Novartis drug Exjade® first treatment approved by FDA for chronic iron overload in patients with non-transfusion-dependent thalassemia

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- -- Pivotal placebo-controlled study data show Exjade significantly decreases iron burden in NTDT patients versus placebo, with similar overall adverse event rate1
- -- Patients with NTDT accumulate excess iron increasing their risk of complications, including liver fibrosis, cirrhosis, blood clots, and bone and vascular disease2
- -- At least three quarters of a million people worldwide have NTDT3-5 and many patients are undiagnosed until serious symptoms arise6

EAST HANOVER, N.J., January 23, 2013 /PRNewswire/ -- Novartis announced today that the US Food and Drug Administration (FDA) has approved Exjade® (deferasirox) for the treatment of chronic iron overload in patients 10 years of age and older with non-transfusion-dependent thalassemia (NTDT) syndromes and with a liver iron concentration of at least 5 mg of iron per gram dry weight and a serum ferritin measurement greater than 300 micrograms per liter. Exjade is the first treatment indicated for patients with these types of thalassemia in the United States.

The approval is based on results from the first prospective placebo-controlled study of iron chelation in NTDT patients, THALASSA, which showed a significant dose-dependent decrease in iron burden compared to placebo ($p<0.001$)[1]. In this pivotal study, Exjade significantly reduced the concentration of iron in the liver, known as liver iron concentration (LIC), as well as the amount of iron anywhere in the body, measured by serum ferritin[1]. The overall adverse event rate for Exjade was similar to the placebo arm[1].

"Patients with NTDT can suffer severe and life-changing complications from chronic iron overload," said Elliott Vichinsky, MD, Medical Director, Hematology/Oncology, Children's Hospital and Research Center, Oakland, California. "In these thalassemia patients, excess iron starts to accumulate at birth yet is often undetected until serious symptoms appear in early adulthood. With this approval of Exjade, physicians will be able to offer NTDT patients a treatment option, helping fulfill a critical unmet need."

Thalassemia refers to a diverse group of genetic disorders that affect red blood cell production, causing anemia. Unlike patients with other types of thalassemia, those with NTDT syndromes don't require regular transfusions, a significant cause of chronic iron overload. However, even without transfusions, NTDT patients still accumulate excess iron through intestinal absorption, leading to debilitating health complications like liver fibrosis and cirrhosis, blood clots, bone disease, pulmonary hypertension, and vascular and endocrine diseases[2,7].

"For years, Exjade has effectively treated chronic iron overload in transfused thalassemia patients," said Alessandro Riva, Global Head, Oncology Development and Medical Affairs, Novartis Oncology. "Now, for the first time, thalassemia patients who do not receive transfusions but suffer the same debilitating effects from chronic iron overload, have an approved treatment option."

According to published studies, at least three quarters of a million people worldwide have NTDT syndromes, although as understanding of the disease increases it is probable the number will grow[3-5]. Because NTDT patients are not symptomatic at birth, when most thalassemias are diagnosed, they are often underdiagnosed and undertreated[6]. Many complications associated with chronic iron overload begin to appear as early as age 10 and become increasingly common as patients reach their 20s or 30s[8]. Most NTDT patients are of South and Southeast Asian, Mediterranean or Middle Eastern origin, with immigration broadening the global prevalence[6,9].

About the THALASSA Study

The THALASSA trial showed that Exjade at a 10 mg/kg per day starting dose significantly reduced LIC from baseline by 3.8 mg of iron per gram of liver dry weight (Fe/g dw) compared to an increase of 0.38 mg Fe/g dw in patients receiving placebo after 52 weeks of treatment ($p<0.001$)[1]. The study also determined that a 10 mg/kg per day dose was superior to a 5 mg/kg per day dose ($p=0.009$)[1]. Additional research has also demonstrated Exjade continues to provide benefit over the longer term, with LIC levels reduced by 7.14 mg Fe/g dw from baseline after 24 months of treatment[10]. The most common reported adverse events (at least 5% in any Exjade or placebo group) were nausea, skin rash, diarrhea and headache[1].

About Exjade

In the US, Exjade is now indicated for the treatment of chronic iron overload in patients 10 years of age and older with non-transfusion-dependent thalassemia (NTDT) syndromes and with a liver iron concentration (LIC) of at least 5 mg of iron per gram dry weight (mg Fe/g dw) and a serum ferritin measurement greater than 300 micrograms per liter. The basis of this indication is data showing achievement of an LIC less than 5 mg Fe/g dw after treatment with Exjade. An improvement in survival or disease-related symptoms has not been established.

Since 2005, Exjade has been approved in the US for the treatment of chronic iron overload due to blood transfusions in adult and pediatric patients (aged 2 years and over). Exjade is approved in over 100 countries including the US, Switzerland, Japan and the countries comprising the European Union. The approved indication may vary depending upon the individual country.

Exjade Important Safety Information

Exjade is contraindicated in patients with creatinine clearance <40 mL/min or serum creatinine >2 times the age-appropriate upper limit of normal; poor performance status and high-risk myelodysplastic syndromes or advanced malignancies: platelet counts <50 x 10^9/L; known hypersensitivity to deferasirox or any component of Exjade.

There have been postmarketing reports of acute renal failure, hepatic failure and cytopenias. Renal failure requiring temporary or permanent dialysis, renal tubulopathy and interstitial nephritis have been reported. Upper gastrointestinal ulceration and hemorrhage, sometimes fatal, have been reported. Caution should be used in elderly patients due to a higher frequency of adverse reactions. Exjade is not recommended in patients with a short life expectancy (e.g., high-risk myelodysplastic syndromes), especially when co-morbidities could increase the risk of adverse events.

Skin rashes, serious hypersensitivity reactions, decreased hearing and lens opacities have been reported. The most common adverse reactions are nausea, vomiting, diarrhea, abdominal pain, rash, non-progressive increases in serum creatinine, increased transaminases, abdominal distension, constipation, dyspepsia, proteinuria and headache.

Please visit www.exjade.com. The full prescribing information including the Boxed Warning for Exjade is

available at http://www.pharma.us.novartis.com/product/pi/pdf/exjade.pdf.

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Located in East Hanover, NJ, Novartis Pharmaceuticals Corporation is an affiliate of Novartis AG, which provides innovative healthcare solutions that address the evolving needs of patients and societies. Headquartered in Basel, Switzerland, Novartis offers a diversified portfolio to best meet these needs: innovative medicines, eye care, cost-saving generic pharmaceuticals, preventive vaccines and diagnostic tools, over-the-counter and animal health products. Novartis is the only global company with leading positions in these areas. In 2011, the Group's continuing operations achieved net sales of USD 58.6 billion, while approximately USD 9.6 billion (USD 9.2 billion excluding impairment and amortization charges) was invested in R&D throughout the Group. Novartis Group companies employ approximately 127,000 full-time-equivalent associates and operate in more than 140 countries around the world. For more information, please visit http://www.novartis.com.

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