

ספטמבר 2021

רופא/ה נבד/ה
רוקח/ת נבד/ה שלום רב,

פרסום עדכון בעלון התכשיר :

Imfinzi 120 mg 159-97-35280-00

Imfinzi 500 mg 159-98-35281-00

הרכב:

Durvalumab 120 mg, 500mg

התוויה:

Urothelial Carcinoma -IMFINZI is indicated for the treatment of patients with PD-L1 high (Tumor cell \geq 25% or IC \geq 25%) locally advanced or metastatic urothelial carcinoma 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.

Non-Small Cell Lung Cancer -IMFINZI is indicated for the treatment of patients with unresectable Stage III non-small cell lung cancer (NSCLC) whose disease has not progressed following concurrent platinum-based chemotherapy and radiation therapy.

Small Cell Lung Cancer -IMFINZI, in combination with etoposide and either carboplatin or cisplatin, is indicated for the first-line treatment of adult patients with extensive-stage small cell lung cancer (ES-SCLC).

חברת אסטרזניקה ישראל מבקשת להודיע על עדכון עלון בהתאם להוראות משרד הבריאות בתאריך **ספטמבר 2021**.

העדכון העיקרי בעלון לרופא הוא:

5 WARNINGS AND PRECAUTIONS

Immune-Mediated Adverse Reactions

IMFINZI is a monoclonal antibody that belongs to a class of drugs that bind to either the programmed death-receptor 1 (PD-1) or the PD-ligand 1 (PD-L1), blocking the PD-1/PD-L1 pathway, thereby removing inhibition of the immune response, potentially breaking peripheral tolerance and inducing immune-mediated adverse reactions. Important immune-mediated adverse reactions listed under Warnings and Precautions may not include all possible severe and fatal immune-mediated reactions.

Immune-mediated adverse reactions, which may be severe or fatal, can occur in any organ system or tissue.

Immune-mediated adverse reactions can occur at any time after starting treatment with a PD-1/PDL1 blocking antibody. While immune-mediated adverse reactions usually manifest during treatment with PD-1/PDL1 blocking

antibodies, immune-mediated adverse reactions can also manifest after discontinuation of PD-1/PD-L1 blocking antibodies.

Early identification and management of immune-mediated adverse reactions are essential to ensure safe use of PD-1/PD-L1 blocking antibodies. Monitor patients closely for symptoms and signs that may be clinical manifestations of underlying immune-mediated adverse reactions. Evaluate liver enzymes, creatinine, and thyroid function at baseline and periodically during treatment. In cases of suspected immune-mediated adverse reactions, initiate appropriate workup to exclude alternative etiologies, including infection. Institute medical management promptly, including specialty consultation as appropriate. Withhold or permanently discontinue IMFINZI depending on severity [See Dosage and Administration (2.2)].

In general, if IMFINZI requires interruption or discontinuation, administer systemic corticosteroid therapy (1 mg to 2 mg/kg/day prednisone or equivalent) until improvement to Grade 1 or less. Upon improvement to Grade 1 or less, initiate corticosteroid taper and continue to taper over at least 1 month. Consider administration of other systemic immunosuppressants in patients whose immune-mediated adverse reactions are not controlled with corticosteroid therapy. Toxicity management guidelines for adverse reactions that do not necessarily require systemic steroids (e.g., endocrinopathies and dermatologic reactions) are discussed below.

