

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use IMJUDO safely and effectively. See full prescribing information for IMJUDO.

IMJUDO® (tremelimumab-actl) injection, for intravenous use
Initial U.S. Approval: 2022

INDICATIONS AND USAGE

IMJUDO is a cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4) blocking antibody indicated in combination with durvalumab, for the treatment of adult patients with unresectable hepatocellular carcinoma (uHCC). (1.1)

DOSAGE AND ADMINISTRATION

- Administer IMJUDO as an intravenous infusion over 60 minutes after dilution. (2.3)
- uHCC:
 - Weight 30 kg and more: IMJUDO 300 mg as a single dose in combination with durvalumab 1,500 mg at Cycle 1/Day 1, followed by durvalumab as a single agent every 4 weeks (2.1)
 - Weight less than 30 kg: IMJUDO 4 mg/kg as a single dose in combination with durvalumab 20 mg/kg at Cycle 1/Day 1, followed by durvalumab as a single agent every 4 weeks (2.1)
- See full Prescribing Information for preparation and administration instructions and dosage modifications for adverse reactions.

DOSAGE FORMS AND STRENGTHS

- Injection: 25 mg/1.25 mL (20 mg/mL) solution in a single-dose vial. (3)
- Injection: 300 mg/15 mL (20 mg/mL) solution in a single-dose vial. (3)

CONTRAINDICATIONS

None. (4)

WARNINGS AND PRECAUTIONS

- Immune-Mediated Adverse Reactions (5.1)
 - Immune-mediated adverse reactions, which may be severe or fatal, can occur in any organ system or tissue, including the following:

immune-mediated pneumonitis, immune-mediated colitis, immune-mediated hepatitis, immune-mediated endocrinopathies, immune-mediated dermatologic adverse reactions, immune-mediated nephritis with renal dysfunction and immune-mediated pancreatitis.

- Monitor for early identification and management. Evaluate liver enzymes, creatinine, adrenocorticotropic hormone level and thyroid function at baseline and before each dose.
- Withhold or permanently discontinue based on severity and type of reaction.
- Infusion-Related Reactions: Interrupt, slow the rate of infusion, or permanently discontinue treatment based on the severity of the reaction. (5.2)
- Embryo-Fetal Toxicity: Can cause fetal harm. Advise females of reproductive potential of the potential risk to a fetus and use of effective contraception. (5.3, 8.1, 8.3)

ADVERSE REACTIONS

Most common adverse reactions ($\geq 20\%$) of patients with uHCC are rash, diarrhea, fatigue, pruritus, musculoskeletal pain, and abdominal pain. Most common laboratory abnormalities ($\geq 40\%$) of patients with uHCC are AST increased, ALT increased, hemoglobin decreased, sodium decreased, bilirubin increased, alkaline phosphatase increased, and lymphocytes decreased. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact AstraZeneca at 1-800-236-9933 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

USE IN SPECIFIC POPULATIONS

Lactation: Advise not to breastfeed. (8.2)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide

Issued: 10/2022

FULL PRESCRIBING INFORMATION: CONTENTS*

1 INDICATIONS AND USAGE

1.1 Hepatocellular Carcinoma

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Dosage for Unresectable Hepatocellular Carcinoma

2.2 Dosage Modifications for Adverse Reactions

2.3 Preparation and Administration

3 DOSAGE FORMS AND STRENGTHS

4 CONTRAINDICATIONS

5 WARNINGS AND PRECAUTIONS

5.1 Severe and Fatal Immune-Mediated Adverse Reactions

5.2 Infusion-Related Reactions

5.3 Embryo-Fetal Toxicity

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

8.2 Lactation

8.3 Females and Males of Reproductive Potential

8.4 Pediatric Use

8.5 Geriatric Use

11 DESCRIPTION

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

12.2 Pharmacodynamics

12.3 Pharmacokinetics

12.6 Immunogenicity

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

14 CLINICAL STUDIES

14.1 Hepatocellular Carcinoma (HCC)

16 HOW SUPPLIED/STORAGE AND HANDLING

17 PATIENT COUNSELING INFORMATION

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

1.1 Hepatocellular Carcinoma

IMJUDO in combination with durvalumab is indicated for the treatment of adult patients with unresectable hepatocellular carcinoma (uHCC).

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Dosage for Unresectable Hepatocellular Carcinoma

The recommended dosage of IMJUDO is presented in Table 1.

Administer IMJUDO as an intravenous infusion after dilution as recommended [*see [Dosage and Administration \(2.3\)](#)*].

Table 1. Recommended dosage of IMJUDO

Indication	Recommended IMJUDO Dosage	Duration of Therapy
uHCC	<p><u>Patients with a body weight of 30 kg and more:</u></p> <ul style="list-style-type: none">• A single dose of IMJUDO¹ 300 mg followed by durvalumab² 1,500 mg at Day 1 of Cycle 1;• Continue durvalumab 1,500 mg as a single agent every 4 weeks <p><u>Patients with a body weight of less than 30 kg:</u></p> <ul style="list-style-type: none">• A single dose of IMJUDO¹ 4 mg/kg followed by durvalumab² 20 mg/kg at Day 1 of Cycle 1;• Continue durvalumab 4 mg/kg as a single agent every 4 weeks	After Cycle 1 of combination therapy, administer durvalumab as a single agent every 4 weeks until disease progression or unacceptable toxicity

¹ Administer IMJUDO prior to durvalumab on the same day.

² Refer to the Prescribing Information for durvalumab dosing information

2.2 Dosage Modifications for Adverse Reactions

No dose reduction for treatment is recommended. In general, withhold treatment regimen for severe (Grade 3) immune-mediated adverse reactions. Permanently discontinue treatment regimen for life-threatening (Grade 4) immune-mediated adverse reactions, recurrent severe (Grade 3) immune-mediated reactions that require systemic immunosuppressive treatment, or an inability to reduce corticosteroid dose to 10 mg or less of prednisone or equivalent per day within 12 weeks of initiating corticosteroids.

Recommended treatment modifications are presented in Table 2.

