CHALLENGING MEDICAL ISSUES
Asthma

WADA TUE SYMPOSIUM 2014

Dr Audrey Kinahan, List Expert Group
The List Expert Group

- Scientific and Medical Experts (13)
- Draft List
- Criteria for inclusion
- Stakeholders comments
- List → HMR Committee → Executive Committee → Final approval
All beta-2 agonists, including all optical isomers, e.g. \( d \)- and \( l \)- where relevant, are prohibited.

Except:

- Inhaled \textbf{salbutamol} (maximum 1600 micrograms over 24 hours);
- Inhaled \textbf{formoterol} (maximum \textit{delivered} dose 54 micrograms over 24 hours); and
- Inhaled \textbf{salmeterol} in accordance with the manufacturers’ recommended therapeutic regimen.
“The presence in urine of salbutamol in excess of 1000 ng/mL or formoterol in excess of 40 ng/mL is presumed not to be an intended therapeutic use of the substance and will be considered as an Adverse Analytical Finding unless the Athlete proves, through a controlled pharmacokinetic study, that the abnormal result was the consequence of the use of the therapeutic inhaled dose up to the maximum indicated above.”
INHALED BETA-2-AGONISTS ON THE PROHIBITED LIST?

**Salbutamol**

**THRESHOLD APPROACH**

**Permitted**
- Inhaled doses \( \leq 1600 \text{ mcg/24 hours} \)
- \(< 1000 \text{ ng/mL in urine} \)

**Prohibited**
- Oral, IV,
- Inhaled doses \( >1600 \text{ mcg/24 hours} \)
- \( >1000 \text{ ng/mL in urine} \) → PK study
Urinary concentrations: Inhaled & Oral Salbutamol

Inhaled salbutamol 0.8 mg

Oral salbutamol 8 mg

Urine Concentrations of Repetitive Doses of Inhaled Salbutamol, J Elers et al,
**Formoterol**

**CORRELATION BETWEEN INHALED DOSE AND URINE CONCENTRATION**

**Permitted**
- Inhaled delivered dose ≤ 54 mcg/24 hours
- < 40 ng/mL in urine

**Prohibited**
- Inhaled delivered dose > 54 mcg/24 hours
- > 40 ng/mL in urine

→ PK study

2012 List: Threshold 36 mcg/24 hours, correlated with urinary threshold of 30 ng/ml
Permitted  Usual inhaled dose of 50 mcg *bd*,
Severe cases –
Max dose 100 mcg *bd*

Prohibited  Doses in excess of 100 mcg bd

*Manufacturer’s recommended therapeutic dose may change from country to country
Urinary concentrations: Inhaled Salmeterol 100 mcg

Highest observed individual urine concentration of salmeterol was 0.74 ng/mL when not corrected for USG

Serum concentrations: Inhaled & Oral Terbutaline

**Inhaled repeat doses**
Terbutaline 1 mg every 2 hours, total 4 mg

**Oral Terbutaline 10 mg**

All other Beta-2-agonists

PROHIBITED

- Fenoterol
- Reproterol
- Procaterol

Ultra-Long Acting Beta-2-Agonists

- Indacaterol (Onbrez® & Ultibro®)
- Vilanterol (Relvar® & Anoro®)
- Olodaterol (Striverdi®)