הודעה על החמרה (מידע בטיחות) בעלון לרופא

תאריך 6.12.2012

שם תכשיר באנגלית_____Erbitux 5mg/ml

מספר רישום_____ _____141-40-31828

שם בעל הרישום_____Merck Serono Ltd.

פרטים על השינוי/ים המבוקש/ים

טקסט חדש	טקסט נוכחי	פרק בעלון
4.1 Therapeutic indications: Erbitux® is indicated for the treatment of patients with epidermal growth factor receptor (EGFR)-expressing, KRAS wild-type metastatic colorectal cancer • In combination with irinotecan-based chemotherapy • In first-line in combination with FOLFOX • as a single agent in patients who have failed oxaliplatin- and irinotecan-based therapy and who are intolerant to irinotecan *for details, see section 5.1*	**4.1 Therapeutic indications:** Erbitux is indicated for the treatment of patients with KRAS wild-type metastatic colorectal cancer • in combination with chemotherapy • as a single agent in patients who have failed oxaliplatin- and irinotecan-based therapy or who are intolerant to irinotecan	**Indications**
Skin reactions: Adding: Skin reactions are very common and treatment interruption or discontinuation may be required. According to clinical practice guidelines prophylactic use of oral tetracyclines (6 - 8 weeks) and topical application of 1% hydrocortisone cream with moisturiser should be considered. Medium to high-potency topical corticosteroids or oral tetracyclines have been used for the treatment of skin reactions. Adding: Eye disorders Patients presenting with signs and		**Special warnings and precautions for use**

symptoms suggestive of keratitis such as acute or worsening: eye inflammation, lacrimation, light sensitivity, blurred vision, eye pain and/or red eye should be referred promptly to an ophthalmology specialist. If a diagnosis of ulcerative keratitis is confirmed, treatment with cetuximab should be interrupted or discontinued. If keratitis is diagnosed, the benefits and risks of continuing treatment should be carefully considered. Cetuximab should be used with caution in patients with a history of keratitis, ulcerative keratitis or severe dry eye. Contact lens use is also a risk factor for keratitis and ulceration.		
Cardiovascular disorders An increased frequency of severe and sometimes fatal cardiovascular events and treatment emergent deaths has been observed in the treatment of non-small cell lung cancer, squamous cell carcinoma of the head and neck and colorectal carcinoma. In some studies association with age ≥ 65 years or performance status has been observed. When prescribing cetuximab, the cardiovascular status and performance status of the patients and concomitant administration of cardiotoxic compounds such as fluoropyrimidines should be taken into account.	Cardiovascular disorders An increased frequency of severe and sometimes fatal cardiovascular events and treatment emergent deaths has been observed in the treatment of non-small cell lung cancer, squamous cell carcinoma of the head and neck and colorectal carcinoma. In some studies non-small cell lung cancer association with age ≥ 65 years has been observed. When prescribing cetuximab, the cardiovascular status of the patients and concomitant administration of cardiotoxic compounds such as fluoropyrimidines should be taken into account.	
Colorectal cancer patients with KRAS mutated tumours Cetuximab should not be used in the treatment of colorectal cancer patients whose tumours have KRAS 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). Similar findings were also reported when cetuximab was given as add-on to XELOX in combination with bevacizumab (CAIRO2). However, in this study no	Colorectal cancer patients with KRAS mutated tumours Cetuximab should not be used in the treatment of colorectal cancer patients whose tumours have KRAS mutations or for whom KRAS tumour status is unknown. Results from clinical studies show a negative benefit-risk balance in tumours with KRAS mutations.	

עיצב:גופן: Verdana, 9 נק', גופן עבור עברית ושפות אחרות: 9 נק', סמן

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positive effects on PFS or OS were demonstrated in patients with KRAS wild-type tumours, either.		
Adding: The combination of Erbitux with oxaliplatin-containing chemotherapy is contraindicated for patients with mutant KRAS metastatic colorectal cancer (mCRC) or for whom KRAS mCRC status is unknown (see also section 4.4).		**Contraindications**
Respiratory, thoracic and mediastinal disorders Uncommon: Pulmonary embolism, interstitial lung disease. Skin and subcutaneous tissue disorders Very common: Skin reactions*. Very rare: Stevens-Johnson syndrome/toxic epidermal necrolysis. Frequency not known: Superinfection of skin lesions*. Skin reactions Adding: necrotising fasciitis	Respiratory, thoracic and mediastinal disorders Uncommon: Pulmonary embolism. Skin and subcutaneous tissue disorders Very common: Skin reactions*. Frequency not known: Superinfection of skin lesions*.	**Undesirable effects**
Adding: In combination with capecitabine and oxaliplatin (XELOX) the frequency of severe diarrhoea may be increased.		**Drug Interactions**
5. PHARMACOLOGICAL PROPERTIES: **5.1 Pharmacodynamic properties:** In metastatic colorectal cancer, the incidence of KRAS mutations is in the range of 30 - 50%. Study data demonstrate that patients with metastatic colorectal cancer and activating KRAS mutations are highly unlikely to benefit from treatment with cetuximab or a combination of cetuximab and chemotherapy and as add-on to FOLFOX4 a significant negative effect on progression-free survival time (PFS) was shown. *Cetuximab in combination with chemotherapy*	**5. PHARMACOLOGICAL PROPERTIES:** **5.1 Pharmacodynamic properties:** In metastatic colorectal cancer, the incidence of KRAS mutations is in the range of 30 - 50%. Recent data demonstrate that patients with KRAS wild-type metastatic colorectal cancer have a significantly higher chance to benefit from treatment with cetuximab or a combination of cetuximab and chemotherapy. *Cetuximab in combination with chemotherapy* • EMR 62 202-013:	**Others**

• EMR 62 202-013: Adding: In particular a negative effect of cetuximab add-on in the KRAS mutant population was observed. Adding: In time related endpoints no trends indicating clinical benefit could be shown for patients who received cetuximab in combination with the XELOX regimen. There were significant dose reductions and delays of capecitabine or oxaliplatin administration mainly due to higher frequency of diarrhoea in the cetuximab containing arm. In addition, significantly fewer patients treated with cetuximab received second-line therapy.		