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**MEDIA RELEASE • COMMUNIQUE AUX MEDIAS • MEDIENMITTEILUNG**

## **Exjade®, a breakthrough once-daily oral iron chelator, receives first approval worldwide in the US**

- *Exjade offers new alternative to burdensome standard therapy in children and adults who require blood transfusions for chronic anemias*
- *Approval makes iron chelation more accessible to patients suffering from diseases such as thalassemia, sickle cell and myelodysplastic syndromes*

**Basel, November 3, 2005** – Novartis announced today the first approval worldwide for Exjade® (deferasirox) – the first and only once-daily oral iron chelator – by the US Food and Drug Administration. Exjade has been approved for the treatment of chronic iron overload due to blood transfusions in adults and children age two and older.

Exjade is the only iron chelator administered as a drink (the tablets are dispersed in a glass of orange juice, apple juice or water), compared to the current standard of care, which often requires a subcutaneous infusion lasting eight to 12 hours per night, for five to seven nights a week for as long as the patient continues to receive blood transfusions or has excess iron within the body. As a result, many patients may have stopped or avoided iron chelation therapy, thus risking the toxic effects of iron overload.

The approval of Exjade is expected to greatly enhance the acceptance of iron chelation therapy, especially for children, and offer a new alternative to the burdensome continuous infusion therapy.

“The approval of Exjade is an advance for people like me, who have been having blood transfusions and iron chelation for most of our lives,” said Jasmine Williams, who has sickle cell disease and participated in a clinical trial of Exjade. “With Exjade I won’t have to worry about using my needle and pump. I just have to drink my medicine and not think about it again until the next day. Exjade has really made a difference in my life.”

Iron overload is a potentially life-threatening and unavoidable consequence of frequent blood transfusions used to treat certain types of rare chronic blood disorders, including thalassemia and sickle cell disease, as well as other rare anemias and myelodysplastic syndromes. Signs of iron overload may be detected after transfusion of about 20 units of blood. If left undiagnosed or untreated, the excess iron in the body is likely to lead to damage to the liver, heart and endocrine glands. The body has no inherent mechanism to remove excess iron, so iron chelation is used as an effective treatment for transfusion-related iron overload.

“We believe Exjade is a significant breakthrough that will fill an important gap in protecting patients from the cumulative toxicity of iron overload by making iron chelation therapy much more acceptable. Until now, patients may have avoided the potentially life-saving benefits of iron chelation because the standard therapy can be difficult to use,” said David Epstein, CEO of Specialty Medicines and President of Novartis Oncology.

Exjade was approved after being granted priority review by the FDA and also after the Blood Products Advisory Committee to the FDA voted unanimously to give Exjade a positive recommendation for approval. Designated an orphan drug in the US, Switzerland, Australia, and the EU, Exjade has also been granted a priority review in Switzerland, Canada, Australia and New Zealand. Additional regulatory submissions have been made around the world.

### **Filing data**

The Exjade filings were based on the results of a clinical trials program that included a Phase III trial, which showed that after one year Exjade produced reductions in liver iron concentration (LIC).

The clinical trials, which included more than 1,000 adults and children, were part of the largest prospective global clinical trials program ever implemented for an investigational iron chelator. LIC is an indicator for body iron content in patients receiving blood transfusions. It is a measure of iron accumulation in the liver. The studies demonstrated that Exjade, at 20-30 mg/kg/day, led to the maintenance or reduction of iron burden in transfused patients with thalassemia and sickle cell disease as well as other rare anemias and myelodysplastic syndromes. In the clinical studies, Exjade was generally well tolerated, with the most frequently reported adverse events being nausea, vomiting, diarrhea, abdominal pain, skin rash and increases in serum creatinine. As with deferoxamine (Desferal<sup>®</sup>), cases of ocular and auditory disturbances have been reported.

Mild, non-progressive increases in serum creatinine, mostly within the normal range, occur in about one-third of Exjade treated patients. These are dose-dependent, often resolve spontaneously and can sometimes be alleviated by reducing the dose. Serum creatinine should be assessed before initiating therapy and should be monitored monthly thereafter to determine if dose modification or discontinuation is necessary. Liver function should be monitored monthly and if there is an unexplained, persistent, or progressive increase in serum transaminase levels Exjade should be interrupted or discontinued.

### **About iron chelation**

In iron chelation, an agent binds to iron in the body and tissues and helps remove it through the urine and/or feces. The goal of iron chelation therapy is to remove the amount of iron administered in transfusions and, as required, to reduce the existing iron burden. In many patients the need for transfusions may be life-long. To date, only deferoxamine is globally available for the first-line treatment of transfusion related iron overload. While deferoxamine is effective, due to its burdensome administration, many patients do not undergo iron chelation therapy, exposing themselves to the dangers of iron overload. Novartis believes the approval of Exjade will not only help patients currently receiving iron chelation, but also extend the benefits of iron chelation to those not currently undergoing therapy.

The foregoing release contains forward-looking statements that can be identified by terminology such as "significant breakthrough/breakthrough," "will fill an important gap," "first," "is expected," "is likely," "potentially," "greatly enhance," or similar expressions, or by express or implied discussions regarding potential additional marketing approvals or future sales of Exjade. Such forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause actual results with Exjade to be materially different from any future results, performance or achievements expressed or implied by such statements. There can be no guarantee that Exjade will receive any additional marketing approvals in any other countries, or that it will reach any particular sales levels. In particular, management's expectations regarding commercialization of Exjade could be affected by, among other things, additional analysis of Exjade clinical data; new clinical data; unexpected clinical trial results; unexpected regulatory actions or delays or government regulation generally; the company's ability to obtain or maintain patent or other proprietary intellectual property protection; competition in general; increased government, industry, and general public pricing pressures; and other risks and factors referred to in the Company's current Form 20-F on file with the U.S. Securities and Exchange Commission. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those anticipated, believed, estimated or expected. Novartis is providing the information in this press release as of this date and does not undertake any obligation to update any

forward-looking statements contained in this press release as a result of new information, future events or otherwise.

For prescribing information on deferoxamine (Desferal®) please contact your local Novartis affiliate.

**More Information For Health-Care Providers:**

Some clinical trials with Exjade are ongoing. To learn more about Exjade clinical trials, health-care providers can call +44 (0) 1506 814899 or +1-800-340-6843 in the US

**About Novartis**

Novartis AG (NYSE: NVS) is a world leader in pharmaceuticals and consumer health. In 2004, the Group's businesses achieved net sales of USD 28.2 billion and pro forma net income of USD 5.6 billion. The Group invested approximately USD 4.1 billion in R&D. Headquartered in Basel, Switzerland, Novartis Group companies employ about 91,700 people and operate in over 140 countries around the world.

For further information please consult <http://www.novartis.com>.

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