Table 2. Recommended Dosage Modifications for Adverse Reactions

Adverse Reaction	Severity ¹	Dosage Modification
Immune-Mediated Adverse Reactions [<i>see Warnings and Precautions (5.1)</i>]		
Pneumonitis	Grade 2	Withhold ²
	Grade 3 or 4	Permanently discontinue
Colitis	Grade 2	Withhold ²
	Grade 3 or 4	Permanently discontinue
Intestinal perforation	Any grade	Permanently discontinue
Hepatitis with no tumor involvement of the liver	ALT or AST increases to more than 3 and up to 8 times the ULN or total bilirubin increases to more than 1.5 and up to 3 times ULN	Withhold ²
	ALT or AST increases to more than 8 times ULN or total bilirubin increases to more than 3 times the ULN	Permanently discontinue
Hepatitis with tumor involvement of the liver ³	AST or ALT is more than 1 and up to 3 times ULN at baseline and increases to more	Withhold ²

Adverse Reaction	Severity ¹	Dosage Modification
	than 5 and up to 10 times ULN or AST or ALT is more than 3 and up to 5 times ULN at baseline and increases to more than 8 and up to 10 times ULN	
	AST or ALT increases to more than 10 times ULN or Total bilirubin increases to more than 3 times ULN	Permanently discontinue
Endocrinopathies	Grade 3 or 4	Withhold until clinically stable or permanently discontinue depending on severity
Nephritis with Renal Dysfunction	Grade 2 or 3 increased blood creatinine	Withhold ²
	Grade 4 increased blood creatinine	Permanently discontinue
Exfoliative Dermatologic Conditions	Suspected SJS, TEN, or DRESS	Withhold ²
	Confirmed SJS, TEN, or DRESS	Permanently discontinue
Myocarditis	Grade 2, 3, or 4	Permanently discontinue
Neurological Toxicities	Grade 2	Withhold ²
	Grade 3 or 4	Permanently discontinue
Other Adverse Reactions		
Infusion-related reactions [<i>see Warnings and Precautions (5.2)</i>]	Grade 1 or 2	Interrupt or slow the rate of infusion
	Grade 3 or 4	Permanently discontinue

ALT = alanine aminotransferase, AST = aspartate aminotransferase, DRESS = Drug Rash with Eosinophilia and Systemic Symptoms, SJS = Stevens Johnson Syndrome, TEN = toxic epidermal necrolysis, ULN = upper limit normal

¹ Based on National Cancer Institute Common Terminology Criteria for Adverse Events, version 4.03.

² Resume in patients with complete or partial resolution (Grade 0 to 1) after corticosteroid taper. Permanently discontinue if no complete or partial resolution within 12 weeks of initiating steroids or an inability to reduce corticosteroid dose to 10 mg of prednisone or less per day (or equivalent) within 12 weeks of initiating corticosteroids.

³ If AST and ALT are less than or equal to ULN at baseline in patients with liver involvement, withhold or permanently discontinue durvalumab based on recommendations for hepatitis with no liver involvement.

2.3 Preparation and Administration

Preparation

- Visually inspect drug product for particulate matter and discoloration. Discard if the solution is cloudy, discolored, or visible particles are observed.
- Do not shake the vial.
- Withdraw the required volume from the vial(s) of IMJUDO and transfer into an intravenous bag containing 0.9% Sodium Chloride Injection, USP or 5% Dextrose Injection, USP. Mix diluted solution by gentle inversion. Do not shake the solution. The maximum final concentration of the diluted solution should not exceed 10 mg/mL. The total volume of diluent for use with each dose and patient weight is presented in Table 3.
- Discard partially used or empty vial(s) of IMJUDO.

Table 3. IMJUDO Infusion Conditions

Dose	Patient Weight	Maximum diluent volume
300 mg	≥ 30 kg	150 mL
4 mg/kg	< 30 kg	80 mL

Storage of Diluted IMJUDO

- IMJUDO does not contain a preservative. Administer infusion solution immediately once prepared. If infusion solution is not administered immediately and needs to be stored, the total time from preparation to the start of administration should not exceed:
 - 24 hours in a refrigerator at 2°C to 8°C (36°F to 46°F)
 - 24 hours at room temperature up to 30°C (86°F)
- Do not freeze.
- Do not shake.

Administration

- Administer IMJUDO infusion solution intravenously over 60 minutes through an intravenous line containing a sterile, low-protein binding 0.2 or 0.22 micron filter.
- Observe patient for 60 minutes following completion of IMJUDO infusion [*see [Warnings and Precautions \(5.2\)](#)*]. Then administer durvalumab as a separate intravenous infusion over 60 minutes on the same day.
- Use separate infusion bags and filters for each infusion.
- Do not co-administer other drugs through the same infusion line.

3 DOSAGE FORMS AND STRENGTHS

Injection: 25 mg/1.25 mL (20 mg/mL) or 300 mg/15 mL (20 mg/mL) clear to slightly opalescent, colorless to slightly yellow solution in a single-dose vial.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Severe and Fatal Immune-Mediated Adverse Reactions

IMJUDO is a monoclonal antibody that blocks T-cell inhibitory signals induced by the CTLA-4 pathway, thereby removing inhibition of the immune response. In combination with durvalumab, a PD-L1 inhibitor, these drugs have the potential for induction of immune-mediated adverse reactions. Immune-mediated adverse reactions listed herein may not be inclusive of 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 IMJUDO in combination with durvalumab. While immune-mediated adverse reactions usually manifest during treatment, immune-mediated adverse reactions can also manifest after discontinuation of IMJUDO and/or durvalumab.

Early identification and management of immune-mediated adverse reactions are essential to ensure safe use of IMJUDO in combination with durvalumab. Monitor for signs and symptoms that may be clinical manifestations of underlying immune-mediated adverse reactions. Evaluate clinical chemistries including liver enzymes, creatinine, adrenocorticotropic hormone (ACTH) level, and thyroid function at baseline and before each dose. Institute medical management promptly, including specialty consultation as appropriate.

Withhold or permanently discontinue IMJUDO and durvalumab depending on severity [*see [Dosage and Administration \(2.2\)](#)*]. In general, if combination of IMJUDO and durvalumab requires interruption or discontinuation, administer systemic corticosteroid therapy (1 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

IMJUDO in combination with durvalumab can cause immune-mediated pneumonitis, which may be fatal.