Immune-Mediated Pneumonitis

~~IMFINZI can cause immune-mediated pneumonitis, defined as requiring use of corticosteroids. Fatal cases have been reported. The incidence of pneumonitis is higher in patients who have received prior thoracic radiation.~~

~~Monitor patients for signs and symptoms of pneumonitis. Evaluate patients with suspected pneumonitis with radiographic imaging. Administer corticosteroids, prednisone 1 to 2 mg per kg per day or equivalent for moderate (Grade 2) pneumonitis or prednisone 1 to 4 mg per kg per day or equivalent for more severe (Grade 3-4) pneumonitis, followed by taper. Interrupt or permanently discontinue IMFINZI based on the severity [see Dosage and Administration (2.3)].~~

~~In clinical studies enrolling 1889 patients with various cancers who received IMFINZI [see Adverse Reactions (6.1)], pneumonitis occurred in 5% of patients, including Grade 3 (0.8%), Grade 4 (< 0.1%) and Grade 5 (0.3%). The median time to onset was 1.8 months (range: 1 day to 13.9 months) and the median time to resolution was 4.9 months (range: 0 days to 13.7 months).~~

~~Pneumonitis led to discontinuation of IMFINZI in 1.5% of the 1889 patients. Pneumonitis resolved in 54% of patients. Systemic corticosteroids were required in 3.5% of the 1889 patients, with 2.5% requiring high-dose corticosteroids (prednisone \geq 40 mg per day or equivalent) and 0.1% requiring infliximab. The frequency and severity of immune-mediated pneumonitis were similar whether IMFINZI was given as a single agent in patients with various cancers or in combination with chemotherapy in patients with ES-SCLC.~~

~~The incidence of pneumonitis (including radiation pneumonitis) was higher in patients in the PACIFIC study who completed treatment with definitive chemoradiation within 42 days prior to initiation of IMFINZI (34%) compared to patients in other clinical studies (2.3%) in which radiation therapy was generally not administered immediately prior to initiation of IMFINZI.~~

~~In the PACIFIC study, the incidence of Grade 3 pneumonitis was 3.4% and of Grade 5 pneumonitis was 1.1% in the IMFINZI arm. The median time to onset of pneumonitis was 1.8 months and the median duration was 2.1 months (range: 3 days to 18.7 months). Pneumonitis led to discontinuation of IMFINZI in 6% of patients. Pneumonitis resolved in 47% of patients experiencing pneumonitis. Systemic corticosteroids were required in 21% of patients, with 12% requiring high-dose corticosteroids and 0.1% requiring infliximab.~~

In Patients Who did Not Receive Recent Prior Radiation

In patients who received IMFINZI on clinical trials in which radiation therapy was generally not administered immediately prior to initiation of IMFINZI, the incidence of immune-mediated pneumonitis was 2.4% (34/1414), including fatal (<0.1%), and Grade 3-4 (0.4%) adverse reactions. Events resolved in 19 of the 34 patients and resulted in permanent discontinuation in 5 patients. Systemic corticosteroids were required in 19 patients (19/34) with pneumonitis who did not receive chemoradiation prior to initiation of IMFINZI.

In Patients Who Received Recent Prior Radiation

The incidence of pneumonitis (including radiation pneumonitis) in patients with unresectable Stage III NSCLC following definitive chemoradiation within 42 days prior to initiation of IMFINZI in PACIFIC was 16.6% (79/475) in patients receiving IMFINZI and 12.8% (30/234) in patients receiving placebo. Of the patients who received IMFINZI (475), 1.1% were fatal and 2.7% were Grade 3-4 adverse reactions. Events resolved in 50 of the 87 patients and resulted in permanent discontinuation in 27 patients.

Systemic corticosteroids were required in 64 patients (64/87) with pneumonitis who had received chemoradiation prior to initiation of IMFINZI, while 2 patients required use of infliximab with high-dose steroids.

The frequency and severity of immune-mediated pneumonitis in patients who did not receive definitive chemoradiation prior to IMFINZI were similar whether IMFINZI was given as a single agent in patients with various cancers in a pooled data set or in patients with ES-SCLC when given in combination with chemotherapy.

