IMFINZI™
durvalumab
Injection for Intravenous Use 50 mg/mL

HCP Guide

TARGET PD-L1 WITH PRECISE BLOCKADE[1]

Enable the immune system.
RECOGNIZE. **RESPOND.**

Ref: 1. PI of IMFINZI for Feb 2018

טרם מתן מרשם יש לעיין בעלון לרופא של התכשיר כפי שאושר ע"י משרד הבריאות

AstraZeneca
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HCP guide

"This Prescriber Guide, format and content has been checked and approved by the Ministry of Health in June 2018"

HCP Guide

IMFINZI™

(durvalumab)

Important safety information to minimize the risks of immune mediated adverse reactions for healthcare professionals

Indication:

- **Urothelial Carcinoma**

  IMFINZI™ is indicated for the treatment of patients with PD-L1 high (Tumor cell ≥ 25% or IC ≥ 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.

This guide is essential to ensure the safe and effective use of durvalumab and appropriate management of Immune-mediated adverse event (imAE) and must be read before prescribing and administering durvalumab.

Important Information

- Durvalumab increases the risk of immune mediated adverse events (imAE), early diagnosis and management is essential to minimize serious consequences
- Routine monitoring of patients for signs and symptoms is essential
- Suspected imAEs must be promptly investigated for alternative causes
- All patients receiving durvalumab should be given a patient guide (including a patient alert card)
- Durvalumab treatment may be withheld or discontinued based on the severity of the imAE and corticosteroid treatment may be introduced (see detailed treatment guidance). It is very important to explain to the patient to carry the alert card at all time and present it to HCP if needed.
- Onset of imAEs can occur up to several months after the last dose of durvalumab

Patient information

It is important to provide the patient guide and the patient alert card to all patients receiving durvalumab. You should discuss durvalumab with the patient/carer emphasizing the importance of reporting any suspected imAR symptoms to their doctor.

The patient guide will help the patient understand what symptoms they need to be aware of and what to do should they experience any of these symptoms.

Please inform patients that if they need a replacement card: *contact their physician*

Where to find further information

IMFINZI™ physician leaflet

You can also contact us on phone number: 09-7406528

To order additional educational materials
you can email to: Safety.Israel@astrazeneca.com or please call: 09-7406528

To report SUSPECTED ADVERSE REACTIONS, contact AstraZeneca

https://aereporting.astrazeneca.com/ or Safety.Israel@astrazeneca.com

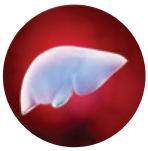
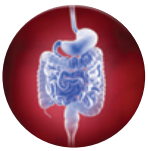
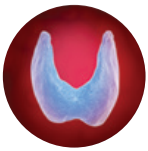
You can also call us on phone number: 09-7406528

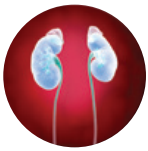
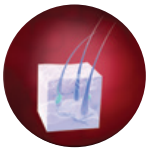
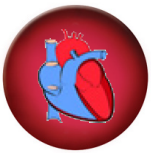
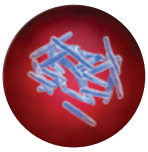
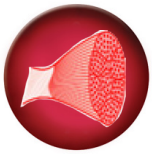
You may also report side effects to the Israeli ministry of health by using online form: WWW.HEALTH.GOV.IL or by entering the link: https://forms.gov.il/globaldata/

getsequence/getsequence.aspx?formType=AdversEffectMedic@moh.gov.il

Immune mediated adverse event check list

Monitoring patients being treated with duvalumab at every visit for signs and symptoms of immune mediated AEs will help ensure the safety of your patients.