Immune-mediated pneumonitis occurred in 1.3% (5/388) of patients receiving IMJUDO in combination with durvalumab, including fatal (0.3%) and Grade 3 (0.2%) adverse reactions. Events resolved in 3 of

the 5 patients and resulted in permanent discontinuation in 1 patient. Systemic corticosteroids were required in all patients, of these 4 patients required high-dose corticosteroid treatment (at least 40 mg prednisone or equivalent per day). One patient (1/5) required other immunosuppressants.

Immune-Mediated Colitis

IMJUDO in combination with durvalumab can cause immune-mediated colitis 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 or diarrhea occurred in 6% (23/388) of patients receiving IMJUDO in combination with durvalumab, including Grade 3 (3.6%) adverse reactions. Events resolved in 22 of the 23 patients and resulted in permanent discontinuation in 5 patients. All patients received systemic corticosteroids, and 20 of the 23 patients received high-dose corticosteroid treatment (at least 40 mg prednisone or equivalent per day). Three patients also received other immunosuppressants.

Intestinal perforation has been observed in other studies of IMJUDO in combination with durvalumab.

Immune-Mediated Hepatitis

IMJUDO in combination with durvalumab can cause immune-mediated hepatitis, which may be fatal.

Immune-mediated hepatitis occurred in 7.5% (29/388) of patients receiving IMJUDO in combination with durvalumab, including fatal (0.8%), Grade 4 (0.3%), and Grade 3 (4.1%) adverse reactions. Events resolved in 12 of the 29 patients and resulted in permanent discontinuation in 9 patients. Systemic corticosteroids were required in all 29 patients and all 29 patients required high-dose corticosteroid treatment (at least 40 mg prednisone or equivalent per day). Eight patients (8/29) required other immunosuppressants.

Immune-Mediated Endocrinopathies

Adrenal Insufficiency: IMJUDO in combination with durvalumab 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 IMJUDO in combination with durvalumab based on the severity [see [Dosage and Administration \(2.2\)](#)].

Immune-mediated adrenal insufficiency occurred in 1.5% (6/388) of patients receiving IMJUDO in combination with durvalumab, including Grade 3 (0.3%) adverse reactions. Events resolved in 2 of the 6 patients. Systemic corticosteroids were required in all 6 patients and of these, 1 patient required high-dose corticosteroid treatment (at least 40 mg prednisone or equivalent per day).

Hypophysitis: IMJUDO in combination with durvalumab 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 IMJUDO in combination with durvalumab depending on severity [see [Dosage and Administration \(2.2\)](#)].

Immune-mediated hypophysitis/hypopituitarism occurred in 1% (4/388) of patients receiving IMJUDO in combination with durvalumab. Events resolved in 2 of the 4 patients. Systemic corticosteroids were required in 3 patients and of these, 1 patient received high-dose corticosteroid treatment (at least 40 mg prednisone or equivalent per day). Two patients also required endocrine therapy.

Thyroid Disorders: IMJUDO in combination with durvalumab 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 IMJUDO in combination with durvalumab based on the severity [see [Dosage and Administration \(2.2\)](#)].

Thyroiditis: Immune-mediated thyroiditis occurred in 1.5% (6/388) of patients receiving IMJUDO in combination with durvalumab. Events resolved in 2 of the 6 patients. Systemic corticosteroids were required in 2 patients (2/6) with immune-mediated thyroiditis, of these 1 patient required high-dose corticosteroid treatment (at least 40 mg prednisone or equivalent per day). All patients required other therapy including hormone replacement therapy, thiamazole, carbimazole, propylthiouracil, perchlorate, calcium channel blocker, or beta-blocker.

Hyperthyroidism: Immune-mediated hyperthyroidism occurred in 4.6% (18/388) of patients receiving IMJUDO in combination with durvalumab, including Grade 3 (0.3%) adverse reactions. Events resolved in 15 of the 18 patients. Two patients (2/18) required high-dose corticosteroid treatment (at least 40 mg prednisone or equivalent per day). Seventeen patients required other therapy (thiamazole, carbimazole, propylthiouracil, perchlorate, calcium channel blocker, or beta-blocker).

Hypothyroidism: Immune-mediated hypothyroidism occurred in 11% (42/388) of patients receiving IMJUDO in combination with durvalumab. Events resolved in 5 of the 42 patients. One patient received high-dose corticosteroid treatment (at least 40 mg prednisone or equivalent per day). All patients required other therapy (thiamazole, carbimazole, propylthiouracil, perchlorate, calcium channel blocker, or beta-blocker).

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 IMJUDO in combination with durvalumab based on the severity [see [Dosage and Administration \(2.2\)](#)].

Two patients (0.5%, 2/388) had events of hyperglycemia requiring insulin therapy that had not resolved at last follow-up.

Immune-Mediated Nephritis with Renal Dysfunction

IMJUDO in combination with durvalumab can cause immune-mediated nephritis.

Immune-mediated nephritis occurred in 1% (4/388) of patients receiving IMJUDO in combination with durvalumab, including Grade 3 (0.5%) adverse reactions. Events resolved in 3 of the 4 patients and resulted in permanent discontinuation in 2 patients. Systemic corticosteroids were required in all patients with immune-mediated nephritis, of these 3 patients required high-dose corticosteroid treatment (at least 40 mg prednisone or equivalent per day).

Immune-Mediated Dermatology Reactions

IMJUDO in combination with durvalumab can cause immune-mediated rash or dermatitis. Exfoliative dermatitis, including Stevens Johnson Syndrome (SJS), drug rash with eosinophilia and systemic symptoms (DRESS), and toxic epidermal necrolysis (TEN), has occurred with CTLA-4 and 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 IMJUDO in combination with durvalumab depending on severity [see [Dosage and Administration \(2.2\)](#)].

Immune-mediated rash or dermatitis occurred in 4.9% (19/388) of patients receiving IMJUDO in combination with durvalumab, including Grade 4 (0.3%) and Grade 3 (1.5%) adverse reactions. Events resolved in 13 of the 19 patients and resulted in permanent discontinuation in 2 patients. Systemic corticosteroids were required in all patients with immune-mediated rash or dermatitis, of these 12 patients required high-dose corticosteroid treatment (at least 40 mg prednisone or equivalent per day). One patient received other immunosuppressants.