Immune-Mediated Hepatitis

~~IMFINZI can cause immune-mediated hepatitis, defined as requiring use of corticosteroids. Fatal cases have been reported.~~

~~Monitor patients for signs and symptoms of hepatitis, during and after discontinuation of IMFINZI, including clinical chemistry monitoring. Administer corticosteroids, prednisone 1 to 2 mg per kg per day or equivalent, followed by taper for Grade 2 or higher elevations of ALT, AST, and/or total bilirubin. Interrupt or permanently discontinue IMFINZI based on the severity [see Dosage and Administration (2.3)].~~

~~In clinical studies enrolling 1889 patients with various cancers who received IMFINZI [see Adverse~~

~~*Reactions (6.1)*~~, hepatitis occurred in 12% of patients, including Grade 3 (4.4%), Grade 4 (0.4%) and Grade 5 (0.2%) immune-mediated hepatitis. The median time to onset was 1.2 months (range: 1 day to 13.6 months). Hepatitis led to discontinuation of IMFINZI in 0.7% of the 1889 patients. Hepatitis resolved in 49% of patients. Systemic corticosteroids were required in 2.7% of patients, with 1.7% requiring high-dose corticosteroids and 0.1% requiring mycophenolate.

Immune-mediated hepatitis occurred in 2.8% (52/1889) of patients receiving IMFINZI, including fatal (0.2%) and Grade 4 (0.3%) adverse reactions. Events resolved in 21 of the 52 patients and resulted in permanent discontinuation of IMFINZI in 6 patients. Systemic corticosteroids were required in all patients with immune-mediated hepatitis, while 2 patient (2/52) required use of mycophenolate with high-dose steroids.

Immune-Mediated Colitis

IMFINZI can cause immune-mediated colitis, defined as requiring use of corticosteroids; that is frequently associated with diarrhea. Cytomegalovirus (CMV) infection/reactivation has been reported in patients with corticosteroid-refractory immune-mediated colitis. In cases of corticosteroid-refractory colitis, consider repeating infectious workup to exclude alternative etiologies.

Immune-mediated colitis occurred in 2% (37/1889) of patients receiving IMFINZI, including Grade 4 (<0.1%) and Grade 3 (0.4%) adverse reactions. Events resolved in 27 of the 37 patients and resulted in permanent discontinuation in 8 patients. Systemic corticosteroids were required in all patients with immune-mediated colitis, while 2 patients (2/37) required other immunosuppressants (e.g. infliximab, mycophenolate).

~~Monitor patients for signs and symptoms of diarrhoea or colitis. Administer corticosteroids, prednisone 1 to 2 mg per kg per day or equivalent, for moderate (Grade 2) or more severe (Grade 3-4) colitis, followed by taper. Interrupt or permanently discontinue IMFINZI based on the severity [see *Dosage and Administration (2.3)*].~~

~~In clinical studies enrolling 1889 patients with various cancers who received IMFINZI [see *Adverse Reactions (6.1)*], diarrhea or colitis occurred in 18% of patients, including Grade 3 (1%) and Grade 4 (0.1%) immune-mediated colitis. The median time to onset was 1.4 months (range: 1 day to 14 months). Diarrhea or colitis lead to discontinuation of IMFINZI in 0.4% of the 1889 patients. Diarrhea~~

~~or colitis resolved in 78% of the patients. Systemic corticosteroids were required in 1.9% of patients, with 1% requiring high-dose corticosteroids and 0.1% requiring other immunosuppressants (e.g., infliximab, mycophenolate).~~

Immune-Mediated Endocrinopathies

IMFINZI can cause immune-mediated endocrinopathies, including thyroid disorders, adrenal insufficiency, type 1 diabetes mellitus and hypophysitis/hypopituitarism.

Adrenal Insufficiency

IMFINZI can cause primary or secondary adrenal insufficiency. For Grade 2 or higher adrenal insufficiency, initiate symptomatic treatment, including hormone replacement as clinically indicated. Withhold or permanently discontinue IMFINZI based on the severity [see *Dosage and Administration (2.2)*]. Immune-mediated adrenal

insufficiency occurred in 0.5% (9/1889) of patients receiving IMFINZI, including Grade 3 (<0.1%) adverse reactions. Events resolved in 1 of the 9 patients and did not lead to permanent discontinuation of IMFINZI in any patients. Systemic corticosteroids were required in all patients with adrenal insufficiency; of these, the majority remained on systemic corticosteroids.

