

NOVARTIS AG  
Form 6-K  
December 12, 2008

## **SECURITIES AND EXCHANGE COMMISSION**

Washington, D.C. 20549

### **FORM 6-K**

**REPORT OF FOREIGN PRIVATE ISSUER**

**PURSUANT TO RULE 13a-16 or 15d-16 OF**

**THE SECURITIES EXCHANGE ACT OF 1934**

**Report on Form 6-K dated December 9, 2008**

**(Commission File No. 1-15024)**

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**Novartis AG**

**(Name of Registrant)**

**Lichtstrasse 35**

**4056 Basel**

**Switzerland**

**(Address of Principal Executive Offices)**

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Yes:  **No:**

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**- Investor Relations Release -**

**Exjade® benefits chronically transfused patients by significantly reducing toxic iron that can damage key organs, according to landmark trial**

- *First prospective, multicenter study to show Exjade removes iron from the heart in beta-thalassemia patients with mild to severe cardiac iron overload*
- *In a subgroup analysis of 341 patients with myelodysplastic syndromes (MDS), Exjade significantly reduced levels of toxic iron*
- *These results are part of the largest prospective trial in iron chelation, which includes more than 1,700 patients with various transfusion-dependent anemias*

**Basel, December 9, 2008** New data from the largest prospective trial in iron chelation demonstrate the efficacy and safety of Exjade® (deferasirox) in treating chronic transfusional iron overload, a potentially life-threatening condition for patients who have had multiple blood transfusions to treat underlying anemias, including beta-thalassemia and myelodysplastic syndromes (MDS).

Data from this landmark trial, known as EPIC, were presented today at the 50th American Society of Hematology (ASH) Annual Meeting and Exposition in San Francisco, California.

The EPIC cardiac substudy showed that Exjade removed iron from the heart in beta-thalassemia patients, based on a statistically significant improvement in T2\* magnetic resonance imaging, a validated technique to assess cardiac iron content (P<0.0001). The one-year substudy included 114 beta-thalassemia patients with cardiac iron overload, the leading cause of death in these patients.

These data clearly demonstrate that deferasirox significantly reduces cardiac iron in beta-thalassemia patients with iron overload, which is a critical goal of treatment for these patients, said Dudley Pennell, MD, Professor of Cardiology, Royal Brompton and Harefield NHS Trust and

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Imperial College, London. Cardiac complications caused by the buildup of toxic iron in the heart can be life-threatening for people living with thalassemia.

A pre-planned analysis of 341 MDS patients enrolled in the study showed that Exjade significantly reduced levels of serum ferritin (SF), a key measure of iron in the body, by 253.0 ng/mL from baseline (P=0.0019). Of the 171 MDS patients whose SF was measured at one year, the decrease from baseline was 606 ng/mL.

Many MDS patients receive regular blood transfusions as part of their ongoing treatment, which puts them at risk for iron overload, said Norbert Gattermann, MD, PhD, Hematology, Oncology and Clinical Immunology, Heinrich Heine University Medical Center, Dusseldorf, Germany.  
This

study, which includes the largest number of MDS patients of any iron chelation study, shows deferasirox can effectively reduce iron burden and is generally well tolerated when used appropriately to treat these patients.

Iron toxicity can lead to permanent damage of the liver, heart and endocrine glands, leading to an increased risk of serious health problems and early death. Previous studies of transfusion-dependent MDS patients have found that increased levels of SF are associated with shortened overall survival.

### **About the EPIC trial**

The EPIC trial was a one-year, open-label, prospective, multicenter trial. EPIC studied the efficacy and safety of a fixed starting dose of Exjade based on transfusional iron intake, with subsequent dose titration at 3-monthly intervals based on serum ferritin (SF) trends. With 1,744 patients, this trial is the largest ever conducted for an iron chelator and included the largest cohorts of underlying anemias in a single trial, including patients with beta-thalassemia, MDS and aplastic anemia. Twelve abstracts from EPIC are being presented at ASH.

### **Study details**

The EPIC cardiac substudy evaluated the cardiac efficacy of Exjade in 114 beta-thalassemia patients with myocardial siderosis ( $T2^* < 20$  ms). Baseline myocardial  $T2^*$  was  $< 10$  milliseconds (ms) in 47 (41%) patients (considered severe cardiac iron overload) and 10–20 ms in 67 (59%) patients (considered mild to moderate). Mean baseline liver iron concentration (LIC) was  $28.2 \pm 10.0$  mg Fe/g dry weight (dw), median SF was 5235 ng/mL, and the mean amount of transfused blood in the year prior to study entry was 185 mL/kg.

Patients experienced a statistically significant increase in myocardial  $T2^*$  indicating a decrease in myocardial iron content. Based on a geometric mean  $\pm$  coefficient of variation, change from baseline ( $11.2$  ms  $\pm 40.5\%$ ) to  $12.9$  ms  $\pm 49.5\%$  represents an increase by a factor of 1.16 from baseline ( $P < 0.0001$ ). Overall, 69.5% of patients taking Exjade had an improvement in  $T2^*$  ( $> 4\%$  increase); there was no change in 14.3%; and worsening ( $> 4\%$  decrease) in 16.2% of patients. Left ventricular ejection fraction remained stable throughout the study. Additionally, LIC and SF levels (both indicators of total body iron) were significantly reduced from baseline by  $6.6 \pm 9.9$  mg Fe/g dw and 1257 ng/mL, respectively ( $P < 0.0001$ ). Four patients discontinued treatment due to adverse events. Most investigator-assessed drug-related adverse events were mild to moderate in severity; rash was the most common (13.2%). There is an ongoing one-year extension of this substudy.

