IMFINZI® durvalumab Injection for Intravenous Use 50 mg/mL | AstraZeneca Access 360™

Dosing, Wastage, and Coding Guide for IMFINZI® (durvalumab)

INDICATIONS

IMFINZI is indicated for the treatment of adult patients with 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.

  This indication is approved under accelerated approval based on tumor response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

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

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).

IMPORTANT SAFETY INFORMATION

There are no contraindications for IMFINZI® (durvalumab).

IMFINZI can cause serious, potentially fatal adverse reactions including immune-mediated pneumonitis, hepatitis, colitis, endocrinopathies, nephritis, dermatologic reactions, other immune-mediated adverse reactions, infection, and infusion-related reactions. Please refer to the full Prescribing Information for important dosage modification and management information specific to adverse reactions.

Immune-Mediated Pneumonitis

IMFINZI can cause immune-mediated pneumonitis, defined as requiring use of corticosteroids. Fatal cases have been reported. Monitor patients for signs and symptoms of pneumonitis and evaluate with radiographic imaging when suspected. Administer corticosteroids for Grade 2 or greater pneumonitis. Withhold IMFINZI for Grade 2 pneumonitis; permanently discontinue for Grade 3 or 4 pneumonitis.

In clinical studies enrolling 1889 patients with various cancers who received IMFINZI, pneumonitis occurred in 5% of patients, including Grade 3 (0.8%), Grade 4 (<0.1%), and Grade 5 (0.3%) pneumonitis. Pneumonitis led to discontinuation of IMFINZI in 1.5% of the 1889 patients. 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. In the PACIFIC study, pneumonitis led to discontinuation of IMFINZI in 6% of patients.

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.

Please read additional Important Safety Information on pages 4-6 and accompanying complete Prescribing Information including Medication Guide.

Dosage

Recommended dosage for ES-SCLC

The recommended dose of IMFINZI® (durvalumab) is 1500 mg in combination with chemotherapy every 3 weeks (21 days) for 4 cycles, followed by 1500 mg every 4 weeks as a single agent until disease progression or unacceptable toxicity.

IMFINZI is supplied as single-use vials

	IMFINZI	NDC
	**120 mg in 2.4 mL** of solution for infusion in a single-use vial	0310-4500-12 (10 digit) 00310-4500-12 (11 digit)
	**500 mg in 10 mL** of solution for infusion in a single-use vial	0310-4611-50 (10 digit) 00310-4611-50 (11 digit)

Recommended dosage for urothelial carcinoma

The recommended dose of IMFINZI is 10 mg/kg administered as an intravenous infusion over 60 minutes every 2 weeks until disease progression or unacceptable toxicity.

Recommended dosage for NSCLC

The recommended dose of IMFINZI is 10 mg/kg administered as an intravenous infusion over 60 minutes every 2 weeks until disease progression, unacceptable toxicity, or a maximum of 12 months.

No dose reductions of IMFINZI are recommended. Withhold or discontinue IMFINZI to manage adverse reactions as described in Table 2 of full Prescribing Information.

Determine the appropriate dose based on patient weight

1. Determine total dose in mg

10 mg/kg × patient weight (kg) = Total mg

2. Identify volume of IMFINZI needed

Total mg ÷ 50 mg/mL = Total IMFINZI volume

3. Calculate the number of single-use vials required

Total IMFINZI volume ÷ 10 mL or 2.4 mL single-use vials = number of single-use vials required

QUICK TIP: Multiply patient weight (kg) by 0.2 to determine volume of IMFINZI (mL) needed

Wastage

A quick guide to determine the vials needed to produce the least amount of wastage

Patient weight (kg)	37-48	49-50	51-60	61-62	63-72	73-74	75-84
Vials needed	x4	x1	x5	x1 x1	x6	x2 x1	x7
Patient weight (kg)	**85-86**	**87-96**	**97-98**	**99-100**	**101-108**	**109-110**	**111-112**
Vials needed	x3 x1	x8	x4 x1	x2	x9	x5 x1	x1 x2
Patient weight (kg)	**113-120**	**121-122**	**123-124**	**125-132**	**133-134**	**135-136**	**137-144**
Vials needed	x10	x6 x1	x2 x2	x11	x7 x1	x3 x2	x12
Patient weight (kg)	**145-146**	**147-148**	**149-150**	**151-156**	**157-158**	**159-160**	**161-162**
Vials needed	x8 x1	x4 x2	x3	x13	x9 x1	x5 x2	x1 x3

See Prescribing Information for further dosing information.

