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Reassured by adult safety study, FDA approves sildenafil for children

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The Food and Drug Administration (FDA) has approved Revatio (sildenafil) for the treatment of pulmonary arterial hypertension (PAH) in pediatric patients ages 1-17 years. It is indicated to improve exercise ability and pulmonary hemodynamics thought to underly improvements in exercise in patients too young to perform standard exercise testing.

The approval comes after the FDA considered additional data that have accrued since its prior decision not to approve Revatio in pediatric patients due to concern for increased mortality risk.

PAH is a rare, serious and progressive disease characterized by increased pulmonary vascular resistance, increased pulmonary artery pressure and right ventricular dysfunction, which lead to right heart failure, morbidity and mortality. PAH can be idiopathic or associated with specific etiologies, including congenital heart disease and developmental lung diseases.

Pediatric clinical trials to assess treatments for PAH have been limited, so the disease remains an area of unmet medical need. Prior to the FDA's approval of Revatio, bosentan was the only drug approved for pediatric patients ages 3-18 years.

The FDA previously approved Revatio for adults with PAH to improve exercise ability and delay clinical worsening. Subsequent studies in pediatric patients with PAH demonstrated efficacy, but results from a long-term safety study led to concerns for increasing mortality with increasing doses.

To evaluate the dose-related risk for mortality, the FDA required the manufacturer to conduct a post-market clinical trial in adults with PAH. The findings from this well-designed study in young adults refuted the earlier observation of increased mortality by dose in pediatric studies. Instead, it demonstrated a decline in mortality at high doses.

The FDA concluded that a causal association for the previously observed dose-related effect on mortality risk in pediatric patients is unlikely, given the clinical and survival benefits observed in adults with increasing doses of Revatio and the expected similarity of disease in pediatric and adult patients with PAH.

The FDA previously evaluated the safety and effectiveness of Revatio in pediatric patients based on a randomized, placebo-controlled, dose-ranging trial and a long-term extension study.

The randomized trial demonstrated that patients receiving Revatio had slightly higher mean increases from baseline in peak volume of oxygen consumed, as assessed by cardiopulmonary exercise testing in pediatric patients 7 years and older, and dose-related improvements in pulmonary vascular resistance index and mean pulmonary arterial pressure compared to patients receiving placebo.

The FDA's Office of Pediatric Therapeutics and Office of New Drug's Division of Pediatrics and Maternal Health and Division of Cardiology and Nephrology contributed to this article.

Resources

- Revatio (sildenafil) labeling
- FDA clinical review of Revatio