Pulmonary • New or worsening cough • Shortness of breath • Chest pain		**Hepatic** • Yellowing of skin or the whites of the eyes • Severe nausea or vomiting; • Pain on the right side of the stomach area (abdomen) • Drowsiness • Dark urine (tea coloured) • Bleeding or bruising more easily than normal • Feeling less hungry than usual	
Gastrointestinal • Diarrhoea or more bowel movements than usual • Stools that are black, tarry, sticky, or have blood or mucus • Severe pain or tenderness in stomach-area (abdomen)		**Endocrine** • Headaches that will not go away or unusual headaches • Extreme tiredness • Weight gain or loss • Dizziness or fainting; • Feeling more hungry or thirsty than usual • Hair loss • Feeling cold • Constipation • Voice getting deeper • Urinating more often than usual • Nausea or vomiting • Stomach area (abdomen) pain • Changes in mood or behaviour	

Renal • Decrease in amount of urine • Blood in urine • Swelling in ankles		**Skin** • Rash • Itching • Skin blistering	
Cardiac • Shortness of breath during exercise or exertion • Fatigue • Heart palpitations and chest pain		**Other** • Neck stiffness • Fever • Changes in mood or behaviour • Blurry vision • Double vision	
Severe infections • Fever • Cough • Frequent urination • Pain when urinating • Flu-like symptoms		**Muscle** • Muscle pain or stiffness • Muscle weakness	

Immune mediated Adverse Event Treatment guidance

Immune mediated adverse reaction	Severity	IMFINZI treatment modification	Corticosteroid treatment unless otherwise specified
Pneumonitis	Grade 1: asymptomatic, clinical or diagnostic observations only.	None	None
	Grade 2: Symptomatic, medical intervention indicated, limiting instrumental ADL	Withold dose[a]	Initial dose of 1 mg/kg/day to 2 mg/kg/day prednisone or equivalent followed by a taper
	Grade 3: Sever symptoms, limiting self-care ADL[b], oxygen indicated	Permanently discontinue	Initial dose of 1 mg/kg/day to 4 mg/kg/day prednisone or equivalent followed by a taper
	Grade 4: life threatening respiratory compromise, urgent intervention indicated		
Colitis	Grade 1: asymptomatic, clinical or diagnostic observations only, intervention not indicated	None	None
	Grade 2: abdominal pain, mucus or blood in stool	Withold dose[a]	Initial dose of 1 mg/kg/day to 2 mg/kg/day prednisone or equivalent followed by a taper
	Grade 3: severe abdominal pain, change in bowel habits, medical intervention indicated, peritoneal signs	Permanently discontinue	
	Grade 4: life threatening consequences, urgent intervention indicated		
Diarrhoea	Grade 1: Increase of <4 stools/day over Baseline Mild increase in ostomy output vs baseline	None	None

Immune mediated adverse reaction	Severity	IMFINZI treatment modification	Corticosteroid treatment unless otherwise specified
Diarrhoea	Grade 2: Increase of 4–6 stools/day over baseline Moderate increase in ostomy output vs baseline	Withhold dose[a]	Initial dose of 1 mg/kg/day to 2 mg/kg/day prednisone or equivalent followed by a taper
	Grade 3: • Increase of ≥7 stools/day over baseline • Incontinence • Hospitalization indicated • Severe increase in ostomy output vs baseline • Limiting self-care ADL[b]	Permanently discontinue	
	Grade 4: • Life-threatening consequences • Urgent intervention indicated		
Hepatitis	Grade 1: ALT/AST ≤ 3x ULN or total bilirubin ≤1.5x ULN	None	None
	Grade 2: ALT or AST >3-5x ULN or total bilirubin >1.5xULN	Withold dose[a]	Initial dose of 1 mg/kg/day to 2 mg/kg/day prednisone or equivalent followed by a taper
	Grade 3: ALT or AST ≤8x ULN or total bilirubin ≤5x ULN		
	Grade 3: ALT or AST >8x ULN or total bilirubin >5x ULN	Permanently discontinue	
	Grade 4: concurrent ALT or AST>3x ULN or total bilirubin >2x ULN with no other cause		

