Bavencio® (Avelumab),
concentrate for solution for infusion vial

רופא/ה, רוקח/ת וצוות רפואי נכבדים,
אנו מבקשים להודיעכם העלון לרופא של התכשיר Bavencio עודכן עם עדכון בטיחות.

ההתוויות המאושרות:

Metastatic Merkel Cell Carcinoma
Bavencio is indicated for the treatment of adult patients with metastatic Merkel cell carcinoma (MCC).

Locally Advanced or Metastatic Urothelial Carcinoma
First-Line Maintenance Treatment of Urothelial Carcinoma
Bavencio is indicated for the maintenance treatment of patients with locally advanced or metastatic urothelial carcinoma (UC) that has not progressed with first-line platinum-containing chemotherapy.

Previously-Treated Urothelial Carcinoma
Bavencio is indicated for the treatment of patients with locally advanced or metastatic urothelial carcinoma (UC) who:
- Have disease progression during or following platinum-containing chemotherapy
- Have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.

Advanced Renal Cell Carcinoma
Bavencio in combination with axitinib is indicated for the first-line treatment of patients with advanced renal cell carcinoma (RCC).

השינויים בעלון לרופא הינם (טקסט שנוסף מופיע עם קו תחתון, החמרות מודגשות בצהוב, טקסט שנמחק מופיע עם ~~קו חוצה~~):

4.8 Undesirable effects
[…]
Tabulated list of adverse reactions
The safety of avelumab as monotherapy has been evaluated in 2,082 patients with solid tumours including metastatic MCC or locally advanced or metastatic UC receiving 10 mg/kg every 2 weeks of avelumab in clinical studies or reported from post-marketing use of avelumab (see Table 2).

These reactions are presented by system organ class and frequency. Frequencies are defined as: very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1,000 to < 1/100); rare (≥ 1/10,000 to < 1/1,000); very rare (< 1/10,000); not known (cannot be estimated from the available data). Within each frequency grouping, adverse reactions are presented in the order of decreasing seriousness.

Table 2: Adverse reactions in patients treated with avelumab as monotherapy

…	
Hepatobiliary disorders	
Uncommon	Autoimmune hepatitis*

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Rare	Acute hepatic failure*, hepatic failure*, hepatitis*, hepatotoxicity*
Not known	Sclerosing cholangitis*
…	
Musculoskeletal and connective tissue disorders	
Very common	Back pain, arthralgia
Common	Myalgia
Uncommon	Myositis*, rheumatoid arthritis*
Rare	Arthritis*, polyarthritis*, oligoarthritis*, Sjogren's syndrome*
Not known	Polymyalgia rheumatica*
…	

[…]

Renal cell carcinoma

[…]

Tabulated list of adverse reactions

Adverse reactions reported for 489 patients with advanced RCC treated in two clinical studies or reported from post-marketing use of ~~with~~ avelumab in combination with axitinib are presented in Table 3.

These reactions are presented by system organ class and frequency. Frequencies are defined as: very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1,000 to < 1/100); rare (≥ 1/10,000 to < 1/1,000); very rare (< 1/10,000); not known (cannot be estimated from the available data). Within each frequency grouping, adverse reactions are presented in the order of decreasing seriousness.

Table 3: Adverse reactions in patients treated with avelumab in combination with axitinib ~~in clinical studies B9991002 and B9991003~~

…	
Hepatobiliary disorders	
Common	Hepatic function abnormal*
Uncommon	Hepatitis*, hepatotoxicity*, immune-mediated hepatitis*, liver disorder*
Not known	Sclerosing cholangitis*
…	
Musculoskeletal and connective tissue disorders	
Very common	Arthralgia, back pain, myalgia
Uncommon	Arthritis*
Not known	Polymyalgia rheumatica*, Sjogren's syndrome*
…	

[…]

~~*Immunogenicity*~~

~~For study EMR107000-003 in the MCC population, out of 204 patients (88 from Part A and 116 from Part B) with at least one valid anti-drug antibodies (ADA) result at any time point treated with avelumab 10 mg/kg as an intravenous infusion every 2 weeks, 189 (79 from Part A and 110 from Part B) were evaluable for treatment-emergent ADA and 16 (8.5%) (7 from Part A and 9 from Part B) tested positive.~~

~~For study B9991001 in the UC population, out of 344 patients with at least one valid ADA result at any time point treated with avelumab 10 mg/kg as an intravenous infusion every 2 weeks plus BSC, 325 were evaluable for treatment-emergent ADA and 62 (19.1%) tested positive.~~

~~For study B9991002 and study B9991003 in the RCC population, out of 480 patients with at least one valid ADA result at any time point treated with avelumab 10 mg/kg as an intravenous infusion every 2 weeks in combination with axitinib 5 mg twice daily~~

~~, 453 were evaluable for treatment-emergent ADA and 66 (14.6%) tested positive.~~

~~Overall, there was no evidence of altered pharmacokinetic profile, increased incidence of infusion reactions or effects on efficacy with anti-avelumab antibody development. The impact of neutralizing antibodies (nAb) is unknown.~~
[…]

5.1 Pharmacodynamic properties
[…]

Immunogenicity

Treatment emergent anti-drug antibodies (ADA) were detected in 8.5% of MCC patients (study EMR107000-003, 8.9% for Part A and 8.2% for Part B), 19% of UC patients (study B9991001) and 16% of RCC patients (study B9991003). The majority of the ADA were of neutralising character. No evidence of ADA or neutralising antibodies (nAb) impact on pharmacokinetics, efficacy or safety was observed.

למידע המלא יש לעיין בעלון לרופא כפי שאושר על ידי משרד הבריאות.

העלון לרופא מפורסם במאגר התרופות שבאתר משרד הבריאות, וניתן לקבלו מודפס על ידי פניה לבעל הרישום מרק סרונו בע"מ, רח' הקישון 18, יבנה 81220, טל' 09-9510737

בברכה,

אורית פוקס
רוקחת ממונה