



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Pharmacovigilance Risk Assessment Committee (PRAC)

New product information wording – Extracts from PRAC recommendations on signals

Adopted at the 8-11 February 2016 PRAC

The product information wording in this document is extracted from the document entitled 'PRAC recommendations on signals' which contains the whole text of the PRAC recommendations for product information update, as well as some general guidance on the handling of signals. It can be found [here](#) (in English only).

New text to be added to the product information is underlined. Current text to be deleted is ~~struck through~~.

1. Bcr-abl tyrosine kinase inhibitors: GLIVEC (imatinib); SPRYCEL (dasatinib); TASIGNA (nilotinib); BOSULIF (bosutinib); ICLUSIG (ponatinib) – Hepatitis B virus (HBV) reactivation (EPITT no 18405)

(Applicable to imatinib, dasatinib and nilotinib)

Summary of Product Characteristics

4.4 Special warnings and precautions for use

Hepatitis B reactivation

Reactivation of hepatitis B in patients who are chronic carriers of this virus has occurred after these patients received BCR-ABL tyrosine kinase inhibitors. Some cases resulted in acute hepatic failure or fulminant hepatitis leading to liver transplantation or a fatal outcome.

Patients should be tested for HBV infection before initiating treatment with (BRANDNAME DRUG). Experts in liver disease and in the treatment of hepatitis B should be consulted before treatment is initiated in patients with positive hepatitis B serology (including those with active disease) and for patients who test positive for HBV infection during treatment. Carriers of HBV who require treatment with BRANDNAME DRUG should be closely monitored for signs and symptoms of active HBV infection throughout therapy and for several months following termination of therapy (see section 4.8).



4.8 Undesirable effects

Table 1 Tabulated summary of adverse reactions

Infections and infestations

Frequency 'not known': Hepatitis B reactivation

Description of selected adverse reactions:

Hepatitis B reactivation has been reported in association with BCR-ABL TKIs. Some cases resulted in acute hepatic failure or fulminant hepatitis leading to liver transplantation or a fatal outcome (see section 4.4).

Package Leaflet

2. What you need to know before you take BRANDNAME DRUG

Talk to your doctor, pharmacist or nurse before taking BRANDNAME DRUG

- if you have ever had or might now have a hepatitis B infection. This is because BRANDNAME DRUG could cause hepatitis B to become active again, which can be fatal in some cases. Patients will be carefully checked by their doctor for signs of this infection before treatment is started.

4. Possible side effects

- Recurrence (reactivation) of Hepatitis B infection when you have had hepatitis B in the past (a liver infection).

(Applicable to bosutinib and ponatinib)

Summary of Product Characteristics

4.4 Special warnings and precautions for use

Hepatitis B reactivation

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Patients should be tested for HBV infection before initiating treatment with (BRANDNAME DRUG). Experts in liver disease and in the treatment of hepatitis B should be consulted before treatment is initiated in patients with positive hepatitis B serology (including those with active disease) and for patients who test positive for HBV infection during treatment. Carriers of HBV who require treatment with BRANDNAME DRUG should be closely monitored for signs and symptoms of active HBV infection throughout therapy and for several months following termination of therapy (see section 4.8).

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4. Possible side effects

- Recurrence (reactivation) of Hepatitis B infection when you have had hepatitis B in the past (a liver infection).

2. DUODOPA (levodopa/carbidopa - intestinal gel) – Intussusception (EPITT no 18424)

Summary of Product Characteristics:

4.4 Special warnings and precautions for use

Reported complications in the clinical studies, and seen post-marketing, include bezoar, ileus, implant site erosion/ulcer, intestinal haemorrhage, intestinal ischaemia, intestinal obstruction, intestinal perforation, intussusception, pancreatitis, peritonitis, pneumoperitoneum and post-operative wound infection. Intussusception has also been reported post marketing. Bezoars are retained concretions of ~~undigested food~~ indigestible material (such as vegetable or fruit non-digestible fibers) in the intestinal tract. Most bezoars reside in the stomach but bezoars may be encountered elsewhere in the intestinal tract. A bezoar around the tip of the jejunal tube may function as a lead point for intestinal obstruction or the formation of intussusception. Abdominal pain may be a symptom of the above listed complications. Some events may result in serious outcomes, such as surgery and/or death. Patients should be advised to notify their physician if they experience any of the symptoms associated with the above events.

4.8 Undesirable effects

Table 1. Adverse Reaction Data Derived From Clinical Trials and Postmarketing Experience

Uncommon (> 1/1,000 to < 1/100)

Device- and Procedure-Related Adverse Reactions

Gastrointestinal disorders

Intussusception

Package Leaflet:*4. Possible side effects*

Side effects from the pump or tube

Uncommon: may affect up to 1 in 100 people

- Inflamed colon (colitis).
- Inflamed pancreas (pancreatitis).
- The tube goes through the wall of the large intestine.
- Blockage (obstruction), bleeding or ulcer in the gut.
- Sliding of one part of the gut into an adjacent part of the gut (intussusception)
- Food getting stuck around the tube causing it to block.
- Pocket of infection (abscess) – this could happen after the tube is placed in your stomach

3. LYSODREN (mitotane) – Sex hormone disturbances and development of ovarian macrocysts (EPITT no 18301)

Summary of Product Characteristics*4.4 Special warnings and precautions for use*

Premenopausal women: Ovarian macrocysts have been observed with higher incidence in this population. Isolated cases of complicated cysts have been reported (adnexal torsion and haemorrhagic cyst rupture). Improvement after mitotane discontinuation has been observed. Women should be urged to seek medical advice if they experience gynecological symptoms such as bleeding and/or pelvic pain.

4.8 Undesirable effects

SOC: Investigations (frequency not known):

- Blood androstenedione decreased (in females)
- Blood testosterone decreased (in females)
- Sex hormone binding globulin increased
- Blood free testosterone decreased (in males)

SOC: Reproductive system and breast disorders (frequency not known):

- Ovarian macrocysts

Premenopausal women: non-malignant ovarian macrocysts (with symptoms such as pelvic pain, bleeding) have been described.

Package Leaflet

2. What you need to know before you take Lysodren

Warnings and precautions

You should tell your doctor if any of the following applies to you:

- If you have gynaecological problems such as bleeding and/or pelvic pain.

4. Possible side effects

Frequency not known

- Ovarian macrocysts (with symptoms such as pelvic pain, bleeding)
- Decreased androstenedione (precursor of sex hormones) in blood tests in females
- Decreased testosterone (sex hormone) in blood tests in females
- Sex hormone binding globulin (a protein which binds sex hormones) increased in blood tests
- Decreased free testosterone (sex hormone) in blood tests in males