Immune-Mediated Pancreatitis

IMJUDO in combination with durvalumab can cause immune-mediated pancreatitis.

Immune-mediated pancreatitis occurred in 2.3% (9/388) of patients receiving IMJUDO in combination with durvalumab, including Grade 4 (0.3%) and Grade 3 (1.5%) adverse reactions. Events resolved in 6 of the 9 patients. Systemic corticosteroids were required in all 9 patients and of these, 7 patients required high-dose corticosteroid treatment (at least 40 mg prednisone or equivalent per day).

Other Immune-Mediated Adverse Reactions

The following clinically significant, immune-mediated adverse reactions occurred at an incidence of less than 1% each in patients who received IMJUDO in combination with durvalumab or were reported with the use of other immune-checkpoint inhibitors.

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: Gastritis, duodenitis.

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

Endocrine: Hypoparathyroidism.

Other (hematologic/immune): Hemolytic anemia, aplastic anemia, hemophagocytic lymphohistiocytosis, systemic inflammatory response syndrome, histiocytic necrotizing lymphadenitis (Kikuchi lymphadenitis), sarcoidosis, and immune thrombocytopenia.

5.2 Infusion-Related Reactions

IMJUDO in combination with durvalumab 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 IMJUDO and durvalumab based on the severity [see [Dosage and Administration \(2.2\)](#)]. For Grade 1 or 2 infusion-related reactions, consider using pre-medications with subsequent doses.

Infusion-related reactions occurred in 10 (2.6%) patients receiving IMJUDO in combination with durvalumab.

5.3 Embryo-Fetal Toxicity

Based on findings from animal studies and its mechanism of action, IMJUDO can cause fetal harm when administered to a pregnant woman. In animal studies, CTLA-4 blockade is associated with higher incidence of pregnancy loss.

Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with IMJUDO and for 3 months after the last dose of IMJUDO [see [Use in Specific Populations \(8.1, 8.3\)](#)].

6 ADVERSE REACTIONS

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

- Immune-Mediated Adverse Reactions [see [Warnings and Precautions \(5.1\)](#)].
- Infusion-Related Reactions [see [Warnings and Precautions \(5.2\)](#)].

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Hepatocellular Carcinoma

The safety of IMJUDO administered in combination with durvalumab was evaluated in a total of 388 patients with uHCC in HIMALAYA, a randomized, open-label, multicenter study [see [Clinical Studies \(14.1\)](#)]. Patients received IMJUDO 300 mg administered as a single intravenous infusion in combination with durvalumab 1,500 mg on the same day, followed by durvalumab every 4 weeks or sorafenib 400 mg given orally twice daily.

Serious adverse reactions occurred in 41% of patients who received IMJUDO in combination with durvalumab. Serious adverse reactions in > 1% of patients included hemorrhage (6%), diarrhea (4%),

sepsis (2.1%), pneumonia (2.1%), rash (1.5%), vomiting (1.3%), acute kidney injury (1.3%), and anemia (1.3%). Fatal adverse reactions occurred in 8% of patients who received IMJUDO in combination with durvalumab, including death (1%), hemorrhage intracranial (0.5%), cardiac arrest (0.5%), pneumonitis (0.5%), hepatic failure (0.5%), and immune-mediated hepatitis (0.5%). The most common adverse reactions (occurring in $\geq 20\%$ of patients) were rash, diarrhea, fatigue, pruritus, musculoskeletal pain, and abdominal pain.

Permanent discontinuation of the treatment regimen due to an adverse reaction occurred in 14% of patients; the most common adverse reactions leading to treatment discontinuation ($\geq 1\%$) were hemorrhage (1.8%), diarrhea (1.5%), AST increased (1%), and hepatitis (1%).

Dosage interruptions or delay of the treatment regimen due to an adverse reaction occurred in 35% of patients. Adverse reactions which required dosage interruption or delay in $\geq 1\%$ of patients included ALT increased (3.6%), diarrhea (3.6%), rash (3.6%), amylase increased (3.4%), AST increased (3.1%), lipase increased (2.8%), pneumonia (1.5%), hepatitis (1.5%), pyrexia (1.5%), anemia (1.3%), thrombocytopenia (1%), hyperthyroidism (1%), pneumonitis (1%), and blood creatinine increased (1%).

Table 4 summarizes the adverse reactions that occurred in patients treated with IMJUDO in combination with durvalumab in the HIMALAYA study.

Table 4. Adverse Reactions Occurring in $\geq 10\%$ Patients in the HIMALAYA study

Adverse Reaction	IMJUDO and Durvalumab (N=388)		Sorafenib (N=374)	
	All Grades (%)	Grade 3-4 (%)	All Grades (%)	Grade 3-4 (%)
Gastrointestinal disorders				
Diarrhea ¹	27	6	45	4.3
Abdominal pain ¹	20	1.8	24	4
Nausea	12	0	14	0
Skin and subcutaneous tissue disorders				
Rash ¹	32	2.8	57	12
Pruritus	23	0	6	0.3
Metabolism and nutrition disorders				
Decreased appetite	17	1.3	18	0.8
General disorders and administration site conditions				
Fatigue ¹	26	3.9	30	6

Adverse Reaction	IMJUDO and Durvalumab (N=388)		Sorafenib (N=374)	
	All Grades (%)	Grade 3-4 (%)	All Grades (%)	Grade 3-4 (%)
Pyrexia ¹	13	0.3	9	0.3
Psychiatric disorders				
Insomnia	10	0.3	4.3	0
Endocrine disorders				
Hypothyroidism ¹	14	0	6	0
Musculoskeletal and Connective Tissue Disorders				
Musculoskeletal pain ¹	22	2.6	17	0.8

¹ Represents a composite of multiple related terms.

Table 5 summarizes the laboratory abnormalities that occurred in patients treated with IMJUDO in combination with durvalumab in the HIMALAYA study.