The pre-planned subgroup analysis of the EPIC study included 341 patients with transfusion-dependent MDS and SF levels  $\geq$

1000 ng/mL, or SF  $< 1000$  ng/mL, but with a history of multiple transfusions ( $> 20$  transfusions or 100 mL/kg of red blood cells) and an R2 MRI-confirmed LIC  $> 2$  mg Fe/g dw. Overall, mean actual dose of Exjade over one year of treatment was  $19.2 \pm 5.4$  mg/kg/day. Based on the last observation carried forward statistical method, at one year, there was a significant reduction in median SF from baseline ( $253.0$  ng/mL;  $P = 0.0019$ ,  $n = 341$ ). Of the 171 MDS patients whose SF was measured at one year, the decrease from baseline was 606 ng/mL. Overall, 48.7% of pts ( $n = 166$ ) discontinued therapy. Most common investigator-assessed drug-related adverse events were mild to moderate in severity and included diarrhea ( $n = 110$ , 32%), nausea ( $n = 45$ , 13%), vomiting ( $n = 26$ , 8%), abdominal pain ( $n = 26$ , 8%), upper abdominal pain ( $n = 25$ , 7%), rash ( $n = 23$ , 7%) and constipation ( $n = 21$ , 6%).

**About Exjade**

Exjade is indicated for the treatment of chronic iron overload due to blood transfusions (transfusional haemosiderosis) in adult and paediatric patients (aged 2 years and over). It is

approved in 90 countries including the U.S., Switzerland, Japan, and the countries comprising the European Union. The approved indication may vary depending upon the individual country.

Exjade is contraindicated in patients with hypersensitivity to the active substance or to any of the excipients.

There have been postmarketing reports of acute renal failure, hepatic failure and cytopenias in patients treated with Exjade. Monthly monitoring of serum creatinine, proteinuria, serum transaminases and blood counts is recommended, and the dose of Exjade should be modified or interrupted if necessary. More frequent creatinine monitoring is recommended in patients with an increased risk of renal complications. Upper gastrointestinal ulceration and hemorrhage have been reported and caution should be exercised when combined with drugs with ulcerogenic potential. Skin rashes, including hypersensitivity reactions, have been reported. Exjade should be interrupted if severe rash develops and discontinued if severe hypersensitivity reaction occurs. Auditory and ophthalmic testing should be conducted annually.

Exjade should not be taken with aluminium-containing antacids. Caution should be exercised when Exjade is combined with drugs metabolized through CYP3A4.

The most common adverse reactions are nausea, vomiting, diarrhea, abdominal pain, rash, non-progressive increase in serum creatinine, increased transaminases, abdominal distension, constipation, dyspepsia, proteinuria and headache.

Please visit [www.exjade.com](http://www.exjade.com) for more information.

#### **Disclaimer**

The foregoing release contains forward-looking statements that can be identified by terminology such as potentially, can, risk, will, may, or similar expressions, or by express or implied discussions regarding potential new indications or labeling for Exjade or regarding potential future revenues from Exjade. You should not place undue reliance on these statements. Such forward-looking statements reflect the current views of management regarding future events, and 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 be approved for any additional indications or labeling in any market. Nor can there be any guarantee that Exjade will achieve any particular levels of revenue in the future. In particular, management's expectations regarding Exjade could be affected by, among other things, unexpected clinical trial results, including unexpected new clinical data and unexpected additional analysis of existing clinical data; 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; government, industry and general public pricing pressures; the impact that the foregoing factors could have on the values attributed to the Novartis Group's assets and liabilities as recorded in the Group's consolidated balance sheet, and other risks and factors referred to in Novartis AG's current Form 20-F on file with the US 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.





**About Novartis**

Novartis AG provides healthcare solutions that address the evolving needs of patients and societies. Focused solely on healthcare, Novartis offers a diversified portfolio to best meet these needs: innovative medicines, cost-saving generic pharmaceuticals, preventive vaccines, diagnostic tools and consumer health products. Novartis is the only company with leading positions in these areas. In 2007, the Group's continuing operations (excluding divestments in 2007) achieved net sales of USD 38.1 billion and net income of USD 6.5 billion. Approximately USD 6.4 billion was invested in R&D activities throughout the Group. Headquartered in Basel, Switzerland, Novartis Group companies employ approximately 97,000 full-time associates and operate in over 140 countries around the world. For more information, please visit <http://www.novartis.com>.

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**SIGNATURES**

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

**Novartis AG**

Date: December 9, 2008

By: /s/ MALCOLM B. CHEETHAM

Name: Malcolm B. Cheetham  
Title: Head Group Financial  
Reporting and Accounting

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