Statement on Concerta and Methylphenidate for the June 30 PAC

The FDA has identified two possible safety concerns with the methylphenidate drug products: psychiatric adverse events and cardiovascular adverse events.

Psychiatric Adverse Events

Post-marketing reports received by FDA regarding Concerta and other methylphenidate products include psychiatric events such as visual hallucinations, suicidal ideation, psychotic behavior, as well as aggression or violent behavior.

We intend to make labeling changes describing these events. In addition, we believe it is critical to examine the other stimulant drug products approved for ADHD, specifically the amphetamine products, and atomoxetine (not a stimulant), to determine if they too are associated with these adverse events. We are currently examining the post-marketing reports for these products. We will bring to this committee a review of the amphetamine adverse events and, we hope, events associated with atomoxetine, in early 2006. Given that both methylphenidates and amphetamines are stimulants used in the treatment of ADHD, it is important we evaluate both stimulant classes in order to avoid potential switching from one class to the other based on incomplete safety assessments.

We are seeking your comments on this approach.
Is there any information that we should provide the public while we are examining the post-marketing reports for the other stimulant products?

Cardiovascular Adverse Events:

In August 2004, the FDA reviewed post-marketing cardiovascular adverse events for all stimulant medications and relabeled Adderall XR to carry a warning about sudden cardiovascular deaths, especially in children with underlying heart disease. At this Pediatric Advisory Committee meeting, the FDA has presented post-marketing reports of adverse cardiovascular (CV) events with the use of Concerta. Examples of these CV events include reports of hypertension, syncope, chest pain, prolonged QTc, arrhythmias, and tachycardia. The agency believes that it is not yet possible to determine whether these events, especially the more serious ones, are causally associated with these treatments. The FDA is pursuing additional means to better characterize the cardiovascular risks for all drug products approved for ADHD. Potential options under consideration include population-based pharmaco-epidemiologic studies, long term safety trials and other targeted CV risk studies.

It is our proposal that the FDA obtain these additional data to help guide the development of any regulatory action regarding potential CV risks of drug products approved for ADHD.

We are seeking your comments on this approach.
Is there any information that should be shared with the public while these studies are being conducted?