Announcement regarding harshment (safety information) in the Physician Leaflet
הודעה על החמרה (מידע בטיחות) בעלון לרופא

תאריך: 04/07/2013

Name of the product:

שם תכשיר באנגלית: Vectibix 20mg/ml

Registration No's:

מספר רישום: 142923295100

Name of the registration owner:

שם בעל הרישום Amgen Europe B.V.

<table>
<tr><th>Current
טקסט נוכחי</th><th>Proposed Text
טקסט חדש</th></tr>
<tr><td></td><td></td></tr>
<tr><td>4.4 Special warnings and precautions for use

Dermatological reactions

Dermatologic related reactions, a pharmacologic effect observed with epidermal growth factor receptor (EGFR) inhibitors, are experienced with nearly all patients (approximately 90%) treated with Vectibix (see section 4.8), the majority are mild to moderate in nature. If a patient develops dermatologic reactions that are grade 3 (NCI-CTC/CTCAE) or higher, or that are considered intolerable, the following dose modification is recommended:</td><td>4.4 Special warnings and precautions for use

Dermatologic<s>al</s> reactions and soft tissue toxicity

Dermatologic related reactions, a pharmacologic effect observed with epidermal growth factor receptor (EGFR) inhibitors, are experienced with nearly all patients (approximately 90%) treated with Vectibix (see section 4.8), the majority are mild to moderate in nature. If a patient develops dermatologic reactions that are grade 3 (NCI-CTC/CTCAE) or higher, or that are considered intolerable, the following dose modification is recommended:</td></tr>
</table>

Occurrence of skin symptom(s): ≥ grade 3[1]	**Administration of Vectibix**	**Outcome**	**Dose regulation**
Initial occurrence	Hold 1 or 2 doses	Improved (< grade 3)	Continuing infusion at 100% of original dose
		Not recovered	Discontinue
At the second occurrence	Hold 1 or 2 doses	Improved (< grade 3)	Continuing infusion at 80% of original dose

Occurrence of skin symptom(s): ≥ grade 3[1]	**Administration of Vectibix**	**Outcome**	**Dose regulation**
Initial occurrence	Hold 1 or 2 doses	Improved -(< grade 3)	Continuing infusion at 100% of original dose
		Not recovered	Discontinue
At the second occurrence	Hold 1 or 2 doses	Improved -(< grade 3)	Continuing infusion at 80% of original dose

		Not recovered	Discontinue
At the third occurrence	Hold 1 or 2 doses	Improved (< grade 3)	Continuing infusion at 60% of original dose
		Not recovered	Discontinue
At the fourth occurrence	Discontinue	-	-

[1]Greater than or equal to grade 3 is defined as severe or life-threatening

In clinical studies, subsequent to the development of severe dermatological reactions (including stomatitis), infectious complications including sepsis, in rare cases leading to death, and local abscesses requiring incisions and drainage were reported. Patients who have severe dermatologic reactions or who develop worsening reactions whilst receiving Vectibix should be monitored for the development of inflammatory or infectious sequelae (including cellulitis), and appropriate treatment promptly initiated. Life threatening and fatal infectious complications including events of necrotizing fasciitis and/or sepsis have been observed in patients treated with Vectibix. Withhold or discontinue Vectibix for dermatologic toxicity with severe or life threatening inflammatory or infectious complications.

Hypersensitivity reactions occurring more than 24 hours after infusion have been reported including a fatal case of angioedema that occurred more than 24 hours after the infusion. Patients should be informed of the possibility of a late onset reaction and instructed to contact their physician if symptoms of a hypersensitivity reaction occur.

		Not recovered	Discontinue
At the third occurrence	Hold 1 or 2 doses	Improved -(< grade 3)	Continuing infusion at 60% of original dose
		Not recovered	Discontinue
At the fourth occurrence	Discontinue	-	-

[1]Greater than or equal to grade 3 is defined as severe or life-threatening

In clinical studies, subsequent to the development of severe dermatologic~~al~~ reactions (including stomatitis), infectious complications including sepsis, in rare cases leading to death, and local abscesses requiring incisions and drainage were reported. Patients who have severe dermatologic reactions or soft tissue toxicity or who develop worsening reactions whilst receiving Vectibix should be monitored for the development of inflammatory or infectious sequelae (including cellulitis), and appropriate treatment promptly initiated. Life threatening and fatal infectious complications including events of necrotizing fasciitis and/or sepsis have been observed in patients treated with Vectibix. Withhold or discontinue Vectibix for dermatologic or soft tissue toxicity associated with severe or life threatening inflammatory or infectious complications.

Hypersensitivity reactions occurring more than 24 hours after infusion have been reported including a fatal case of angioedema that occurred more than 24 hours after the infusion. Patients should be informed of the possibility of a late onset reaction and instructed to contact their physician if symptoms of a hypersensitivity reaction occur.