Immune mediated adverse reaction	Severity	IMFINZI treatment modification	Corticosteroid treatment unless otherwise specified
Hypothyroidism	Grade 1: Asymptomatic Clinical or diagnostic observations only Intervention not indicated	None	None
	Grade 2: Symptomatic Thyroid replacement indicated Limiting instrumental ADL[c]	No change	Initiate thyroid hormone replacement as clinically indicated
	Grade 3: Severe symptoms Limiting self-care ADL[b] Hospitalization indicated		
	Grade 4: Life-threatening consequences Urgent intervention indicated		
Hyperthyroidism	Grade 1: Asymptomatic Clinical or diagnostic observations only Intervention not indicated	None	None
	Grade 2: Symptomatic Thyroid suppression therapy indicated Limiting instrumental ADL[c]	Withold until clinically stable	Symptomatic management
	Grade 3: Severe symptoms Limiting self-care ADL[b] Hospitalization indicated		
	Grade 4: Life-threatening consequences Urgent intervention indicated		
Adrenal insufficiency	Grade 1: Asymptomatic Clinical or diagnostic observations only Intervention not indicated	None	None
	Grade 2: Moderate symptoms Medical intervention indicated	Withold dose until clinically stable	Initial dose of 1 mg/kg/day to 2 mg/kg/day prednisone or equivalent followed by a taper and hormone replacement therapy as clinically indicated

Immune mediated adverse reaction	Severity	IMFINZI treatment modification	Corticosteroid treatment unless otherwise specified
Adrenal insufficiency	Grade 3: Severe symptoms Hospitalization indicated	Withold dose until clinically stable	Initial dose of 1 mg/kg/day to 2 mg/kg/day prednisone or equivalent followed by a taper and hormone replacement therapy as clinically indicated
	Grade 4: Life-threatening consequences Urgent intervention indicated		
Hypophysitis/ hypopituitarism[e]	Grade 1: • Asymptomatic or mild symptoms clinical or diagnostic observations only • Intervention not indicated	None	
	Grade 2: • Moderate • Minimal, local, or noninvasive intervention indicated • Limiting age appropriate instrumental ADL[c]	Withold dose until clinically stable	Initial dose of 1 mg/kg/day to 2 mg/kg/day prednisone or equivalent followed by a taper and hormone replacement therapy as indicated
	Grade 3: • Severe or medically significant, but not immediately life threatening • Hospitalization or prolongation of existing hospitalization indicated • Disabling • Limiting self-care ADL[b]		
	Grade 4: • Life-threatening consequences • Urgent intervention indicated		

Immune mediated adverse reaction	Severity	IMFINZI treatment modification	Corticosteroid treatment unless otherwise specified
Type 1 Diabetes mellitus[f]	Grade 1: • Fasting glucose value >ULN –160 mg/dL • Fasting glucose value >ULN –8.9 mmol/L	None	
	Grade 2: • Fasting glucose value >160–250 mg/dL • Fasting glucose value >8.9–13.9 mmol/L	Withold dose until clinically stable	Initiate treatment with insulin as clinically indicated
	Grade 3: • >250–500 mg/dL • >13.9–27.8 mmol/L • Hospitalization indicated		
	Grade 4: • >500 mg/dL • >27.8 mmol/L • Life-threatening consequences		
Nephritis	Grade 1: Nephritis[d] • Asymptomatic or mild symptoms • Clinical or diagnostic observations only • Intervention not indicated • With creatinine • ≤1.5x ULN	None	
	Grade 2: Nephritis[d] • Moderate, local, or non-invasive intervention indicated • Limiting instrumental ADLc • With creatinine • >1.5–3x ULN	Withold dose[a]	Initial dose of 1 mg/kg/day to 2 mg/kg/day prednisone or equivalent followed by a taper

