WORLD ANTI-DOPING AGENCY
play true

WADA Technical Letter – TL16

Document Number:	TL16 (replaces TL2018/05)	Version Number:	2.0
Written by:	*WADA* LabEG	Approved by:	*WADA* LabEG*
Date:	20 December 2018	Effective Date:	20 December 2018

**The approval by the WADA Executive Committee is applicable only to Technical Letters issued after November 2019.*

TRETOQUINOL

The *World Anti-Doping Agency* wishes to draw the attention of the Laboratories to the following issue that may affect Laboratory operations. This pertains, in particular, to the detection and reporting of **Tretoquinol** [Trimetoquinol; 1-(3',4',5'-trimethoxybenzyl)-6,7-dihydroxy-1,2,3,4-tetrahydroisoquinoline] in urine *Samples*.

Tretoquinol is a non-selective beta-2 agonist, which has been explicitly listed as an example of prohibited beta-2 agonists under class S3 of the 2019 *Prohibited List*. Tretoquinol is used therapeutically for the treatment of asthma (sold as Inolin® in some Asian countries) and is also used as an ingredient of over-the-counter (OTC) cold and flu medications.

Studies on Tretoquinol metabolism[1, 2] have shown that it is excreted in urine either as free form (minor) or phase-II conjugates (glucuronide and sulfate); in addition, Tretoquinol is metabolized by catechol-O-methyl transferase (COMT) into 6- and 7-methoxytetroquinol, which are also excreted in urine either unchanged or after phase-II conjugation (Figure 1). However, not much has been published about the kinetics of urinary excretion of Tretoquinol or its *Metabolites* and, therefore, there has been no information available about the expected urinary concentrations after administration.

A recent study performed by the Tokyo *WADA*-accredited Laboratory, in which volunteers were administered 6 mg of oral Tretoquinol hydrochloride hydrate (as per manufacturer's recommendations) has helped shed light on the excretion kinetics and provides the basis for this initial recommendation for a conservative reporting limit for Tretoquinol (free plus glucuronide conjugate) as outlined below. These recommendations are provided to avoid the reporting of an *Adverse Analytical Finding* for Tretoquinol, which may have resulted from the inadvertent use of Tretoquinol-containing OTC medications before the coming into effect of the 2019 *Prohibited List* (1 January 2019).

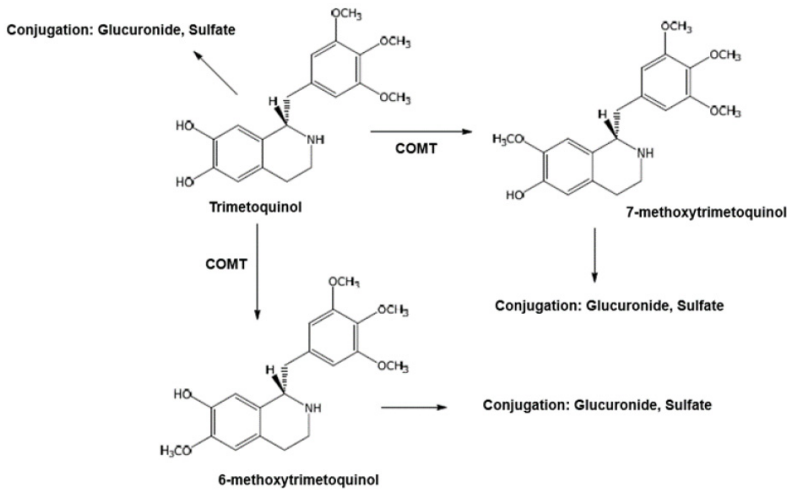

Figure 1. Metabolic pathway of Tretoquinol (Trimetoquinol).

WORLD ANTI-DOPING AGENCY
play true

WADA Technical Letter – TL16

Document Number:	TL16 (replaces TL2018/05)	Version Number:	2.0
Written by:	*WADA* LabEG	Approved by:	*WADA* LabEG*
Date:	20 December 2018	Effective Date:	20 December 2018

**The approval by the WADA Executive Committee is applicable only to Technical Letters issued after November 2019.*

WADA recommends the following in regard to the analysis and reporting of Tretoquinol findings, starting in 2019:

- Laboratories shall target the analysis of the Tretoquinol **parent compound** and its **glucuronoconjugated *Metabolite*** only, following urine enzymatic hydrolysis with β-glucuronidase (from *E. Coli*);
- Report findings for Tretoquinol as *Adverse Analytical Findings* in *ADAMS* only when the following conditions are met:
  - The *Sample* has been collected after 15 January 2019;
  - The total estimated concentration of Tretoquinol (free + glucuronidated conjugate) is higher than 20 ng/mL.

In order to assess the prevalence of Tretoquinol use, Laboratories are also requested to record all samples, which contain Tretoquinol at levels below the recommended 20 ng/mL reporting limit, and report such findings to *WADA*, upon request, at the beginning of 2020.

Should you have any further questions, please do not hesitate to contact the *WADA* Science Department.