Hypophysitis

IMFINZI can cause immune-mediated hypophysitis. Hypophysitis can present with acute symptoms associated with mass effect such as headache, photophobia, or visual field cuts. Hypophysitis can cause hypopituitarism. Initiate symptomatic treatment including hormone replacement as clinically indicated. Withhold or permanently discontinue IMFINZI depending on severity [see Dosage and Administration (2.2)]. Grade 3 hypophysitis / Hypopituitarism occurred in <0.1% (1/1889) patients who received IMFINZI. Treatment with systemic corticosteroids was administered in this patient. The event did not lead to permanent discontinuation of IMFINZI.

Thyroid Disorders

IMFINZI can cause immune-mediated thyroid disorders. Thyroiditis can present with or without endocrinopathy. Hypothyroidism can follow hyperthyroidism. Initiate hormone replacement therapy for hypothyroidism or institute medical management of hyperthyroidism as clinically indicated. Withhold or discontinue IMFINZI based on the severity [see Dosage and Administration (2.2)]. Monitor thyroid function prior to and periodically during treatment with IMFINZI. Initiate hormone replacement therapy or medical management of hyperthyroidism as clinically indicated. Continue IMFINZI for hypothyroidism and interrupt for hyperthyroidism based on the severity [see Dosage and Administration (2.3)].

In clinical studies enrolling 1889 patients who received IMFINZI [see Adverse Reactions (6.1)], hypothyroidism occurred in 11% of patients and hyperthyroidism occurred in 7% of patients. Thyroiditis occurred in 0.9% of patients, including Grade 3 (< 0.1%) thyroiditis. Hypothyroidism was preceded by thyroiditis or hyperthyroidism in 25% of patients.

Thyroiditis: Immune-mediated thyroiditis occurred in 0.5% (9/1889) of patients receiving IMFINZI, including Grade 3 (<0.1%) adverse reactions. Events resolved in 4 of the 9 patients and resulted in permanent discontinuation in 1 patient. Systemic corticosteroids were required in 3 patients (3/9) with immune-mediated thyroiditis, while 8 patients (8/9) required endocrine therapy.

Hyperthyroidism: Immune-mediated hyperthyroidism occurred in 2.1% (39/1889) of patients receiving IMFINZI. Events resolved in 30 of the 39 patients and did not lead to permanent discontinuation of IMFINZI in any patients. Systemic corticosteroids were required in 9 patients (9/39) with immune mediated hyperthyroidism, while 35 patients (35/39) required endocrine therapy.

Hypothyroidism: Immune-mediated hypothyroidism occurred in 8.3% (156/1889) of patients receiving IMFINZI, including Grade 3 (<0.1%) adverse reactions. Events resolved in 31 of the 156 patients and did not lead to permanent discontinuation of IMFINZI in any patients. Systemic corticosteroids were required in 11 patients (11/156) and the majority of patients (152/156) required long-term thyroid hormone replacement.

Adrenal Insufficiency

Monitor patients for clinical signs and symptoms of adrenal insufficiency. For Grade 2 or higher adrenal insufficiency, initiate prednisone 1 to 2 mg per kg per day or equivalent, followed by corticosteroid taper and hormone replacement as clinically indicated. Interrupt IMFINZI based on the severity [see Dosage and Administration (2.3)].

In clinical studies enrolling 1889 patients who received IMFINZI, adrenal insufficiency occurred in 0.7% of patients, including Grade 3 (< 0.1%). Systemic corticosteroids were required in 0.4% of patients, including 0.1% of patients who required high-dose corticosteroids.