Immune mediated adverse reaction	Severity	IMFINZI treatment modification	Corticosteroid treatment unless otherwise specified
Nephritis	Grade 3: • Severe or medically significant, but not immediately life threatening • Hospitalization or prolongation of existing hospitalization indicated • Disabling • Limiting self-care ADLb • With creatinine • >3–6x ULN	Permanently discontinue	Initial dose of 1 mg/kg/day to 2 mg/kg/day prednisone or equivalent followed by a taper
	Grade 4: • Life-threatening consequences • Urgent intervention indicated • With creatinine • >6x ULN		
Rash or dermatitis	Grade 1: • Covering <10% BSA	None	
	Grade 2 for > 1 week • Covering 10%–30% BSA	Withold dose[a]	Initial dose of 1 mg/kg/day to 2 mg/kg/day prednisone or equivalent followed by a taper
	Grade 3: • Covering >30% BSA		
	Grade 4: • Covering >30% BSA • Life-threatening consequences • Urgent intervention needed	Permanently discontinue	

Immune mediated adverse reaction	Severity	IMFINZI treatment modification	Corticosteroid treatment unless otherwise specified
Myocarditis	Grade 1: • Asymptomatic with laboratory or cardiac imaging abnormalities (e.g., BNP [B-Natriuretic Peptide])	None	
	Grade 2: • Symptoms with mild to moderate activity or exertion	None	
	Grade 3: • Severe with symptoms at rest or with minimal activity or exertion; • Intervention indicated	Withold dose[a]	Initial dose of 1 mg/kg/day to 2 mg/kg/day prednisone or equivalent followed by a taper and hormone replacement therapy as indicated
	Grade 4: • Life-threatening consequences • Urgent intervention indicated (e.g., • continuous IV therapy or mechanical hemodynamic support)	Permenantly discontinue	
Other	Grade 1	None	Symptomatic management
	Grade 2		
	Grade 3	Withold until ≤ Grade 1 or resolved and corticosteroid dose is prednisone 10 mg equivalent or less	
	Grade 4	Permanently discontinue	

Immune mediated adverse reaction	Severity	IMFINZI treatment modification	Corticosteroid treatment unless otherwise specified
Infusion related infections	Grade 1 :Mild transient reaction; infusion interruption not indicated; intervention not indicated	Interrupt or slow the rate of infusion	May consider pre-medications for prophylaxis of subsequent infusion reactions
	Grade 2: Therapy or infusion interruption indicated but responds promptly to symptomatic treatment (e.g., antihistamines, NSAIDS, narcotics, IV fluids); prophylactic medications indicated for <=24 hrs		
	Grade 3: Prolonged (e.g., not rapidly responsive to symptomatic medication and/ or brief interruption of infusion); recurrence of symptoms following initial improvement; hospitalization indicated for clinical sequelae	Permanently discontinue	
	Grade 4 Life-threatening consequences; urgent intervention indicated		

ADL: activities of daily living, BSA: Body surface area

[a]Consider increasing dose of corticosteroids and/or using other systemic immunosuppressants if there is worsening or no improvement. Upon improvement to ≤Grade 1, corticosteroid taper should be initiated and continued over at least 1 month. For ADRs that do not result in permanent discontinuation resume treatment if the adverse reactions improve to ≤Grade 1 and the corticosteroid dose has been reduced to ≤10 mg prednisone or equivalent per day.

[b]Self-care ADL refer to bathing, dressing and undressing, self-feeding, using the toilet, taking medications, and not being bedridden.

[c] Instrumental ADL refer to preparing meals, shopping for groceries or clothes, using the telephone, managing money, etc.

[d]If no improvement within 3 to 5 days despite corticosteroids, promptly start additional immunosuppressive therapy. Upon resolution (Grade 0), corticosteroid taper should be initiated and continued over at least 1 month, after which IMFINZI can be resumed based on clinical judgment.

[d]Permanently discontinue if adverse reaction does not resolve to ≤Grade 1 within 30 days or if there are signs of respiratory insufficiency.

The reference from witch the grad is taken from is “CTCAE V 4.03”

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