Table 5. Laboratory Abnormalities Worsening from Baseline Occurring in $\geq 20\%$ of Patients in the HIMALAYA study

Laboratory Abnormality	IMJUDO and Durvalumab		Sorafenib	
	Any grade ¹ (%) ²	Grade 3 ¹ or 4 (%) ²	Any grade ¹ (%) ²	Grade 3 ¹ or 4 (%) ²
Chemistry				
Aspartate Aminotransferase increased	63	27	55	21
Alanine Aminotransferase increased	56	18	53	12
Sodium decreased	46	15	40	11
Bilirubin increased	41	8	47	11
Alkaline Phosphatase increased	41	8	44	5
Glucose increased	39	14	29	4

Laboratory Abnormality	IMJUDO and Durvalumab		Sorafenib	
	Any grade ¹ (%) ²	Grade 3 ¹ or 4 (%) ²	Any grade ¹ (%) ²	Grade 3 ¹ or 4 (%) ²
Calcium decreased	34	0	43	0.3
Albumin decreased	31	0.5	37	1.7
Potassium increased	28	3.8	21	2.6
Creatinine increased	21	1.3	15	0.9
Hematology				
Hemoglobin decreased	52	4.8	40	6
Lymphocytes decreased	41	11	39	10
Platelets decreased	29	1.6	35	3.1
Leukocytes decreased	20	0.8	30	1.1

¹ Graded according to NCI CTCAE version 4.03.

² Each test incidence is based on the number of patients who had both baseline and at least one on-study laboratory measurement available: IMJUDO with durvalumab (range: 367-378) and sorafenib (range: 344-352).

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk summary

Based on findings from animal studies and its mechanism of action, IMJUDO can cause fetal harm when administered to a pregnant woman [see [Clinical Pharmacology \(12.1\)](#)]. There are no available data on the use of IMJUDO in pregnant women. In animal studies, CTLA-4 blockade is associated with increased risk of immune-mediated rejection of the developing fetus and fetal death (see *Data*).

Human immunoglobulin G2 (IgG2) is known to cross the placental barrier; therefore, IMJUDO has the potential to be transmitted from the mother to the developing fetus. Advise pregnant women and females of reproductive potential of the potential risk to a fetus.

In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Data

Animal Data

In reproduction studies, administration of tremelimumab-actl to pregnant cynomolgus monkeys during the period of organogenesis through delivery was not associated with maternal toxicity or effects on embryo-fetal development at exposure levels approximately 31-times higher than those observed at a recommended dose of 300 mg (based on AUC). CTLA-4 plays a role in maintaining maternal immune tolerance to the fetus to preserve pregnancy and in immune regulation of the newborn. In a murine model of pregnancy, CTLA-4 blockade resulted in increased resorptions and reduced live fetuses. Mated genetically engineered mice heterozygous for CTLA-4 (CTLA-4+/-) gave birth to CTLA-4+/- offspring and offspring deficient in CTLA-4 (homozygous negative, CTLA-4-/-) that appeared healthy at birth. The CTLA-4-/- homozygous negative offspring developed signs of a lymphoproliferative disorder and died by 3 to 4 weeks of age with multiorgan tissue destruction. Based on its mechanism of action, fetal exposure to tremelimumab-actl may increase the risk of developing immune-mediated disorders or altering the normal immune response.

8.2 Lactation

Risk Summary

There are no data on the presence of tremelimumab-actl in human milk, its effects on a breastfed child, or on milk production. Maternal IgG is known to be present in human milk. The effects of local gastrointestinal exposure and limited systemic exposure in the breastfed child to IMJUDO are unknown. Because of the potential for serious adverse reactions in the breastfed child, advise women not to breastfeed during treatment with IMJUDO and for 3 months after the last dose. Refer to the Prescribing Information for agents administered in combination with IMJUDO for breastfeeding recommendations, as appropriate.

8.3 Females and Males of Reproductive Potential

IMJUDO can cause fetal harm when administered to a pregnant woman [*see [Use in Specific Populations \(8.1\)](#)*].

Pregnancy Testing

Verify pregnancy status of females of reproductive potential prior to initiating treatment with IMJUDO.

Contraception

Advise females of reproductive potential to use effective contraception during treatment with IMJUDO and for 3 months after the last dose. Refer to the Prescribing Information for the agents administered in combination with IMJUDO for recommended contraception duration, as appropriate

8.4 Pediatric Use

The safety and effectiveness of tremelimumab-actl have not been established in pediatric patients.

8.5 Geriatric Use

Of the 393 patients with uHCC treated with IMJUDO in combination with durvalumab, 50% of patients were 65 years or older and 13% of patients were 75 years or older. No overall differences in safety or efficacy of IMJUDO have been observed between patients 65 years or older and younger adult patients.

11 DESCRIPTION

Tremelimumab-actl, a cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4) blocking human IgG2 monoclonal antibody, is produced by recombinant DNA technology in NS0 cell suspension culture and has a molecular weight of 149 kDa.

IMJUDO (tremelimumab-actl) injection is a sterile, preservative-free, clear to slightly opalescent, colorless to slightly yellow solution in a single-dose vial for intravenous infusion after dilution. IMJUDO contains tremelimumab-actl at a concentration of 20 mg/mL in either a 25 mg/1.25 mL or a 300 mg/15 mL single-dose vial.

Each mL contains 20 mg of tremelimumab-actl, and edetate disodium (0.09 mg), histidine (0.68 mg), L-histidine hydrochloride monohydrate (3.3 mg), polysorbate 80 (0.2 mg), trehalose (76 mg), and Water for Injection, USP. The pH is approximately 5.5.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

CTLA-4 is a negative regulator of T-cell activity. Tremelimumab-actl is a monoclonal antibody that binds to CTLA-4 and blocks the interaction with its ligands CD80 and CD86, releasing CTLA-4-mediated inhibition of T-cell activation. In synergistic mouse tumor models, blocking CTLA-4 activity resulted in decreased tumor growth and increased proliferation of T cells in tumors.

12.2 Pharmacodynamics

The exposure-response relationship and time course of pharmacodynamic response for the safety and effectiveness of tremelimumab-actl have not been fully characterized.

12.3 Pharmacokinetics

The pharmacokinetics of tremelimumab-actl was studied in patients with other solid tumors following administration of doses 1 mg/kg, 3 mg/kg, and 10 mg/kg (1- to 10-times the approved recommended dosage) administered once every 4 weeks for 4 doses. The pharmacokinetics of tremelimumab-actl as a single dose of 300 mg were evaluated in patients with HCC.

