הודעה על החמרה (מידע בטיחות) בעלון לרופא

(מעודכן 05.2013)

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שם תכשיר באנגלית ומספר הרישום Kadcyla® 151.63.33939.00

שם בעל הרישום רוש פרמצבטיקה (ישראל) בע"מ

טופס זה מיועד לפרוט ההחמרות בלבד !

ההחמרות המבוקשות		
טקסט חדש	**טקסט נוכחי**	**פרק בעלון**
Hepatic impairment No adjustment to the starting dose is required for patients with mild or moderate hepatic impairment. Trastuzumab emtansine was not studied in patients with severe hepatic impairment. Treatment of patients with hepatic impairment should be undertaken with caution due to known hepatotoxicity observed with trastuzumab emtansine (see section 4.4 and 5.2).	*Patients with hepatic impairment* The safety and efficacy have not been studied in patients with hepatic impairment. No specific dose recommendations can be made (see section 4.4).	**4.2 Posology and method of administration**
In order to improve traceability of biological medicinal products, the tradename and the batch number of the administered product should be clearly recorded (or stated) in the patient file […] *Hepatotoxicity* […] Trastuzumab emtansine has not been studied in patients with serum transaminases > 2.5 × ULN or total bilirubin > 1.5 × ULN prior to initiation of treatment. Treatment in patients with serum transaminases > 3 × ULN and concomitant total bilirubin > 2 × ULN should be permanently discontinued. Treatment of patients with hepatic impairment should be undertaken with caution (see sections 4.2 and 5.2).	In order to improve traceability of biological medicinal products, the tradename of the administered product should be clearly recorded (or stated) in the patient file […] *Hepatotoxicity* […] Trastuzumab emtansine has not been studied in patients with serum transaminases > 2.5 × ULN or total bilirubin > 1.5 × ULN prior to initiation of treatment. Treatment in patients with serum transaminases > 3 × ULN and concomitant total bilirubin > 2 × ULN should be permanently discontinued.	**4.4 Special warnings and precautions for use**

Summary of the safety profile The safety of trastuzumab emtansine has been evaluated in 1871 breast cancer patients in clinical studies. In this patient population: • the most common serious ADRs (> 0.5% of patients) were haemorrhage, pyrexia, dyspnoea musculoskeletal pain, thrombocytopenia, , abdominal pain and vomiting. • the most common adverse drug reactions (ADRs) (≥25%) with trastuzumab emtansine were nausea, fatigue, and headache. The majority of ADRs reported were of Grade 1 or 2 severity. • the most common National Cancer Institute - Common Terminology Criteria for Adverse Events (NCI-CTCAE) Grade≥ 3 ADRs (> 2%) were thrombocytopenia, increased transaminases, anaemia, neutropenia, fatigue, hypokalaemia, musculoskeletal pain and haemorrhage.	Summary of the safety profile The safety of trastuzumab emtansine has been evaluated in 884 breast cancer patients in clinical studies. In this patient population: • the most common serious ADRs were pyrexia, thrombocytopenia, vomiting, abdominal pain, nausea, constipation, diarrhoea, dyspnoea and pneumonitis. • the most common adverse drug reactions (ADRs) (≥25%) with trastuzumab emtansine were haemorrhage (including epistaxis), increased transaminases, fatigue, musculoskeletal pain, and headache. The majority of ADRs reported were of Grade 1 or 2 severity. • the most common National Cancer Institute - Common Terminology Criteria for Adverse Events (NCI-CTCAE) Grade 3 or 4 ADRs (> 2%) were thrombocytopenia, fatigue, increased transaminases, anaemia, hypokalaemia, musculoskeletal pain and neutropenia.	**4.8 Undesirable effects**
Description of selected adverse reactions *Left ventricular dysfunction* Left ventricular dysfunction was reported in 2.2% of patients in clinical studies with trastuzumab emtansine. The majority of events were asymptomatic Grade 1 or 2 decrease in LVEF. Grade 3 or 4 events were reported in 0.4% of patients. .. *Infusion-related reactions* ... Infusion-related reactions were reported in 4.0% of patients in clinical studies with trastuzumab emtansine, with six Grade 3 and no Grade 4 events reported… *Hypersensitivity reactions* Hypersensitivity was reported in	Description of selected adverse reactions *Left ventricular dysfunction* Left ventricular dysfunction was reported in 2.0% of patients in clinical studies with trastuzumab emtansine. The majority of events were asymptomatic Grade 1 or 2 decrease in LVEF. Grade 3 or 4 events were reported in 0.3% of patients… *Infusion-related reactions* ... Infusion-related reactions were reported in 4.5% of patients in clinical studies with trastuzumab emtansine, with one Grade 3 and no Grade 4 events reported... *Hypersensitivity reactions* Hypersensitivity was reported in	

2.6% of patients in clinical studies with trastuzumab emtansine, with one Grade 3 and one Grade 4 events reported... *Thrombocytopenia* Thrombocytopenia or decreased platelet counts were reported in 24.9% of patients in clinical studies with trastuzumab emtansine and was the most common adverse reaction leading to treatment discontinuation (2.6%). .. The incidence of severe haemorrhagic events (Grade ≥3) occurred in 2.2% of the overall trastuzumab emtansine treated patients and 1.8% of Asian trastuzumab emtansine treated patients. .. *Extravasation* Reactions secondary to extravasation have been observed in clinical studies with trastuzumab emtansine. These reactions were usually mild or moderate and comprised erythema, tenderness, skin irritation, pain, or swelling at the infusion site. These reactions have been observed more frequently within 24 hours of infusion. Specific treatment for trastuzumab emtansine extravasation is unknown at this time.	2.6% of patients in clinical studies with trastuzumab emtansine, with no Grade 3 or 4 events reported… *Thrombocytopenia* Thrombocytopenia or decreased platelet counts were reported in 31.4% of patients in clinical studies with trastuzumab emtansine and was the most common adverse reaction leading to treatment discontinuation (1.4%)... The incidence of severe haemorrhagic events (Grade ≥3) occurred in 1.7% of the overall trastuzumab emtansine treated patients and 1% of Asian trastuzumab emtansine treated patients. .. *Extravasation* Reactions secondary to extravasation have been observed in clinical studies with trastuzumab emtansine. These reactions were usually mild and comprised erythema, tenderness, skin irritation, pain, or swelling at the infusion site. These reactions have been observed more frequently within 24 hours of infusion. Specific treatment for trastuzumab emtansine extravasation is unknown at this time.	
Table 7 Laboratory abnormalities observed in patients treated with trastuzumab emtansine in study TDM4370g/BO21977 Increased bilirubin – All Grades (%)-21 Increased AST- Grade 3 (%)-8 Decreased platelets All Grades (%)-85 Decreased haemoglobin- All Grades (%)- 63 Decreased haemoglobin- Grade 3 (%)-5 Decreased neutrophils- All Grades (%)- 41 Decreased potassium -All Grades (%)- 35	**Table 7 Laboratory abnormalities observed in patients treated with trastuzumab emtansine in study TDM4370g/BO21977** Increased bilirubin – All Grades (%)- 20 Increased AST- Grade 3 (%)-7 Decreased platelets All Grades (%)- 84 Decreased haemoglobin- All Grades (%)- 62 Decreased haemoglobin- Grade 3 (%)-4 Decreased neutrophils- All Grades (%)- 39 Decreased potassium -All Grades (%)- 34	