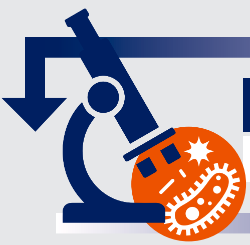
NOVARTIS DEVELOPS NEW IRON CHELATOR:

THE PATH TO JADENU

Jadenu™ (deferasirox) tablets are an iron chelation therapy approved for the treatment of chronic iron overload due to blood transfusions and non–transfusion–dependent thalassemia (NTDT). It is a new formulation of Exjade® (deferasirox) tablets for oral suspension that removes excess iron from the body with once-daily oral tablets that can be swallowed whole.

Novartis has a history of leading the way in iron chelation therapy. Jadenu is the latest example of a long-term commitment to research and treatment innovation for patients with chronic iron overload.



1963

Desferal: Discovery of First Iron-Chelating Agent

Desferal® (deferoxamine mesylate USP) is discovered as an iron chelator that could be used in the treatment of iron overload[1].

APRIL 1968

Desferal: FDA Approval

Novartis begins its long-term commitment to iron chelation therapy with the approval of Desferal by the US Food and Drug Administration (FDA) for the treatment of acute iron intoxication and of chronic iron overload due to transfusion-dependent anemias[2].

Administration is by subcutaneous injection over a period of 8-12 hours 5-7 nights per week.

APRIL 1991

Desferal: Prolongs Survival in Beta-Thalassemia Major Patients

In a study of survival among patients with beta-thalassemia major, researchers found that treatment with deferoxamine, when used in amounts proportional to iron burden, delayed cardiac complications and improved longevity[3].

2002-2004

Exjade: Research and Development of First Oral Iron Chelation Therapy

Novartis continues its research on the treatment of chronic iron overload and develops Exjade – the first iron chelation therapy that can be taken orally as a dispersible tablet in liquid, without the need for an injection or infusion[1].

OCT 2004

Desferal: Improves Survival of Thalassemia Major Patients

Seven Italian centers reported data on survival, causes of death and appearance of complications in patients with thalassemia major treated with transfusion and deferoxamine and found that survival continued to improve[4].

MAY 2005

Exjade: New Drug Applications Submitted

Novartis files regulatory submissions for Exjade in the US and European Union (EU).

JUNE 2005

Exjade: FDA Priority Review Granted

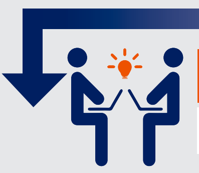
The FDA grants priority review to Novartis for the Exjade application due to the potential of Exjade fulfilling an unmet medical need for patients with chronic iron overload[5]. Exjade also receives Orphan Drug status in the US, EU, and Australia.

NOV 2005

Exjade: FDA Approval

Exjade becomes the first orally administered medication to be approved by the FDA for the treatment of chronic iron overload due to blood transfusions in adults and children age two and older[6].

Exjade is an oral iron chelator taken once daily, after dispersing tablets in a glass of water, apple or orange juice.



2006-2008

Novartis Begins to Explore New Formulation Development

Novartis begins to explore new ways of delivering deferasirox to help simplify iron chelation therapy administration for patients.

JAN 2013

Exjade: FDA NTDT Approval Expands Treatment to Other Patients with Chronic Iron Overload

Exjade becomes the first therapy approved by the FDA for the treatment of chronic iron overload in patients with non–transfusion–dependent thalassemia[7].

2015

Exjade: 10 Years of Iron Chelation Treatment with over 200,000 Patient-years

Exjade is celebrating 10 years of iron chelation treatment, with over 200,000 patient-years of experience on Exjade therapy[8].

MARCH 2015

Jadenu: FDA Approves New Formulation

Jadenu is approved by the FDA for the treatment of chronic iron overload due to blood transfusions and chronic iron overload in non–transfusion–dependent thalassemia syndromes.

Jadenu is a new formulation of deferasirox that removes iron from the body with oral film-coated tablets taken once-daily, swallowed whole.

PRESENT

Novartis continues its commitment to research in chronic iron overload

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JADENU™

(deferasirox) TABLETS

90 mg, 180 mg, 360 mg

ABOUT JADENU (DEFERASIROX) TABLETS FOR ORAL USE

Jadenu is an iron chelator indicated for the treatment of chronically elevated levels of iron in the blood caused by repeated blood transfusions (transfusional hemosiderosis) in patients ages 2 years and older. Jadenu is also indicated to treat patients ages 10 years and older who have chronic iron overload resulting from a genetic blood disorder called non–transfusion–dependent thalassemia (NTDT). These indications are approved under accelerated approval based on a reduction of iron levels in the liver (measured by liver iron concentration) and blood (measured by serum ferritin levels). Continued approval for these indications may be contingent upon verification and description of clinical benefit in confirmatory trials. There are ongoing studies to find out how Jadenu works over a longer period of time.