The AUC of tremelimumab-actl increased proportionally from 1 mg/kg to 10 mg/kg every 4 weeks (1 to 10-times the approved recommended dosage) and steady state was achieved at approximately 12 weeks.

Distribution

The geometric mean (% coefficient of variation [CV%]) of tremelimumab-actl for central (V1) and peripheral (V2) volume of distribution was 3.45 (24%) and 2.66 (34%) L, respectively.

Elimination

The geometric mean (CV%) terminal half-life of tremelimumab-actl was 16.9 days (19%) after a single dose and 18.2 days (19%) during steady state. The geometric mean (CV%) clearance of tremelimumab-actl was 0.286 L/day (32%) after a single dose and 0.263 L/day (32%) during steady state.

Specific Populations

There were no clinically significant differences in the pharmacokinetics of tremelimumab-actl based on body weight (34 to 149 kg), age (18 to 87 years), sex, race (White, Black, Asian, Native Hawaiian, Pacific Islander, or American Indian), serum albumin levels (0.3 to 396 g/L), lactate dehydrogenase levels (12 to 5570 U/L), soluble PD-L1 (67 to 349 pg/mL), organ dysfunction including mild to moderate renal impairment (CLcr 30 to 89 mL/min), and mild to moderate hepatic impairment (bilirubin < 3 x ULN and any AST).

The effect of severe renal impairment (CLcr 15 to 29 mL/min) or severe hepatic impairment (bilirubin > 3 x ULN and any AST) on the pharmacokinetics of tremelimumab-actl is unknown.

12.6 Immunogenicity

The observed incidence of anti-drug antibodies (ADA) is highly dependent on the sensitivity and specificity of the assay. Differences in assay methods preclude meaningful comparisons of the incidence of ADA in the studies described below with the incidence of ADA in other studies, including those of tremelimumab-actl.

In the HIMALAYA study, of the 182 patients who were treated with a single dose of tremelimumab-actl in combination with durvalumab once in every 4 weeks therapy and evaluable for the presence of ADAs against tremelimumab-actl at predose week 0 and week 4, 11% (20/182) of patients tested positive for anti-tremelimumab-actl antibodies. Among the 20 patients who tested positive for ADAs 40% (8/20) tested positive for neutralizing antibodies against tremelimumab-actl. There was no identified clinically significant effect of anti-tremelimumab antibodies on the pharmacokinetics or safety of tremelimumab-actl; however, the effect of ADAs and neutralizing antibodies on the effectiveness of tremelimumab-actl is unknown.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

The carcinogenic and genotoxic potential of tremelimumab-actl have not been evaluated.

Animal fertility studies have not been conducted with tremelimumab-actl.

14 CLINICAL STUDIES

14.1 Hepatocellular Carcinoma (HCC)

The efficacy of IMJUDO in combination with durvalumab was evaluated in the HIMALAYA study (NCT03298451), a randomized (1:1:1), open-label, multicenter study in patients with confirmed uHCC who had not received prior systemic treatment for HCC. Patients were randomized to one of two investigational arms (IMJUDO plus durvalumab or durvalumab) or sorafenib. Study treatment consisted of IMJUDO as a one-time single intravenous infusion of 300 mg in combination with durvalumab 1,500 mg on the same day, followed by durvalumab every 4 weeks; durvalumab 1,500 mg every 4 weeks (an unapproved regimen for uHCC); or sorafenib 400 mg given orally twice daily, until disease progression or unacceptable toxicity. The efficacy assessment of IMJUDO is based on patients randomized to the IMJUDO plus durvalumab arm versus the sorafenib arm. Randomization was stratified by macrovascular

invasion (MVI) (yes or no), etiology of liver disease (hepatitis B virus vs. hepatitis C virus vs. others) and ECOG performance status (0 vs. 1).

The study enrolled patients with BCLC Stage C or B (not eligible for locoregional therapy). The study excluded patients with co-infection of viral hepatitis B and hepatitis C; active or prior documented gastrointestinal (GI) bleeding within 12 months; ascites requiring non-pharmacologic intervention within 6 months; hepatic encephalopathy within 12 months before the start of treatment; active or prior documented autoimmune or inflammatory disorders. Esophagogastroduodenoscopy was not mandated prior to enrollment but adequate endoscopic therapy, according to institutional standards, was required for patients with a history of esophageal variceal bleeding or those assessed as high risk for esophageal variceal bleeding by the treating physician.

Study treatment was permitted beyond disease progression if the patient was clinically stable and was deriving clinical benefit as determined by the investigator.

The major efficacy outcome measure was overall survival (OS) between the IMJUDO plus durvalumab arm versus the sorafenib arm. Additional efficacy outcomes were investigator-assessed progression-free survival (PFS), objective response rate (ORR) and duration of response (DoR) according to RECIST v1.1. Tumor assessments were conducted every 8 weeks for the first 12 months and then every 12 weeks thereafter.

The baseline demographics of the IMJUDO plus durvalumab and sorafenib arms were as follows: male (85%), age < 65 years (50%), median age of 65 years (range: 18 to 88 years), White (46%), Asian (49%), Black or African American (2%), Native Hawaiian or other Pacific Islander (0.1%), race Unknown (2%), Hispanic or Latino (5%), Not Hispanic or Latino (94%), ethnicity Unknown (1%), ECOG PS 0 (62%); Child-Pugh Class score A (99%), macrovascular invasion (26%), extrahepatic spread (53%), viral etiology hepatitis B (31%), hepatitis C (27%), uninfected (42%).

Efficacy results are presented in Table 6 and Figure 1.

