Invirase (saquinavir)

Full Safety and Drug Utilization Review
Provided in Background Materials

Pediatric Advisory Committee Meeting, March 24, 2015
Invirase - Background

• Invirase is an inhibitor of human immunodeficiency virus (HIV) protease.
• It was first approved in 1995 and is indicated in combination with ritonavir and other antiretroviral agents for the treatment of HIV-1 infection in adults, >16 years of age.
• 11/30/2012 Pediatric labeling: Invirase did not receive a pediatric indication.
Invirase - Recent safety labeling update

1/7/2015 FDA requested that the following new safety information be included in class labeling for HIV protease inhibitors:

• Warning and Precautions Section 5.1 Drug Interactions - Initiation of INVIRASE/ritonavir, a CYP3A inhibitor, in patients receiving medications metabolized by CYP3A or initiation of medications metabolized by CYP3A in patients already receiving INVIRASE/ritonavir, may increase plasma concentrations of medications metabolized by CYP3A or may decrease concentrations of INVIRASE. These interactions may lead to:
  – Clinically significant adverse reactions potentially leading to severe, life threatening, or fatal events from greater exposures of concomitant drugs or INVIRASE.
  – Loss of therapeutic effect of INVIRASE and possible development of resistance
Invirase
Justification for Abbreviated Presentation

• 15 pediatric SAEs, including deaths (1/1/2002 to 7/31/2014). The last US FAERS case was reported in 2009.
  ✓ 5 deaths
    o 4 attributed to underlying disease progression (3 infections pneumococcal meningitis, urosepsis, chronic gastroenteritis and acinetobacter baumannii sepsis and 1 failed therapy)
    o 1 due to hepatic failure in a patient with advanced liver disease treated concomitantly with multiple hepatotoxic drugs

*Unlabeled events are underlined
Invirase

Justification for Abbreviated Presentation

✓ 10 Nonfatal SAEs

- 2 GI disorders, 1 case each of Cushing’s syndrome from drug-drug interaction, pneumonia, epiglottitis, pneumocystis jiroveci pneumonia, spontaneous abortion, UTI/sepsis/convulsion, paranoid/hallucination/nightmares, treatment failure/drug resistance

• Use in pediatrics < 1% and not expected to increase

• No new safety signal identified

• Product labeling is appropriate

*Unlabeled events are underlined
Invirase (saquinavir)
Pediatric (0-16 years) Drug Utilization

• In Outpatient Retail Pharmacy Settings
  – In Year 2002: approximately 300 pediatric patients
    • <2% of total patients
  – In Year 2013: <10 pediatric patients,
    • <1% of total patients

Source: IMS Health Total Patient Tracker®(TPT),Y2013, Extracted Oct 2014,
Invirase (saquinavir)

FDA Assessment:
• No new safety signal identified.
• Product labeling is appropriate.

FDA Recommendation:
• Continue standard ongoing safety monitoring.

Question:
• Does the Pediatric Advisory Committee concur?