



### K2 New $\beta$ 2-Agonists in Sports Doping

Anil Aggrawal, MD\*, Maulana Azad Medical College, New Delhi 110002, INDIA

**Learning Overview:** After attending this presentation, attendees will gain insight into new  $\beta$ 2-agonists that are being used in sports doping. Attendees will also learn about the investigational aspects of these new doping agents.

**Impact on the Forensic Science Community:** This presentation will impact the forensic science community by stimulating further inquiry and research into the investigational aspects of new  $\beta$ 2-agonists being used in sports.

$\beta$ 2-Agonists are derivatives of phenyl- $\beta$ -ethanol amines with different substituents on the aromatic ring and on the terminal amino group. The exact positions of different substituents further characterize  $\beta$ 2-agonists as catecholamines, resorcinols, or saligenins.

The  $\beta$ 2-agonists exist as two drug classes: the Short-Acting  $\beta$ 2-Agonists (SABA) (first generation, e.g., salbutamol, terbutaline, fenoterol, isoproterenol), and the Long-Acting  $\beta$ 2-Agonists (LABA) (second generation, e.g., salmeterol, formoterol). Recently, the term “Ultra-LABA” has been used to describe the third-generation products of this drug class. In addition to novel Ultra-LABAs, Long-acting Antimuscarinic Agents (LAMAs), phosphodiesterase inhibitors, and Inhaled Corticosteroids (ICSs) are utilized in combination therapy. Using drugs in combination may lower doses of individual agents, decrease adverse effects, simplify medication regimens, and improve compliance.

The most prominent representatives of  $\beta$ 2-agonists are clenbuterol and salbutamol. They are used primarily for the treatment of asthma and related bronchial spasms. Because about 10%–15% of Olympic athletes exhibit asthma syndromes, the use of  $\beta$ 2-agonists is relatively high among them.  $\beta$ 2-agonists exhibit muscle anabolic and lipolytic properties not as their intended effects, but as side effects. Because of relatively low adverse effects of the  $\beta$ 2-agonists, they are considered by some athletes as a “safe” alternative to anabolic androgenic steroids.

Interestingly, although demonstrable in animal experiments, there is little evidence that  $\beta$ 2-agonists can really improve performance in trained athletes. Despite this, in recent years several new  $\beta$ 2-agonist molecules have emerged. Some of these are AZD-3199, AZD-9708, carmoterol, indacaterol, LAS-100977, milveterol, olodaterol, PF-610355, trantinterol, and vilanterol.

In some countries,  $\beta$ 2-agonists are even used to increase the muscle mass of animals, so they can yield more meat. Thus, athletes visiting these countries either for training or simply for tourism may inadvertently consume meat derived from such animals. This may cause them to test positive for  $\beta$ 2-agonists. The German national anti-doping agency has even published a clenbuterol (the most controversial  $\beta$ 2-agonist) warning for athletes traveling to Mexico or China recommending particular vigilance with food.

This presentation discusses the use of  $\beta$ 2-agonists in sports doping, in particular, the new molecules as mentioned above, as well as their use in cattle fattening.

#### Doping, Sports, Toxicology