הודעה על החמרה (מידע בטיחות) בעלון לרופא

(מעודכן 05.2013)

תאריך 27/07/2014

שם תכשיר באנגלית ומספר הרישום Actemra 20 mg/ml [142-21-31931-00]

שם בעל הרישום רוש פרמצבטיקה (ישראל) בע"מ

טופס זה מיועד לפרוט ההחמרות בלבד !

ההחמרות המבוקשות - עלון לרופא		
טקסט חדש	**טקסט נוכחי**	**פרק בעלון**
Actemra treatment must not be initiated in patients with active infections (see section 4.3).	Actemra treatment should not be initiated in patients with active infections (see section 4.3).	**Special warnings and precautions for use**
Interaction studies have only been performed on adults. …	…	**Interaction with other medicinal products and other forms of interaction**
RA Patients … The most serious ADRs were serious infections, complications of diverticulitis, and hypersensitivity reactions. … **Paediatric population** The safety of toclizumab in the pediatric population in the sections on pJIA and sJIA below. In general, the ADRs in pJIA and sJIA patients were similar in type to those see in RA patients, see section 4.8. The ADRs in the pJIA and sJIA patients treated with tocilizumab are described below and are presented in the Table 2 by system organ class and frequency categories, defined using the following convention: very common (≥ 1/10); common (≥ 1/100 to < 1/10) or uncommon (≥ 1/1,000 to <1/100) ***Table 2: Summary of ADRs occurring in patients with sJIA or pJIA receiving tocilizumab as monotherapy or in combination with MTX.*** The content of table 2 is detailed in Annex I *pJIA Patients* The safety of tocilizumab in pJIA has been studied in 188 patients from 2 to 17 years of age. The total patient exposure was 184.4 patient years. The frequency of ADRs in pJIA patients can be found in Table 2 . The	**RA Patients** … **Paediatric population**	**Undesirable effects**

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types of ADRs in pJIA patients were similar to those seen in RA and sJIA patients, see section 4.8. When compared to the adult RA population, events of nasopharyngitis, headache, nausea, and decreased neutrophil count were more frequently reported in the pJIA population. Events of cholesterol increased were less frequently reported in the pJIA population than in the adult RA population. *Infections* The rate of infections in the tocilizumab all exposure population was 163.7 per 100 patient years. The most common events observed were nasopharyngitis and upper respiratory tract infections. The rate of serious infections was numerically higher in patients weighing <30 kg treated with 10 mg/kg tocilizumab (12.2 per 100 patient years) compared to patients weighing ≥30 kg, treated with 8 mg/kg tocilizumab (4.0 per 100 patient years). The incidence of infections leading to dose interruptions was also numerically higher in patients weighing <30 kg treated with 10 mg/kg tocilizumab (21.4%) compared to patients weighing ≥30 kg, treated with 8 mg/kg tocilizumab (7.6%). *Infusion Reactions* In pJIA patients, infusion related reactions are defined as all events occurring during or within 24 hours of an infusion. In the tocilizumab all exposure population, 11 patients (5.9%) experienced infusion reactions during the infusion and 38 patients (20.2%) experienced an event within 24 hours of an infusion. The most common events occuring during infusion were headache, nausea and hypotension and within 24 hours of infusion were dizziness and hypotension. In general, the adverse drug reactions observed during or within 24 hours of an infusion were similar in nature to		

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those seen in RA and sJIA patients, see section 4.8. No clinically significant hypersensitivity reactions associated with tocilizumab and requiring treatment discontinuation were reported. *Immunogenicity* One patient in the 10 mg/kg < 30kg group developed positive anti-tocilizumab antibodies without developing a hypersensitivity reaction and subsequently withdrew from the study. *Neutrophils* During routine laboratory monitoring in the tocilizumab all exposure population, a decrease in neutrophil count below 1×10^9/L occurred in 3.7% of patients. *Platelets* During routine laboratory monitoring in the tocilizumab all exposure population, 1% of patients had a decrease in platelet count to $\leq 50 \times 10^3$/µL without associated bleeding events. *Hepatic transaminase elevations* During routine laboratory monitoring in the tocilizumab all exposure population, elevation in ALT or AST ≥ 3xULN occurred in 3.7% and <1% of patients, respectively. *Lipid parameters* During routine laboratory monitoring in the tocilizumab all exposure population, elevation in total cholesterol >1.5-2 x ULN occurred in one patient (0.5%) and elevation in LDL >1.5-2 x ULN in one patient (0.5%). *sJIA Patients* The safety of tocilizumab in sJIA has been studied in 112 patients from 2 to 17 years of age. In the 12 week double-blind, controlled phase, 75	*sJIA Patients* The safety of tocilizumab in sJIA has been studied in 112 patients from 2 to 17 years of age. In the 12 week	

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patients received treatment with tocilizumab (8 mg/kg or 12 mg/kg based upon body weight). After 12 weeks or at the time of switching to tocilizumab, due to disease worsening, patients were treated in the ongoing open label extension phase. In general, the ADRs in sJIA patients were similar in type to those seen in RA patients, see section 4.8. The frequency of ADRs in sJIA patients can be found in Table 2. When compared to the adult RA population, patients with sJIA experienced a higher frequency of nasopharyngitis, decrease in neutrophil counts, hepatic transaminases increased, and diarrhea. Events of cholesterol increased were less frequently reported in the sJIA population than in the adult RA population.	double-blind, controlled phase, 75 patients received treatment with tocilizumab (8 mg/kg or 12 mg/kg based upon body weight). After 12 weeks or at the time of switching to tocilizumab, due to disease worsening, patients were treated in the ongoing open label extension phase. In general, the ADRs in sJIA patients were similar in type to those seen in RA patients, see section 4.8.	

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 27/07/2014

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Annex I

Table 2: Summary of ADRs occurring in patients with sJIA or pJIA receiving tocilizumab as monotherapy or in combination with MTX.

SOC	**PT**	**Frequency**		
Infections and Infestations		Very Common	Common	Uncommon
	Upper Respiratory Tract Infections	pJIA, sJIA		
	Nasopharyngitis	pJIA, sJIA		
Gastrointestinal Disorders				
	Nausea		pJIA	
	Diarrhea		pJIA, sJIA	
General disorders and administration site conditions				
	Infusion related reactions		pJIA[1], sJIA[2]	
Nervous system disorders				
	Headache	pJIA	sJIA	
Investigations				
	Hepatic transaminases increased		pJIA	
	Decrease in neutrophil count	sJIA	pJIA	

	Platelet count decreased		sJIA	pJIA
	Cholesterol increased		sJIA	pJIA

1. Infusion related reaction events in pJIA patients included but were not limited to headache, nausea and hypotension
2. Infusion related reaction events in sJIA patients included but were not limited to rash, urticaria, diarrhea, epigastric discomfort, arthralgia and headache