July 14th, 2013

Dear Healthcare Professional:

Subject: Updated information regarding the possible risk of developing atherosclerosis-related diseases with the use of TASIGNA* (Nilotinib)

Novartis Pharmaceuticals Saudi Arabia ("Novartis"), in collaboration with the Saudi FDA, would like to inform you about updated information regarding the possible risks of atherosclerosis related events in patients treated with TASIGNA* (Nilotinib).

Summary

TASIGNA*belongs to the pharmacological class of protein-tyrosine kinase inhibitors. It has received marketing authorization for the treatment of adult patients with newly diagnosed Philadelphia chromosome positive chronic myeloid leukemia (Ph+CML) in chronic phase. TASIGNA* has also received marketing authorization for the treatment of adult patients with Ph+ chronic and accelerated phase CML who are resistant to or intolerant of at least one prior therapy, including Imatinib.

Information for Health Care Providers

- Cases of atherosclerosis-related diseases and elevated glucose and cholesterol have been reported during clinical trials and post marketing experience with the use of TASIGNA*.
- Patients should be monitored for signs of atherosclerosis-related diseases and elevated glucose and cholesterol during treatment with TASIGNA*.
- Monitoring of lipid and glucose profiles should also be performed before and as clinically indicated during treatment with TASIGNA. If test results warrant therapy, physicians should follow their local standards of practice and treatment guidelines for treating elevated glucose and lipids.

Further Information

An open-label, multicentre, randomised Phase III study (A2303) was conducted to determine the efficacy of Nilotinib versus Imatinib in 846 adult patients with cytogenetically confirmed newly diagnosed Ph+CML in the chronic phase and patients have been followed for at least 4 years.

In the A2303 study, atherosclerosis related events such as peripheral arterial occlusive disease, femoral artery stenosis, coronary artery stenosis, and carotid artery stenosis, were reported in patients taking TASIGNA* (5.0% for TASIGNA* 300 mg BID and 6.1% for TASIGNA* 400 mg BID). All information on cardiovascular events has already been included in the Tasigna label. Novartis will continue monitoring for the atherosclerosis events and will report all events to global Health Authorities on an ongoing basis.

A review of the Novartis global safety database search (between January 1st. 2005 and May 26, 2013) identified a total of 277 cases of atherosclerosis related events, of which one case was reported from Saudi Arabia. The cumulative patient exposure, from the most recent Periodic Safety Update Report (PSUR), submitted April 2013, is estimated to be approximately 39,299 patient-years (since the first launch of TASIGNA in 2007).

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In the 48-months follow-up of A2303 data, 1.1% of the patients treated with 400 mg nilotinib twice a day, had a grade 3/4 elevation in cholesterol. There were no grade 3/4 elevations in the 300 mg twice a day dose group. Based on this analysis, the frequency of the adverse drug reactions 'dyslipidemia' and 'lipoprotein increased' was changed from unknown to uncommon in the product label. A new term 'hypertriglyceridemia' has been added with the frequency of common to the product label. Monitoring of lipid profiles should also be performed before during treatment with TASIGNA* as clinically indicated. If test results warrant therapy, physicians should follow their local standards of practice and treatment guidelines for treating elevated cholesterol.

In addition, 5.8% of the newly diagnosed CML patients treated with 400 mg nilotinib twice a day had a grade 3/4 elevation in blood glucose; and 6.5% of the patients treated with 300 mg nilotinib twice a day had a grade 3/4 elevation in blood glucose. It is recommended that the glucose level should be assessed before initiating treatment with Tasigna and monitored during treatment as clinically indicated.

After a recent review of the Tasigna 48 month update (June 2013), the European Committee for Medicinal Products for Human use (CHMP, regulatory body for the European Members states) concluded that the overall benefit/risk balance for first line treatment of chronic CML is considered unchanged and remains positive. In addition the CHMP concluded that clinically relevant effects continue at 48 months.

It is recommended that health care professionals follow current clinical guidelines for the diagnosis and management of patients with signs and symptoms due to atherosclerosis. Any safety reports related to TASIGNA* should be reported to Novartis or the Saudi National Pharmacovigilance and Drug Safety Center. Novartis will continue to monitor the atherosclerosis, related events and appreciates your collaboration in ensuring the monitoring of patients and continued reporting of any potential adverse drug reactions to:

Call for Reporting

Novartis Pharmaceuticals Saudi Arabia.

Fax: +96611 4653179

E-mail: adverse.events@novartis.com

Or

Saudi FDA, Saudi National Pharmacovigilance & Drug Safety Center.

Fax: +966112057662.

E-mail: npc.drug@sfda.gov.sa

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