause inflammation of the skin and mucous membranes, and is irritating to the eyes (Council of Europe 2008, Sigma-Aldrich, Guidechem).</p> <p>A patch test with a 7% solution gave no effect after 30 minutes, but 40% positive response observed at 48 hours. Some cases of contact dermatitis and a few contact allergies have been reported, indicating that tioxolone is a weak sensitizer. However, it could cause a severe contact dermatitis (Council of Europe 2008).</p>
Systemic toxic effects Acute Repeated dose Mutagenicity /genotoxicity Carcinogenicity Reprotoxicity / teratogenicity Other effects	<p>The hazard codes used for tioxolone are "harmful" (X_n) and "irritant" (X_i), and these symbols are used interchangeably (Sigma-Aldrich, Guidechem, Chemical Book).</p> <p>The Environmental Working Group (EWG) has given the substance a score 0 (low hazard, lowest possible score), but at the same time stating that there is a data gap for tioxolone.</p> <p>The LD₅₀ by oral administration is 6200-17800 mg/kg bw in rats. The dermal LD₅₀ in rabbits is >20000 mg/kg bw (Council of Europe 2008).</p> <p>Negative results on mutagenicity/genotoxicity tests were obtained (Council of Europe 2008).</p> <p>No data available on carcinogenicity.</p> <p>No data available on neither reprotoxicity nor teratogenicity.</p> <p>During use of tioxolone as a cosmetic ingredient, no toxic effects have been observed on humans, provided it is used as instructed.</p>

5. Exposure estimate and critical NOAEL / NOEL

NOAEL/NOEL critical	Not possible to estimate a NOEL/NOAEL on the currently existing data.
Exposure cosmetic	Rough estimates of the systemic exposure dose (SED) for leave-on

products	<p>face and rinse-off hair products are given below:</p> <p>For leave-on face products the surface area is estimated to 565 cm² (face surface area) Amount of product per cm²: 1 mg (SCCS guidelines 2011, assumed leave-on, not rinse-off) Number of applications per day: 2 Concentration of tioxolone in products: 1 % (worst case) Skin penetration rate: assumed 100 % (worst case) as no data are available (SCCS guidelines) Body weight: 60 kg (SCCS guidelines)</p> <p>SED face product: $565 \times 1 \times 0.01 \times 1/60 = 0.09 \text{ mg/kg bw/day}$</p> <p>For rinse-off hair products (shampoos) the calculated daily exposure is 1.51 mg/kg bw/day (SCCS guidelines 2011) Skin penetration rate: assumed 100 % (worst case) as no data are available (SCCS guidelines) Concentration of tioxolone in products: 1 % (worst case)</p> <p>SED shampoo: $1.51 \text{ mg/kg bw/day} \times 1 \times 0.01 = 0.015 \text{ mg/kg bw/day}$</p>
Margin of Safety (MoS)	Not calculated.

6. Other sources of exposure than cosmetic products

Food stuffs	No data available.
Pharmaceuticals	Anti-acne preparations have previously been available; e.g. Stepin® in Germany and Camyna® in Sweden (Martindale).
Other sources	No data available.
Adverse side effects - from uses other than cosmetics	Tioxolone in medicinal products has been reported to cause skin irritation and sensitisation (Council of Europe 2008).

7. Assessment

Tioxolone has been in use for many years, previously as an active substance in medicinal products and now in cosmetics. However, the use in cosmetic products seems to be low according to available sources. The only cosmetic product available is a solution for application on impure and fatty skin.

During this time, apparently no toxic or serious adverse effects have been identified. This can indicate that use of the substance in low (up to 1%) concentrations is acceptable. But despite long term use, the data available for tioxolone is limited.

The contra-indication labelling (acute dermatitis and acute seborrheic eczema) for a former medicinal product can possibly indicate toxic effects of tioxolone.

The currently available data do not indicate any major concerns with the use of tioxolone in cosmetic products, provided the concentration levels are not exceeded.

However, there is a lack of data on the safety of tioxolone used in cosmetic products. The Norwegian Food Safety Authority therefore supports the evaluation made by the Council of Europe; it is not possible to reach a conclusion about the safety of tioxolone used in cosmetic products, based on the currently available documentation.

8. Conclusion

The lack of data on possible toxic effects of tioxolone should warrant a restrictive use of this substance in cosmetic products, to protect the consumers. A regulation reflecting this is needed, until further data possibly can document a low hazard risk for tioxolone.

We suggest prohibiting tioxolone in cosmetic products, until further data documenting its safety are available.

9. References

Council of Europe's Committee of Experts on Cosmetic Products. Tioxolone, monograph no. 40. Active ingredients used in cosmetics: safety survey, Council of Europe Publishing. 2008; 381-383.

Online:

Chemical Book: Tioxolone; http://www.chemicalbook.com/ProductIndex_EN.aspx (accessed 8th Aug 2011).

Codecheck © 2011: Tioxolone; <http://www.codecheck.info> (accessed 13th Feb 2012).

CosIng database: EU, DG Sanco, Consumers: Tioxolone; <http://ec.europa.eu/consumers/cosmetics/cosing/> (accessed 2nd Aug 2011).

Environmental Working Group; Tioxolone: <http://www.ewg.org/> (accessed 9th Aug 2011).

European chemical Substances Information System (ESIS): Tioxolone; <http://esis.jrc.ec.europa.eu/> (accessed 1st Jul 2011).

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Martindale: The Complete Drug Reference, Lexicomp online: Tioxolone, 12th Mar 2011; <http://www.helsebiblioteket.no/> (accessed 27th Jun 2011)

Scientific Committee on Consumer Safety (SCCS), EU DG Health & Consumers; SCCS/1416/11: 7th Rev. 2010: http://ec.europa.eu/health/scientific_committees/consumer_safety/docs/sccs_s_004.pdf (accessed 16th Feb 2012).

Sigma-Aldrich Co: Tioxolone (6-Hydroxy-1,3-benzoxathiol-2-one); <http://www.sigmaaldrich.com> (accessed 13th Feb 2012).

US National Library of Medicine, Toxnet: Tioxolone; <http://toxnet.nlm.nih.gov/> (accessed 27th Jun 2011).

10. Annexes

Council of Europe's Committee of Experts on Cosmetic Products. Tioxolone, monograph no. 40. Active ingredients used in cosmetics: safety survey, Council of Europe Publishing. 2008; 381-383.