Revatio (sildenafil) is FDA approved for adults with group 1 PAH (pulmonary arterial hypertension). Further, sildenafil is approved in Europe by the European Medicines Agency for use in adults and children with PAH. On August 30th 2012, the FDA placed a safety warning on prescription of sildenafil in pediatric PAH patients (http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm317743.htm). The ruling, now part of the package insert for Revatio, states that Revatio should not be started in patients 1-17 years of age.

This decision is based on results of the sildenafil monotherapy STARTS trials. In the STARTS-2 study, the blinded dose extension study of the 16 week double-blind placebo controlled STARTS-1 study, patients randomized to high dose sildenafil in the 16 week STARTS-1 study, had an overall increased mortality at 3-years compared to the lower dose groups (Eur Heart J (2012) 33 (suppl 1): 979).

The study included several groups of PAH patients including those with idiopathic and heritable PAH and PAH associated with congenital heart disease (CHD). Risk factors for death included patients with idiopathic or heritable PAH and those with higher mean pulmonary artery pressure and higher pulmonary vascular resistance at baseline. Children with APAH- Congenital Heart Disease and those weighing less than 20 kg did not appear at an increased risk with high dose sildenafil.

The safety and/or efficacy in PAH children on combination therapy is unknown as all of the children studied were only treated with sildenafil monotherapy per study protocol.

While acknowledging and respecting the FDA’s decision, the Scientific Leadership Council of the Pulmonary Hypertension Association, in response to concern expressed by PH care providers, patients, and caregivers, would like to provide some perspective.

-The results from the STARTS-2 trial do not account for the differences in disease severity at the time of enrollment or subgroups of PAH children who might respond more favorably.

-With respect to long-term survival, there was no control group (untreated group) for comparison. The overall survival for the sildenafil treated patients is very favorable compared to historical controls (untreated patients reported in previous studies). Survival is also favorable in current cohorts of treated patients despite the reported association between high dose sildenafil and increased mortality.

-The SLC recognizes the highly complex decision-making process that involves appropriate treatment of pediatric PAH when there are so few options available.

-The SLC urges patients/parents to discuss this issue and their treatment regimen with their PH treating physician as soon as possible and warns against abruptly stopping sildenafil, as this may be associated with severe clinical worsening or death.

This situation continues to underscore the need for ongoing clinical research in pediatric PAH to identify safe, effective therapies. The PH community is currently working on how to best address this problem and will keep you informed of any updates.