Santhera Questions – Family Friendly Version

1. What is Catena® and how does it work?

Catena® is the US brand name for Santhera's 150 mg film-coated idebenone tablets. Catena is given orally (as tablets) three times a day.

Idebenone works in Duchenne to increase the energy output of the cells' mitochondria—the factories that fuel all of a cells activities. Specifically, the drug acts as an electron carrier to provide additional electrons to the mitochondria, which use them as fuel in the cells. It also activates an additional, rarely used enzyme cycle in cells, which leads to the production of even more energy. Idebenone can carry and drop off electrons within the mitochondria numerous times. In addition to helping cells make extra energy, idebenone is a powerful antioxidant and can neutralize destructive free radicals in cells.

All of these activities help dystrophic muscle cells to maintain their cellular energy supply, which is reduced as a result of the lack of dystrophin and protect cells from oxidative stress.

In mice that lack dystrophin, idebenone has been shown to reduce the damage to the heart and to improve their exercise performance.

In Phase II and Phase III clinical trials idebenone has shown efficacy in delaying the loss of respiratory function in patients not currently treated with steroids (patients in clinical trials were 8 years and older).

2. What is the difference between idebenone and coenzymeQ10?

Unlike the common dietary supplement CoenzymeQ10 (CoQ10), which is a large molecule that is not water soluble, idebenone has been optimized to dissolve equally well in water or in lipids (oil-like fat that makes up cell membranes). This means that idebenone can get into muscle cells efficiently and go back and forth across cell membranes and drop off electrons in the mitochondria multiple times. Its water solubility also means that idebenone is "recognized" by the enzyme that loads it with electrons to be dropped off in the mitochondria.

Idebenone and CoQ10 have critical differences in their chemical structures even though they share some similarities. CoQ10 has a much longer "tail," which makes it very soluble in lipids while idebenone has a shorter tail making it water-soluble. The two molecules are not interchangeable in their abilities. There are no placebo-controlled studies that demonstrate that CoQ10 is effective in delaying the loss of respiratory function in Duchenne—these only exist for idebenone.

3. Is there any reason I shouldn't just order idebenone off the internet?

Idebenone sources sold via the internet are chemicals misbranded as vitamins, food supplements, nutrients or the like. They are not medicinal products. The FDA has not approved any of these products for human use nor are these products monitored for quality by the FDA. Therefore patients/families cannot be sure whether these products work or whether any constituent might indeed be harmful.

In a press release issued by the FDA on May 22, 2014 on illegal internet sources, the director of FDA's Office of Enforcement and Import Operations stated:

> "When consumers buy prescription drugs from outside the legitimate supply chain, they cannot know if the medicines they receive are counterfeit or even if they contain the right active ingredient in the proper dosages," said Douglas Stearn, director of the FDA's Office of Enforcement and Import Operations. "Consumers have little or no legal recourse if they experience a reaction to the unregulated medication or if they receive no therapeutic benefit at all. In addition to health risks, these pharmacies pose other risks to consumers, including credit card fraud, identity theft or computer viruses."

4. Can you tell us anything about the label that will be sought for the approval? (i.e. age restrictions? Ambulation restrictions? Steroid restrictions?)

A drug's "label" describes the evidence of efficacy and side effects and for whom a drug should be prescribed, and frequently determines for whom an insurance company or government healthcare system will provide reimbursement for the drug. The decision about the exact label will have to be discussed and agreed upon with the FDA.

Currently, Santhera anticipates that the label sought will be restricted to patients who are not using steroids and who have signs of impaired respiratory function. Regulatory agencies often base the label upon the available data at hand and it should be kept in mind that all of the data collected in the idebenone phase III trial is from participants who were age 10 and older at the time. Santhera does not anticipate that a boy's ability to walk will be a restriction.

5. In what countries is Santhera applying for approval of Catena™?

Santhera prepares for filing of marketing authorization in North America and in Europe (under the brand name Raxone®)

6. What are the results of the phase III study?

Data of the Phase III DELOS trial will be presented at WMS conference in Berlin and during a webinar hosted by Parent Project Muscular Dystrophy on October 15 at 12pm eastern (6pm CDT). Click here for more details.

In the Phase III (DELOS) clinical trial idebenone has shown efficacy in delaying the loss of respiratory function in patients not currently treated with steroids (patients in DELOS were 10 years and older; no selection for specific dystrophin gene mutations; more than 90% were non-ambulatory)

7. What are next steps for Santhera in North American and in Europe?

Santhera has initiated discussions with European regulators and has started to compile the dossier for filing. It is anticipated that filing for an indication in DMD could be achieved in the first half of 2015.

8. How can I stay up to date on information about Catena™?

Please visit www.santhera.com for regular updates and news

Santhera will keep the Duchenne community in the loop about major developments.