Type 1 Diabetes Mellitus which can present with diabetic ketoacidosis: Monitor patients for hyperglycemia or other signs and symptoms of diabetes. Initiate treatment with insulin as clinically indicated. ~~Withhold or permanently discontinue~~ Interrupt IMFINZI based on the severity [see Dosage and Administration (2.3)].

Grade 3 immune-mediated In clinical studies enrolling 1889 patients who received IMFINZI, type 1 diabetes mellitus occurred in <0.1% (1/1889) of patients receiving IMFINZI. This patient required long-term insulin therapy and IMFINZI was permanently discontinued. <0.1% of patients. The median time to onset was 1.4 months. Two additional patients (0.1%, 2/1889) had events of hyperglycemia requiring insulin therapy that did not resolve at the time of reporting.

Hypophysitis

For Grade 2 or higher hypophysitis, initiate prednisone 1 to 2 mg per kg per day or equivalent, followed by corticosteroid taper and hormone replacement therapy as clinically indicated. Interrupt IMFINZI based on the severity [see Dosage and Administration (2.3)].

Hypopituitarism leading to adrenal insufficiency and diabetes insipidus occurred in < 0.1% of 1889 patients who received IMFINZI in clinical studies.

Immune-Mediated Nephritis with Renal Dysfunction

5.3 Immune-Mediated Nephritis

IMFINZI can cause immune-mediated nephritis, defined as evidence of renal dysfunction requiring use

of corticosteroids. Fatal cases have occurred:

Monitor patients for abnormal renal function tests prior to and periodically during treatment with IMFINZI. Initiate prednisone 1 to 2 mg per kg per day or equivalent, for moderate (Grade 2) or severe (Grade 3-4) nephritis, followed by taper. Interrupt or permanently discontinue IMFINZI based on the severity [see Dosage and Administration (2.3)].

In clinical studies enrolling 1889 patients with various cancers who received IMFINZI [see Adverse Reactions (6.1)], nephritis (reported as any of the following increased creatinine or urea, acute kidney injury, renal failure, decreased glomerular filtration rate, tubulointerstitial nephritis, decreased creatinine clearance, glomerulonephritis, and nephritis) occurred in 6.3% of patients including Grade 3 (1.1%), Grade 4 (0.2%) and Grade 5 (0.1%) immune-mediated nephritis. The median time to onset was 2 months (range: 1 day to 14.2 months). IMFINZI was discontinued in 0.3% of the 1889 patients. Nephritis resolved in 50% of patients. Systemic corticosteroids were required in 0.6% of patients, with 0.4% receiving high-dose corticosteroids.

Immune-mediated nephritis occurred in 0.5% (10/1889) of patients receiving IMFINZI, including Grade (<0.1%) adverse reactions. Events resolved in 5 of the 10 patients and resulted in permanent discontinuation in 3 patients. Systemic corticosteroids were required in all patients with immune mediated nephritis.

Immune-Mediated Dermatologic Reactions

IMFINZI can cause immune-mediated rash or dermatitis. Exfoliative dermatitis. ~~Other dermatologic reactions have occurred with other products in this class~~ including Stevens Johnson Syndrome (SJS) drug rash with eosinophilia and systemic symptoms (DRESS), and ~~toxic epidermal necrolysis (TEN) has occurred with PD-1/L-1 blocking antibodies.~~ Topical emollients and/or topical corticosteroids may be adequate to treat mild to moderate non-exfoliative rashes. Withhold or permanently discontinue IMFINZI depending on severity [see Dosage and Administration (2.2)] ~~see Warnings and Precautions (5.7)].~~

Immune-mediated rash or dermatitis occurred in 1.8% (34/1889) of patients receiving IMFINZI, including Grade 3 (0.4%) adverse reactions. Events resolved in 19 of the 34 patients and resulted in permanent discontinuation in 2 patients. Systemic corticosteroids were required in all patients with immune-mediated rash or dermatitis.

