**הודעה על החמרה ( מידע בטיחות) בעלון לרופא**

**תאריך: 12 בנובמבר 2014**

**שם תכשיר באנגלית:Integrilin 0.75 mg/ml. 2 mg/ml**

**מספר רישום: 112-71-29528-11, 112-72-29529-11**

**שם בעל הרישום: חברת מרק שארפ ודוהם (ישראל-1996) בע"מ**

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| **ההחמרות המבוקשות** |
| **פרק בעלון לרופא** | **טקסט נוכחי** | **טקסט חדש** |
| **CONTRAINDICATIONS** | Known hypersensitivity to any component of the product. | Hypersensitivity to INTEGRILIN or any component of the product hypersensitivity reactions that occurred included anaphylaxis and urticaria). |
| **Warnings and precautions-** *Bleeding* | Because eptifibatide inhibits platelet aggregation, caution should be employed when it is used with other drugs that affect hemostasis, including thrombolytics, oral anticoagulants, nonsteroidal anti-inflammatory drugs, and dipyridamole. To avoid potentially additive pharmacologic effects, concomitant treatment with other inhibitors of platelet receptor GP IIb/IIIa should be avoided | Use of Thrombolytics, Anticoagulants, and Other Antiplatelet Agents-Risk factors for bleeding include older age, a history of bleeding disorders, and concomitant use of drugs that increase the risk of bleeding (thrombolytics, oral anticoagulants, nonsteroidal anti-inflammatory drugs, and P2Y12 inhibitors). Concomitant treatment with other inhibitors of platelet receptor glycoprotein (GP) IIb/IIIa should be avoided. In patients treated with heparin, bleeding can be minimized by close monitoring of the aPTT and ACT *[see Dosage and Administration (2)]*. |
| **Warnings and precautions-** *Thrombocytopenia* | In the event of acute profound thrombocytopenia or a confirmed platelet decrease to <100,000/mm3, discontinue INTEGRILIN and heparin (unfractionated or low-molecular-weight). Monitor serial platelet counts, assess the presence of drug-dependent antibodies, and treat as appropriate (see ADVERSE REACTIONS, Immunogenicity).There has been no clinical experience with eptifibatide initiated in patients with a baseline platelet count <100,000/mm3. If a patient with low platelet counts is receiving INTEGRILIN, their platelet count should be monitored closely. | There have been reports of acute, profound thrombocytopenia (immune-mediated and non-immune mediated) with INTEGRILIN. In the event of acute profound thrombocytopenia or a confirmed platelet decrease to <100,000/mm3, discontinue INTEGRILIN and heparin (unfractionated or low-molecular weight). Monitor serial platelet counts, assess the presence of drug-dependent antibodies, and treat as appropriate *[see Adverse Reactions (6.1)]*.There has been no clinical experience with INTEGRILIN initiated in patients with a baseline platelet count <100,000/mm3. If a patient with low platelet counts is receiving INTEGRILIN, their platelet count should be monitored closely. |
| **ADVERSE REACTIONS-** *Postmarketing Experience* | Additional adverse events reported during use of INTEGRILIN include anaphylaxis, rash and application site disorders such as urticaria. Very rare cases of fatal bleeding have also been reported. Cases of acute profound thrombocytopenia have been reported very rarely. Very rare cases of fatal bleeding have been reported. Cases of pulmonary hemorrhage havealso been reported very rarely. Acute profound thrombocytopenia, as well as immune-mediated thrombocytopenia, has been reported (see ADVERSE REACTIONS, Immunogenicity). | The following adverse reactions have been reported in postmarketing experience, primarily with INTEGRILIN in combination with heparin and aspirin: cerebral, GI, and pulmonary hemorrhage; anaphylaxis, rash and application site disorders such as urticaria. Cases of pulmonary hemorrhage havealso been reported very rarely. Fatal bleeding reactions have been reported. Acute profound thrombocytopenia, as well as immune-mediated thrombocytopenia, has been reported *[see Adverse Reactions (6.1)]*. |
| **DRUG INTERACTIONS** | Enoxaparin dosed as a 1.0-mg/kg subcutaneous injection q12h for 4 doses did not alter the pharmacokinetics of eptifibatide or the level of platelet aggregation in healthy adults | **Use of Thrombolytics, Anticoagulants, and Other Antiplatelet Agents-** Coadministration of antiplatelet agents, thrombolytics, heparin, aspirin, and chronic NSAID use increases the risk of bleeding. Concomitant treatment with other inhibitors of platelet receptor GP IIb/IIIa should be avoided. |