הודעה על החמרה (מידע בטיחות) בעלון לרופא
(מעודכן 3102.50)

תאריך ____20.2.2014____

שם תכשיר באנגלית ומספר הרישום 141-40-31828 Erbitux 5mg/mL

שם בעל הרישום _____ MERCK SERONO Ltd.

טופס זה מיועד לפרוט ההחמרות בלבד !

ההחמרות המבוקשות		
טקסט חדש	**טקסט נוכחי**	**פרק בעלון**
Erbitux® is indicated for the treatment of patients with epidermal growth factor receptor (EGFR)-expressing, RAS wild-type metastatic colorectal cancer	Erbitux® is indicated for the treatment of patients with epidermal growth factor receptor (EGFR)-expressing, KRAS wild-type metastatic colorectal cancer	**Indication**
		contraindications
Posology Prior to the first infusion, patients must receive premedication with an antihistamine and a corticosteroid at least 1 hour prior to administration of cetuximab. This premedication is recommended prior to all subsequent infusions. Colorectal cancer: In patients with metastatic colorectal cancer, cetuximab is used in combination with chemotherapy or as a single agent (see section 5.1). Evidence of wild-type RAS (KRAS and NRAS) status is required before initiating treatment with Erbitux. Mutational status should be determined by an experienced laboratory using validated test methods for detection of KRAS and NRAS (exons 2, 3, and 4) mutations (see section 4.4 and 5.1). Method of Administration: The initial dose should be given slowly and speed of infusion must not exceed 5 mg/min (see section 4.4). The recommended infusion period is 120 minutes. For the subsequent weekly doses, the recommended infusion period is 60 minutes. The infusion rate must not exceed 10 mg/min .	Posology Prior to the first infusion, patients must receive premedication with an antihistamine and a corticosteroid. This premedication is recommended prior to all subsequent infusions. Colorectal cancer: In patients with metastatic colorectal cancer, cetuximab is used in combination with chemotherapy or as a single agent (see section 5.1). Wild-type KRAS tumour status must be verified prior to the first cetuximab infusion. It is important that a validated test method is used by an experienced laboratory (see section 4.4 and 5.1). Method of Administration: For the initial dose, the recommended infusion period is 120 minutes. For the subsequent weekly doses, the	**Posology, dosage & administration**

	recommended infusion period is 60 minutes. The maximum infusion rate must not exceed 10 mg/min	
Infusion-related, including anaphylactic, reactions Severe infusion-related reactions, including anaphylactic reactions, may commonly occur, in some cases with fatal outcome. Occurrence of a severe infusion-related reaction requires immediate and permanent discontinuation of cetuximab therapy and may necessitate emergency treatment. Some of these reactions may be anaphylactic or anaphylactoid in nature or represent a cytokine release syndrome (CRS). Symptoms may occur during the first infusion and for up to several hours afterwards or with subsequent infusions. It is recommended to warn patients of the possibility of such a late onset and instruct them to contact their physician if symptoms or signs of an infusion-related reaction occur. Symptoms may include bronchospasm, urticaria, increase or decrease in blood pressure, loss of consciousness or shock. In rare cases, angina pectoris, myocardial infarction or cardiac arrest have been observed. Anaphylactic reactions may occur as early as within a few minutes of the first infusion e.g. due to preformed IgE antibodies cross-reacting with cetuximab. These reactions are commonly associated with bronchospasm and urticaria. They can occur despite the use of premedication. The risk for anaphylactic reactions is much increased in patients with a history of allergy to red meat or tick bites or positive results of tests for IgE antibodies against cetuximab (α-1-3-galactose). In these patients cetuximab should be administered only after a careful assessment of benefit/risk, including alternative treatments, and only under close supervision of well trained personnel with resuscitation equipment ready. The first dose should be administered slowly and the speed must not exceed 5 mg/min whilst all vital signs are closely monitored for at least two hours. If during the first infusion, an infusion-related reaction occurs within the first 15 minutes, the infusion should be stopped. A careful benefit/risk assessment should be undertaken including consideration whether the patient may have preformed IgE antibodies before a subsequent infusion is given. If an infusion-related reaction develops later during the infusion or at a subsequent infusion further management will depend on its severity: a) Grade 1: continue slow infusion	Infusion-related reactions If the patient experiences a mild or moderate infusion-related reaction, the infusion rate may be decreased. It is recommended to maintain this lower infusion rate in all subsequent infusions. Severe infusion-related reactions have been reported in patients treated with cetuximab (see section 4.8). Symptoms usually occurred during the first infusion and up to 1 hour after the end of infusion, but may occur after several hours or with subsequent infusions. It is recommended to warn patients of the possibility of such a late onset and instruct them to contact their physician if symptoms of an infusion-related reaction occur. Occurrence of a severe infusion-related reaction requires immediate and permanent discontinuation of cetuximab therapy and may necessitate emergency treatment. Special attention is recommended for patients with reduced performance status and pre-existing cardio-pulmonary disease.	**Special Warnings and Special Precautions for Use**

under close supervision b) Grade 2: continue slow infusion and immediately administer treatment for symptoms c) Grade 3 and 4: stop infusion immediately, treat symptoms vigorously and contraindicate further use of cetuximab A cytokine release syndrome (CRS) typically occurs within one hour after infusion and is less commonly associated with bronchospasm and urticaria. CRS is normally most severe in relation to the first infusion. Mild or moderate infusion-related reactions are very common comprising symptoms such as fever, chills, dizziness, or dyspnoea that occur in a close temporal relationship mainly to the first cetuximab infusion. If the patient experiences a mild or moderate infusion-related reaction, the infusion rate may be decreased. It is recommended to maintain this lower infusion rate in all subsequent infusions. A close monitoring of patients, particularly during the first administration, is required. Special attention is recommended for patients with reduced performance status and pre-existing cardio-pulmonary disease. Colorectal cancer patients with RAS mutated tumours Cetuximab should not be used in the treatment of colorectal cancer patients whose tumours have RAS mutations or for whom RAS tumour status is unknown. Results from clinical studies show a negative benefit-risk balance in tumours with RAS mutations. In particular, in these patients negative effects on progression-free survival (PFS) and overall survival (OS) were seen as add-on to FOLFOX4 (see section 5.1).	Colorectal cancer patients with KRAS mutated tumours Cetuximab should not be used in the treatment of colorectal cancer patients whose tumours have RAS mutations or for whom KRAS tumour status is unknown. Results from clinical studies show a negative benefit-risk balance in tumours with KRAS mutations. In particular, in these patients negative effects on progression-free survival (PFS) and overall survival (OS) were seen as add-on to FOLFOX4 (see section 5.1).	
		Interaction with

		Other Medicaments and Other Forms of Interaction
		pregnancy Fertility, and Lactation
General disorders and administration site conditions Common: Severe infusion-related reactions, in some cases with fatal outcome (see section 4.4); fatigue.	General disorders and administration site conditions Common:Severe infusion-related reactions, fatigue	**Adverse events**

מצ"ב העלון, שבו מסומנות ההחמרות המבוקשות על רקע צהוב.
שינויים שאינם בגדר החמרות סומנו (בעלון) בצבע שונה. יש לסמן רק תוכן מהותי ולא שינויים במיקום הטקסט.

הועבר בדואר אלקטרוני בתאריך 24.2.2014

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