Monitor for signs and symptoms of rash. Initiate prednisone 1 to 2 mg per kg per day or equivalent, for moderate (Grade 2) rash or dermatitis lasting for more than 1 week or severe (Grade 3-4) rash or dermatitis followed by taper. Interrupt or permanently discontinue IMFINZI based on the severity *[see Dosage and Administration (2.3)]*.

In clinical studies enrolling 1889 patients with various cancers who received IMFINZI *[see Adverse Reactions (6.1)]*, 26% of patients developed rash or dermatitis. Rash or dermatitis led to discontinuation of IMFINZI in 0.1% of the 1889 patients. Rash resolved in 62% of patients. Systemic corticosteroids were required in 2.0% of patients, including high-dose corticosteroids in 1% of patients.

Other Immune-Mediated Adverse Reactions

IMFINZI can cause severe and fatal immune-mediated adverse reactions. These immune-mediated reactions may involve any organ system. While immune-mediated reactions usually manifest during treatment with IMFINZI, immune-mediated adverse reactions can also manifest after discontinuation of IMFINZI.

For suspected Grade 2 immune-mediated adverse reactions, exclude other causes and initiate corticosteroids as clinically indicated. For severe (Grade 3 or 4) adverse reactions, administer corticosteroids, prednisone 1 to 4 mg per kg per day or equivalent, followed by taper. Interrupt or permanently discontinue IMFINZI, based on the severity of the reaction *[see Dosage and Administration (2.3)]*. If uveitis occurs in combination with other immune-mediated adverse reactions, evaluate for Vogt-Koyanagi-Harada syndrome, which has been observed with other products in this class and may require treatment with systemic steroids to reduce the risk of permanent vision loss.

The following clinically significant, immune-mediated adverse reactions occurred at an incidence of less than 1% each in 1889 patients who received IMFINZI or were reported with the use of other PD-1/PD-L1 blocking antibodies: aseptic meningitis, hemolytic anemia, immune thrombocytopenic purpura, myocarditis, myositis, and ocular inflammatory toxicity, including uveitis and keratitis *[see Adverse Reactions (6.1)]*. In patients who received IMFINZI in clinical studies outside of the pooled dataset, myasthenia gravis occurred at an incidence of less than 0.1%.

The following clinically significant, immune-mediated adverse reactions have been reported with other products in this class: bullous dermatitis, Stevens Johnson Syndrome (SJS)/toxic epidermal necrolysis (TEN), pancreatitis, systemic inflammatory response syndrome, rhabdomyolysis, histiocytic necrotizing lymphadenitis, vasculitis, hemolytic anemia, iritis, encephalitis, facial and abducens nerve paresis, demyelination, polymyalgia rheumatica, autoimmune neuropathy, Guillain-Barré syndrome and Vogt-Koyanagi-Harada syndrome:

Cardiac/vascular: Myocarditis, pericarditis, vasculitis,

Nervous system: Meningitis, encephalitis, myelitis and demyelination, myasthenic syndrome/myasthenia gravis (including exacerbation), Guillain-Barré syndrome, nerve paresis, autoimmune neuropathy,

Ocular: Uveitis, iritis, and other ocular inflammatory toxicities can occur. Some cases can be associated with retinal detachment. Various grades of visual impairment to include blindness can occur. If uveitis occurs in combination with other immune-mediated adverse reactions, consider a Vogt-Koyanagi-Harada like syndrome, as this may require treatment with systemic steroids to reduce the risk of permanent vision loss.

Gastrointestinal: Pancreatitis including increases in serum amylase and lipase levels, gastritis, duodenitis,

Musculoskeletal and connective tissue disorders: Myositis/polymyositis, rhabdomyolysis and associated sequelae including renal failure, arthritis, polymyalgia rheumatic,

Endocrine: Hypoparathyroidism

Other (hematologic/immune): Hemolytic anemia, aplastic anemia, hemophagocytic lymphohistiocytosis, systemic inflammatory response syndrome, histiocytic necrotizing lymphadenitis (Kikuchi lymphadenitis), sarcoidosis, immune thrombocytopenia, solid organ transplant rejection,

5.4 Infection

IMFINZI can cause serious infections, including fatal cases.

