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IMPORTANT INNOHEP® (tinzaparin sodium injection) SAFETY INFORMATION

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Dear Health Care Professional,

Celgene would like to update you on important information concerning INNOHEP®. A controlled clinical study suggests that INNOHEP® may increase the risk for death, compared to unfractionated heparin (UFH) when used to treat elderly patients with renal insufficiency. Consider alternatives to INNOHEP® when treating these patients for deep vein thrombosis (DVT) with or without pulmonary embolism (PE).

Celgene distributed a letter on 28 July 2008 informing you of the revised label that reflected analysis of interim data from a clinical study (IRIS; INNOHEP® in Renal Insufficiency Study). Our revised label highlighted risks only for certain patients 90 years of age or older. We now regard the risks for INNOHEP® as applying to all elderly patients with renal insufficiency and have further revised the label to include this information as a Warning.

INNOHEP® is indicated for the treatment of acute symptomatic deep vein thrombosis with or without pulmonary embolism when administered in conjunction with warfarin sodium. The safety and effectiveness of INNOHEP® were established in hospitalized patients.

The IRIS study compared INNOHEP® (175 IU/kg once daily) and UFH in the initial treatment of DVT and/or PE in elderly patients with renal insufficiency (i.e., patients ≥ 70 years with estimated creatinine clearance of ≤ 30 mL/min calculated by Cockcroft Gault formula or patients ≥ 75 years with estimated creatinine clearance of ≤ 60 mL/min). Oral anticoagulants were co-administered beginning on Days 1-3 and study treatment was continued for at least five days until the international normalized ratio (INR) was between 2-3 on two successive days; oral anticoagulants were then continued alone and patients were followed until 90 days after the start of treatment. Overall in this study, the mortality rate was 6.3% in patients treated with UFH (N=268) and 11.2% in patients treated with INNOHEP® (N=269).

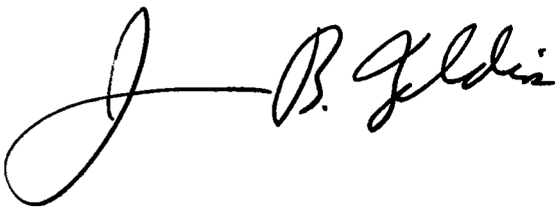
This information is now reflected in the following sections of the prescribing information:

- CLINICAL PHARMACOLOGY, *Special Populations*, Elderly
- WARNINGS
- PRECAUTIONS, Geriatric Use

In addition, as previously informed in the 28 July 2008 letter regarding the identification of two cases of epidural hematoma from post-marketing surveillance, the following sentence is now added to the ADVERSE REACTIONS Section of the label to clarify this information: "Spinal epidural hematoma in association with neuraxial anesthesia or spinal puncture with INNOHEP® has been reported."

Celgene is committed to providing you with the most current information to help you in the management of your patients. Please review the accompanying full prescribing information that incorporates this important change. For further information, or to report an adverse event with INNOHEP®, please call 866-742-7646. Serious adverse events can also be reported to the FDA MedWatch Program by phone at (800)-FDA-1088, or online at www.fda.gov/medwatch.

Sincerely,



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