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

תאריך 21/09/2015

שם תכשיר באנגלית ומספר הרישום Avastin [131-59-31060-00]

שם בעל הרישום: Roche Pharmaceuticals (Israel) Ltd

טופס זה מיועד לפרוט ההחמרות בלבד !

ההחמרות המבוקשות - עלון לרופא		
טקסט חדש	**טקסט נוכחי**	**פרק בעלון**
Paediatric population Avastin is not approved for use in patients under the age of 18 years.	N/A	**4.2 Posology and method of administration**
Gastrointestinal (GI) perforations and Fistulae (see section 4.8) […] Prior radiation is a risk factor for GI perforation in patients treated for persistent, recurrent or metastatic cervical cancer with Avastin and all patients with GI perforation had a history of prior radiation. Therapy should be permanently discontinued in patients who develop gastrointestinal perforation. *GI-vaginal Fistulae in study GOG-0240* Patients treated for persistent, recurrent, or metastatic cervical cancer with Avastin are at increased risk of fistulae between the vagina and any part of the GI tract (Gastrointestinal-vaginal fistulae). Prior radiation is a major risk factor for the development of GI-vaginal fistulae and all patients with GI-vaginal fistulae had a history of prior radiation. Recurrence of cancer within the field of prior radiation is an additional important risk factor for the development of GI-vaginal fistulae. […] *Neutropenia and infections* (see section 4.8) Increased rates of severe neutropenia, febrile neutropenia, or infection with or without severe neutropenia (including some fatalities) have been observed in patients treated with some myelotoxic chemotherapy regimens plus Avastin in comparison to chemotherapy alone. This has mainly been seen in combination with platinum- or taxane-based therapies in the treatment of NSCLC, mBC, and in combination with paclitaxel and topotecan in persistent, recurrent, or metastatic cervical cancer.	*Gastrointestinal perforations* and fistulae (see section 4.8) […] Therapy should be permanently discontinued in patients who develop gastrointestinal perforation. Patients treated for persistent, recurrent, or metastatic cervical cancer with Avastin may be at increased risk of fistulae between the vagina and any part of the GI tract (Gastrointestinal-vaginal fistulae). […] *Neutropenia and infections* (see section 4.8) Increased rates of severe neutropenia, febrile neutropenia, or infection with or without severe neutropenia (including some fatalities) have been observed in patients treated with some myelotoxic chemotherapy regimens plus Avastin in comparison to chemotherapy alone. This has mainly been seen in combination with platinum- or taxane-based therapies in the treatment of NSCLC and mBC.	**4.4 Special warnings and precautions for use**

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Table 1 Adverse Reactions by Frequency […] **Musculoskeletal and connective tissue disorders** Frequency Not Known : Non - mandibular osteonecrosis[a,f] **Congenital, familial, and genetic disorder** Frequency Not Known: Foetal abnormalities[a,b] [e]Recto-vaginal fistulae are the most common fistulae in the GI-vaginal fistula category. **Table 2: Severe Adverse Reactions by Frequency** […] **Musculoskeletal and connective tissue Disorders** Common: Fistula[a,b,] […] **Congenital, familial, and genetic disorder** Frequency Not Known: Foetal abnormalities[a,c] [d]Recto-vaginal fistulae are the most common fistulae in the GI-vaginal fistula category […] *Description of selected serious adverse reactions* […] *GI-vaginal Fistulae in study GOG-0240* In a trial of patients with persistent, recurrent or metastatic cervical cancer, the incidence of GI-vaginal fistulae was 8.3% in Avastin treated patients and 0.9% in control patients, all of whom had a history of prior pelvic radiation. The frequency of GI-vaginal fistulae in the group treated with Avastin + chemotherapy was higher in patients with recurrence within the field of prior radiation (16.7%) compared with patients with recurrence outside the field of prior radiation (3.6%). The corresponding frequencies in the control group receiving chemotherapy alone were 1.1% vs. 0.8%, respectively. […] *Haemorrhage* (see section 4.4) […] From a clinical trial in patients with persistent, recurrent, or metastatic cervical cancer (study GOG-0240), grade 3-5 bleeding reactions have been	**Table 1 Adverse reactions by frequency** **Table 2: Severe Adverse Reactions by Frequency** **[…]** **Musculoskeletal and connective tissue Disorders** Frequency Not Known: Fistula[a,b,] […] *Description of selected serious adverse reactions* […] In a trial of patients with persistent, recurrent or metastatic cervical cancer, the incidence of GI-vaginal fistulae was 8.3% in Avastin treated patients and 0.9% in control patients, all of whom had a history of prior pelvic radiation.	**4.8 Undesirable effects**

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reported in up to 8.3% of patients treated with Avastin in combination with paclitaxel and topotecan compared with up to 4.6% of patients treated with paclitaxel and topotecan. […] *Venous thromboembolism:* […] From a clinical trial in patients with persistent, recurrent, or metastatic cervical cancer (study GOG-0240), grade 3-5 venous thromboembolic events have been reported in up to 15.6% of patients treated with Avastin in combination with paclitaxel and cisplatin compared with up to 7.0% of patients treated with paclitaxel and cisplatin. […] *Infections* From a clinical trial in patients with persistent, recurrent, or metastatic cervical cancer (study GOG-0240), grade 3-5 infections have been reported in up to 24% of patients treated with Avastin in combination with paclitaxel and topotecan compared with up to 13% of patients treated with paclitaxel and topotecan. […] *Paediatric population* The safety of Avastin in children and adolescents has not been established. Avastin is not approved for use in patients under the age of 18 years. In published literature reports, cases of non-mandibular osteonecrosis have been observed in patients under the age of 18 years treated with Avastin. Post-marketing experience **Table 3: Adverse reactions reported in post-marketing setting** **Musculoskeletal and connective tissue disorders** Cases of non-mandibular osteonecrosis have been observed in Avastin treated paediatric patients (see section 4.8, Paediatric population). *Reporting of suspected adverse reactions* Any suspected adverse events should be	[…] *Venous thromboembolism:* […] From a clinical trial in patients with persistent, recurrent, or metastatic cervical cancer (study GOG-0240), grade 3-5 venous thromboembolic events have been reported in up to 10.6% of patients treated with chemotherapy and bevacizumab compared with up to 5.4% in patients with chemotherapy alone. *Paediatric population* The safety of Avastin in children and adolescents has not been established	

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פרק בעלון	**טקסט נוכחי**	**טקסט חדש**
		reported to the Ministry of Health according to the National Regulation by using an online form (http://forms.gov.il/globaldata/getsequence/getsequence.aspx?formType=AdversEffectMedic@moh.health.gov.il) or by email (adr@MOH.HEALTH.GOV.IL)

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: 21 בספטמבר 2015

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