Table 6. Efficacy Results for HIMALAYA Study

Endpoint	IMJUDO and Durvalumab (N=393)	Sorafenib (N=389)
OS		
Number of deaths (%)	262 (66.7)	293 (75.3)
Median OS (months) (95% CI)	16.4 (14.2, 19.6)	13.8 (12.3, 16.1)
HR (95% CI) ¹	0.78 (0.66, 0.92)	
p-value ^{2,3}	0.0035	
PFS		
Number of events (%)	335 (85.2)	327 (84.1)
Median PFS (months) (95% CI)	3.8 (3.7, 5.3)	4.1 (3.7, 5.5)
HR (95% CI) ¹	0.90 (0.77, 1.05)	

Endpoint	IMJUDO and Durvalumab (N=393)	Sorafenib (N=389)
ORR		
ORR % (95% CI) ^{4,5}	20.1 (16.3, 24.4)	5.1 (3.2, 7.8)
Complete Response n (%)	12 (3.1)	0
Partial Response n (%)	67 (17.0)	20 (5.1)
DoR		
Median DoR (months) (95% CI)	22.3 (13.7, NR)	18.4 (6.5, 26.0)
% with duration ≥ 6 months	82.3	78.9
% with duration ≥ 12 months	65.8	63.2

¹ HR (IMJUDO and durvalumab vs. sorafenib) based on the stratified Cox proportional hazard model.

² Based on a stratified log-rank test.

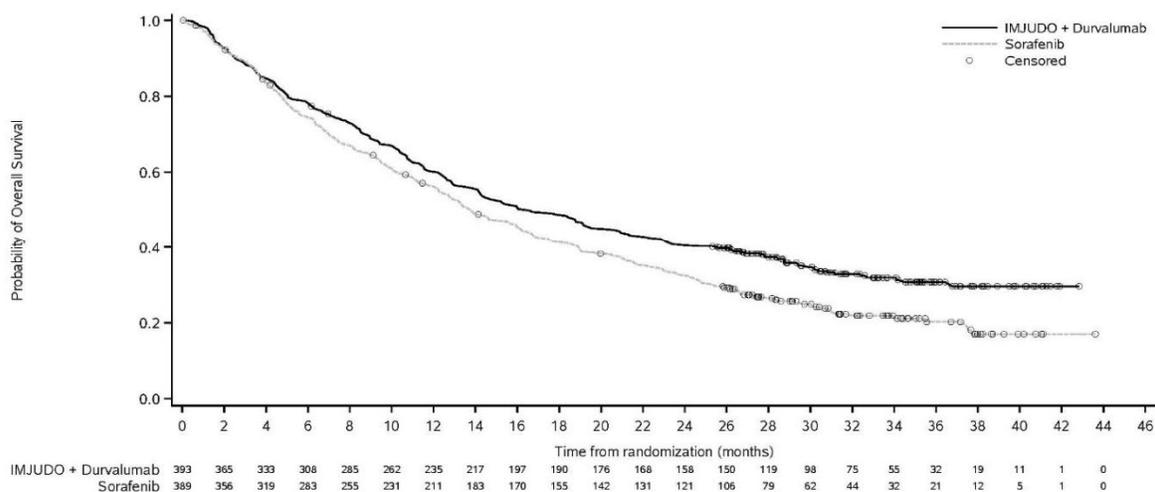
³ Based on a Lan-DeMets alpha spending function with O'Brien Fleming type boundary and the actual number of events observed, the boundary for declaring statistical significance for IMJUDO and durvalumab vs. sorafenib was 0.0398 (Lan and DeMets 1983).

⁴ Confirmed complete response or partial response.

⁵ Based on Clopper-Pearson method.

CI=Confidence Interval, HR=Hazard Ratio, NR=Not Reached

Figure 1. Kaplan-Meier curve of OS



16 HOW SUPPLIED/STORAGE AND HANDLING

IMJUDO (tremelimumab-actl) injection is a clear to slightly opalescent, colorless to slightly yellow solution supplied in a carton containing one single-dose vial in the following concentrations:

- 25 mg/1.25 mL (20 mg/mL) (NDC 0310-4505-25)
- 300 mg/15 mL (20 mg/mL) (NDC 0310-4535-30)

Store in a refrigerator at 2°C to 8°C (36°F to 46°F) in original carton to protect from light. Do not freeze. Do not shake.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Medication Guide).

Immune-Mediated Adverse Reactions

Inform patients of the risk of immune-mediated adverse reactions that may require corticosteroid treatment and interruption or discontinuation of IMJUDO in combination with durvalumab, including [see [Warnings and Precautions \(5.1\)](#)]:

- Pneumonitis: Advise patients to contact their healthcare provider immediately for any new or worsening cough, chest pain, or shortness of breath.
- Colitis: Advise patients to contact their healthcare provider immediately for diarrhea, blood or mucus in stools, or severe abdominal pain.
- Hepatitis: Advise patients to contact their healthcare provider immediately for jaundice, severe nausea or vomiting, pain on the right side of abdomen, lethargy, or easy bruising or bleeding.
- Endocrinopathies: Advise patients to contact their healthcare provider immediately for signs or symptoms of hypothyroidism, hyperthyroidism, adrenal insufficiency, type 1 diabetes mellitus, or hypophysitis.
- Nephritis: Advise patients to contact their healthcare provider immediately for signs or symptoms of nephritis.
- Dermatological Reactions: Advise patients to contact their healthcare provider immediately for signs or symptoms of severe dermatological reactions.
- Pancreatitis: Advise patients to contact their healthcare provider immediately for signs or symptoms of pancreatitis.
- Other Immune-Mediated Adverse Reactions: Advise patients to contact their healthcare provider immediately for signs or symptoms of aseptic meningitis, immune thrombocytopenia, myocarditis, hemolytic anemia, myositis, uveitis, keratitis, and myasthenia gravis.

Infusion-Related Reactions:

- Advise patients to contact their healthcare provider immediately for signs or symptoms of infusion-related reactions [see [Warnings and Precautions \(5.2\)](#)].

Embryo-Fetal Toxicity:

- Advise females of reproductive potential that IMJUDO can cause harm to a fetus and to inform their healthcare provider of a known or suspected pregnancy [see [Warnings and Precautions \(5.3\)](#) and [Use in Specific Populations \(8.1, 8.3\)](#)].
- Advise females of reproductive potential to use effective contraception during treatment and for 3 months after the last dose of IMJUDO [see [Use in Specific Populations \(8.3\)](#)].

Lactation:

- Advise female patients not to breastfeed while taking IMJUDO and for 3 months after the last dose [see [Warnings and Precautions \(5.3\)](#) and [Use in Specific Populations \(8.2\)](#)].

