NOVARTIS

Date: 29 October 2011

Subject: Aclasta® injection is contraindicated in patients with a creatinine clearance < 35 mL/min

Dear Healthcare Professional,

Novartis Pharmaceuticals Corporation would like to inform you of an update to the **Aclasta** prescribing information to reinforce the selection of appropriate patients for **Aclasta** infusion. A contraindication has been added for patients with a creatinine clearance < 35 mL/min and in those with evidence of acute renal impairment. In addition, the renal section of Warnings and Precautions will be updated.

Aclasta is an intravenous bisphosphonate indicated for the treatment and prevention of osteoporosis in postmenopausal women, to increase bone mass in men with osteoporosis, for treatment and prevention of glucocorticoid-induced osteoporosis and for the treatment of Paget's disease of bone in men and women. During post-marketing surveillance, cases of renal failure have continued to be reported with an estimated reporting rate of 11 cases per 100,000 patient-years of treatment.

Acute renal failure requiring hospitalization and/or dialysis or fatal outcome has occurred in patients with underlying moderate to severe renal impairment or with other risk factors such as advanced age, concomitant nephrotoxic medicines and dehydration secondary to fever, sepsis, gastrointestinal losses or diuretic therapy.

Please review the following important considerations regarding renal adverse events.

- **Aclasta** is contraindicated in patients with a creatinine clearance <35 mL/min and in those with evidence of acute renal impairment.
- If history or physical signs suggest dehydration, **Aclasta** should be withheld until normovolemic status has been achieved.
- Risk of acute renal impairment may increase in patients with underlying renal disease, advanced age, concomitant nephrotoxic medications, diuretic therapy, or severe dehydration occurring before or after **Aclasta** administration.
- Acute renal failure has been observed in patients after a single administration.
- Creatinine clearance should be calculated based on actual body weight before each **Aclasta** dose. Transient increase in serum creatinine may be greater in patients with underlying impaired renal function; interim monitoring of creatinine clearance should be performed in at-risk patients.
- A single dose of **Aclasta** should not exceed 5 mg and the duration of infusion should be no less than 15 minutes.

NOVARTIS

There is no safety or efficacy data to support the adjustment of the **Aclasta** dose based on baseline renal function. Therefore, no dose adjustment is required in patients with a creatinine clearance ≥ 35 mL/min. Please note that this presentation of the risk profile for **Aclasta** is not comprehensive.

To report adverse events potentially associated with **Aclasta**, Please contact Novartis at 00966-1-4658882 Ext: 218 or fax on 00966 1 4648127 or email osama.makram@novartis.com

In addition you can also report all ADRs to the SFDA's through either of the following:
National Pharmacovigilance and Drug safety Center (NPC)Saudi Food and Drug authority-Drug sector 3292 Northern Ring Toad Al Nafal District Riyadh 13312-6288 Kingdom of Saudi Arabia
Tel : 00966-1-2759222 ext : 2353 ,2356, 2317, 2354 ,5769
Fax : 00966-1-205-7662 Email: npc.drug@sfda.gov.sa

Please contact Novartis at 00966-1-4658882 Ext: 218 osama.makram@novartis.com if you have any questions about Aclasta or this information.

Sincerely,

Makram Osama
Digitally signed by Makram Osama
DN: cn=Makram Osama, ou=people, PH, serialNumber=928971, dc=com, novartis
Date: 2011.10.29 16:09:53 +03'00'

Osama Makram, MD Medical Advisor Novartis Saudi Arabia

NOVARTIS