It is not known if Jadenu is safe or effective when taken with other iron chelation therapy. Controlled clinical trials of deferasirox in patients with myelodysplastic syndromes (a serious blood disorder) and chronic iron overload due to blood transfusions have not been performed.

In the United States, Jadenu is available by prescription only.

IMPORTANT SAFETY INFORMATION ABOUT JADENU (DEFERASIROX) TABLETS FOR ORAL USE

Jadenu contains deferasirox, the same active ingredient in Exjade (deferasirox) tablets for oral suspension. Deferasirox may cause serious kidney problems, liver problems, and bleeding in the stomach or intestines. In some cases, these problems were fatal. Kidney problems occurred particularly in patients with multiple medical conditions and those who were very ill because of their disease. Bleeding in the stomach or intestines occurred more often in elderly patients. Liver problems were more likely to happen in patients older than 55 years.

Jadenu should not be taken by patients with pre-existing severe kidney and liver problems; high-risk myelodysplastic syndromes; advanced cancer; low platelet counts; or an allergy to Jadenu.

Since deferasirox has been on the market, there have been reports of serious reactions, sometimes leading to death. Severe blood disorders (including neutropenia, agranulocytosis, worsening anemia and thrombocytopenia), serious allergic reactions (including swelling of the throat), severe skin reactions (including Stevens Johnson syndrome and erythema multiforme), decreased hearing and vision changes have been reported. These serious reactions and deaths have happened most often when deferasirox was taken by elderly patients. The most commonly reported side effects related to deferasirox in clinical trials were nausea, vomiting, diarrhea, stomach pain, increases in kidney laboratory values, and skin rash.

Please see full Prescribing Information including Boxed WARNING available at www.jadenu.com.

ABOUT EXJADE (DEFERASIROX) TABLETS FOR ORAL SUSPENSION

Exjade is an iron chelator indicated for the treatment of chronically elevated levels of iron in the blood caused by repeated blood transfusions (transfusional hemosiderosis) in patients ages 2 years and older. Exjade is also indicated to treat patients ages 10 years and older who have chronic iron overload resulting from a genetic blood disorder called non–transfusion–dependent thalassemia (NTDT). In patients Exjade lowered the levels of iron in the blood (measured by serum ferritin levels) and liver (measured by liver iron concentration). An improvement in survival or disease symptoms resulting from reduction in elevated iron levels, however, has not been proven.

It is not known if deferasirox is safe or effective when taken with other iron chelation therapy. Controlled clinical trials of Exjade in patients with myelodysplastic syndromes (a serious blood disorder) and chronic iron overload due to blood transfusions have not been performed.

In the United States, Exjade is available by prescription only.

IMPORTANT SAFETY INFORMATION ABOUT EXJADE (DEFERASIROX) TABLETS FOR ORAL SUSPENSION

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Please see full Prescribing Information including Boxed WARNING available at www.exjade.com.

ABOUT DESFERAL (DEFEROXAMINE MESYLATE USP)

Prescription Desferal is indicated for the treatment of acute iron intoxication and of chronic iron overload due to transfusion-dependent anemias.

IMPORTANT SAFETY INFORMATION ABOUT DESFERAL (DEFEROXAMINE MESYLATE USP)

Desferal should not be taken by patients with pre-existing severe kidney disease, the inability to urinate or are allergic to Desferal. Before using Desferal, patients should tell their doctor if they have kidney disease, heart disease, liver disease, vision or hearing problems, asthma or other breathing disorders, low levels of calcium in their blood (hypocalcemia), or a parathyroid disorder. Long-term use of Desferal can slow a child's growth.

Patients should call their doctor immediately if they have any of signs of an allergic reaction, breathing problems, severe abdominal pain, yellowing of the skin or eyes while taking Desferal. Since Desferal may cause blurred vision and may impair thinking, patients should be careful when driving or do anything that requires alertness and the ability to see clearly. Commonly reported side effects include dizziness, flushing, skin rash, reddish colored urine, nausea, vomiting, diarrhea, stomach pain, and pain/swelling where the medicine was injected.

If Desferal is injected into a vein through an IV, the medicine must be given slowly through an IV infusion, and may be given for several hours in a row. Desferal is also sometimes injected into a muscle using an infusion pump.

Please see full Prescribing Information for Desferal available at www.pharma.us.novartis.com/product/pi/pdf/desferal.pdf.

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