Manufactured for:
AstraZeneca Pharmaceuticals LP
Wilmington, DE 19850

Manufactured By:

AstraZeneca AB
Södertälje, Sweden SE-15185
US License No. 2059

IMJUDO® is a registered trademark of AstraZeneca group of companies.
© AstraZeneca 2022

MEDICATION GUIDE
IMJUDO® (im-JEW-doh)
(tremelimumab-actl)
injection

What is the most important information I should know about IMJUDO?

IMJUDO is a medicine that may treat a certain type of liver cancer by working with your immune system.

IMJUDO in combination with durvalumab can cause your immune system to attack normal organs and tissues in any area of your body and can affect the way they work. These problems can sometimes become severe or life-threatening and can lead to death. You can have more than one of these problems at the same time. These problems may happen anytime during treatment or even after your treatment has ended.

Call or see your healthcare provider right away if you develop any new or worsening signs or symptoms, including:

Lung problems.

- Cough
- shortness of breath
- chest pain

Intestinal problems.

- diarrhea (loose stools) or more frequent bowel movements than usual
- stools that are black, tarry, sticky, or have blood or mucus
- severe stomach-area (abdomen) pain or tenderness

Liver problems.

- yellowing of your skin or the whites of your eyes
- severe nausea or vomiting
- pain on the right side of your stomach-area (abdomen)
- dark urine (tea colored)
- bleeding or bruising more easily than normal

Hormone gland problems.

- headaches that will not go away or unusual headaches
- eye sensitivity to light
- eye problems
- rapid heartbeat
- increase sweating
- extreme tiredness
- weight gain or weight loss
- feeling more hungry or thirsty than usual
- urinating more often than usual
- hair loss
- feeling cold
- constipation
- your voice gets deeper
- dizziness or fainting
- changes in mood or behavior, such as decreased sex drive, irritability, or forgetfulness

Kidney problems.

- decrease in your amount of urine
- blood in your urine
- swelling of your ankles
- loss of appetite

Skin problems.

- rash
- itching
- skin blistering or peeling
- painful sores or ulcers in mouth or nose, throat, or genital area
- fever or flu-like symptoms
- swollen lymph nodes

Pancreas problems.

- Pain in your upper stomach-area (abdomen)
- severe nausea or vomiting
- loss of appetite

Problems can also happen in other organs and tissues. These are not all of the signs and symptoms of immune system problems that can happen with IMJUDO. Call or see your healthcare provider right away for any new or worsening signs or symptoms, which may include:

- chest pain, irregular heartbeats, shortness of breath or swelling of ankles
- confusion, sleepiness, memory problems, changes in mood or behavior, stiff neck, balance problems, tingling or numbness of the arms or legs
- double vision, blurry vision, sensitivity to light, eye pain, changes in eye sight
- persistent or severe muscle pain or weakness, muscle cramps
- low red blood cells, bruising

Infusion reactions that can sometimes be severe or life-threatening. Signs and symptoms of infusion reactions may include:

- chills or shaking
- itching or rash
- flushing
- shortness of breath or wheezing
- dizziness
- feel like passing out
- fever
- back or neck pain

Getting medical treatment right away may help keep these problems from becoming more serious.

Your healthcare provider will check you for these problems during your treatment with IMJUDO. Your healthcare provider may treat you with corticosteroid or hormone replacement medicines. Your healthcare provider may also need to delay or completely stop treatment with IMJUDO, if you have severe side effects.

What is IMJUDO?

IMJUDO is a prescription medicine used in combination with durvalumab to treat adults with:

- a type of liver cancer that cannot be removed by surgery (unresectable hepatocellular carcinoma or uHCC).

It is not known if IMJUDO is safe and effective in children.

Before you receive IMJUDO, tell your healthcare provider about all of your medical conditions, including if you:

- have immune system problems such as Crohn's disease, ulcerative colitis, or lupus
- have a condition that affects your nervous system, such as myasthenia gravis or Guillain-Barré syndrome
- are pregnant or plan to become pregnant. IMJUDO can harm your unborn baby.
- are breastfeeding or plan to breastfeed. It is not known if IMJUDO passes into your breast milk. Do not breastfeed during treatment and for 3 months after your last dose of IMJUDO.

Females who are able to become pregnant

- Your healthcare provider should do a pregnancy test before you start treatment with IMJUDO.
- You should use an effective method of birth control during your treatment and for 3 months after your last dose of IMJUDO. Talk to your healthcare provider about birth control methods that you can use during this time.
- Tell your healthcare provider right away if you become pregnant or think you may be pregnant during treatment with IMJUDO.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

How will I receive IMJUDO?

- Your healthcare provider will give you IMJUDO into your vein through an intravenous (IV) line over 60 minutes. Then durvalumab is also given through an intravenous (IV) line over 60 minutes.
- IMJUDO is given to you as a single dose.
- Your healthcare provider will test your blood to check you for certain side effects.
- If you miss your appointment, call your healthcare provider as soon as possible to reschedule your appointment.

What are the possible side effects of IMJUDO?

IMJUDO can cause serious side effects, including:

See “What is the most important information I should know about IMJUDO?”

The most common side effects of IMJUDO when used in combination with durvalumab include:

- rash
- diarrhea
- feeling tired
- itchiness
- muscle or bone pain
- stomach (abdominal) pain

Tell your healthcare provider if you have any side effect that bothers you or that does not go away.

These are not all the possible side effects of IMJUDO. Ask your healthcare provider or pharmacist for more information.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

General information about the safe and effective use of IMJUDO.

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. If you would like more information about IMJUDO, talk with your healthcare provider. You can ask your healthcare provider for information about IMJUDO that is written for health professionals.

What are the ingredients in IMJUDO?

Active ingredient: tremelimumab-actl

Inactive ingredients: edetate disodium, histidine, L-histidine hydrochloride monohydrate, polysorbate 80, trehalose, and Water for Injection, USP.

Manufactured for: AstraZeneca Pharmaceuticals LP, Wilmington, DE 19850

Manufactured by: AstraZeneca AB, Södertälje, Sweden SE-15185

US License No. 2059

IMJUDO® is a registered trademark of AstraZeneca group of companies.

For more information, call 1-800-236-9933 or go to www.IMJUDO.com

© AstraZeneca 2022

This Medication Guide has been approved by the U S Food and Drug Administration

Issued: October 2022

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

PAUL G KLUETZ
10/31/2022 03:36:23 PM