Monitor patients for signs and symptoms of infection. For Grade 3 or higher infections, withhold

IMFINZI and resume once clinically stable [see Dosage and Administration (2.3)].

In clinical studies enrolling 1889 patients with various cancers who received IMFINZI [see Adverse Reactions (6.1)], infections occurred in 43% of patients, including Grade 3 (8%), Grade 4 (1.9%), and Grade 5 (1%). In the urothelial carcinoma cohort in Study 1108 the most common Grade 3 or higher infection was urinary tract infections which occurred in 4% of patients. In the PACIFIC study the most common Grade 3 or higher infection was pneumonia, which occurred in 5% of patients. The overall incidence of infections in IMFINZI-treated patients (56%) in the PACIFIC study was higher compared to patients in other studies (38%) in which radiation therapy was generally not administered immediately prior to initiation of IMFINZI.

5.2 Infusion-Related Reactions

IMFINZI can cause severe or life-threatening infusion-related reactions.

Monitor for signs and symptoms of infusion-related reactions. Interrupt, slow the rate of, or permanently discontinue IMFINZI based on the severity [see Dosage and Administration (2.3)]. For Grade 1 or 2 infusion-related reactions, consider using pre-medications with subsequent doses.

In clinical studies enrolling 1889 patients with various cancers [see Adverse Reactions (6.1)], infusion-related reactions occurred in 2.2% (42/1889) of patients receiving IMFINZI, including Grade 3 (0.3%) adverse reactions.

5.3 Complications of Allogeneic HSCT after IMFINZI

Fatal and other serious complications can occur in patients who receive allogeneic hematopoietic stem cell transplantation (HSCT) before or after being treated with a PD-1/L-1 blocking antibody. Transplant related complications include hyperacute graft-versus-host-disease (GVHD), acute GVHD, chronic GVHD, hepatic veno-occlusive disease (VOD) after reduced intensity conditioning, and steroid-requiring febrile syndrome (without an identified infectious cause). These complications may occur despite intervening therapy between PD-1/L-1 blockade and allogeneic HSCT.

Follow patients closely for evidence of transplant-related complications and intervene promptly. Consider the benefit versus risks of treatment with a PD-1/L-1 blocking antibody prior to or after an allogeneic HSCT.

6 ADVERSE REACTIONS

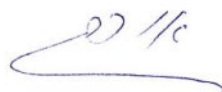
The following adverse reactions are discussed in greater detail in other sections of the labeling.

- Immune-Mediated Adverse Reactions Pneumonitis [see Warnings and Precautions (5.1)].
- ~~Immune-Mediated Hepatitis [see Warnings and Precautions (5.2)].~~
- ~~Immune-Mediated Colitis [see Warnings and Precautions (5.3)].~~
- ~~Immune-Mediated Endocrinopathies [see Warnings and Precautions (5.4)].~~
- ~~Immune-Mediated Nephritis [see Warnings and Precautions (5.5)].~~
- ~~Immune-Mediated Dermatologic Reactions [see Warnings and Precautions (5.6)].~~
- ~~Other Immune-Mediated Adverse Reactions [see Warnings and Precautions (5.7)].~~
- ~~Infection [see Warnings and Precautions (5.8)].~~
- Infusion-Related Reactions [see Warnings and Precautions (5.9)].

העלונים מפורסמים במאגר התרופות שבאתר משרד הבריאות, וניתן לקבלם מודפסים על ידי פניה לבעל הרישום.

בכבוד רב,

אורה סטוליק
רוקחת ממונה
אסטרזהניקה (ישראל) בע"מ



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