Coding

An important modifier[1]

Modifiers provide a means to report or indicate that a service or procedure has been altered by some specific circumstance but not changed in its definition or code. The JW modifier below may be applicable to the provision of IMFINZI in physician offices and hospital outpatient departments.

Modifier	Description	Indication and placement
JW	Drug or biological amount discarded/not administered to any patient	• Unused drug remains after applicable dose is administered from single-use vial • CMS has issued a discarded drug policy, local MAC/ other payer requirements may vary • Payers may have different requirements on how to code unused drug with miscellaneous HCPCS drug codes • Typically, the modifier is appended to the drug code on a line separate from that reporting the administered dose

IMPORTANT SAFETY INFORMATION (Cont'd)

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 for Grade 2 or higher elevations of ALT, AST, and/or total bilirubin. Withhold IMFINZI for ALT or AST greater than 3 but less than or equal to 8 times the ULN or total bilirubin greater than 1.5 but less than or equal to 5 times the ULN; permanently discontinue IMFINZI for ALT or AST greater than 8 times the ULN or total bilirubin greater than 5 times the ULN or concurrent ALT or AST greater than 3 times the ULN and total bilirubin greater than 2 times the ULN with no other cause.

In clinical studies enrolling 1889 patients with various cancers who received IMFINZI, hepatitis occurred in 12% of patients, including Grade 3 (4.4%), Grade 4 (0.4%), and Grade 5 (0.2%) hepatitis. Hepatitis led to discontinuation of IMFINZI in 0.7% of the 1889 patients.

Immune-Mediated Colitis
IMFINZI can cause immune-mediated colitis, defined as requiring use of corticosteroids. Administer corticosteroids for Grade 2 or greater colitis or diarrhea. Withhold IMFINZI for Grade 2 colitis or diarrhea; permanently discontinue for Grade 3 or 4 colitis or diarrhea.

In clinical studies enrolling 1889 patients with various cancers who received IMFINZI, colitis or diarrhea occurred in 18% of patients, including Grade 3 (1.0%) and Grade 4 (0.1%) immune-mediated colitis. Diarrhea or colitis led to discontinuation of IMFINZI in 0.4% of the 1889 patients.

Immune-Mediated Endocrinopathies
IMFINZI can cause immune-mediated endocrinopathies, including thyroid disorders, adrenal insufficiency, type 1 diabetes mellitus, and hypophysitis/hypopituitarism. Monitor patients for clinical signs and symptoms of endocrinopathies.

- **Thyroid disorders**—Monitor thyroid function prior to and periodically during treatment. Initiate hormone replacement therapy or medical management of hyperthyroidism as clinically indicated. Withhold IMFINZI for Grades 2–4 hyperthyroidism, until clinically stable. Continue IMFINZI for hypothyroidism.

  In clinical studies enrolling 1889 patients with various cancers who received IMFINZI, hypothyroidism occurred in 11% of patients, while 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.

- **Adrenal insufficiency**—Administer corticosteroids as clinically indicated and withhold IMFINZI until clinically stable for Grade 2 or higher adrenal insufficiency. In clinical studies enrolling 1889 patients with various cancers who received IMFINZI, adrenal insufficiency occurred in 0.7% of patients, including Grade 3 (<0.1%) adrenal insufficiency.

- **Type 1 diabetes mellitus**—Initiate treatment with insulin as clinically indicated. Withhold IMFINZI for Grades 2–4 type 1 diabetes mellitus, until clinically stable. In clinical studies enrolling 1889 patients with various cancers who received IMFINZI, type 1 diabetes mellitus occurred in <0.1% of patients.

- **Hypophysitis**—Administer corticosteroids and hormone replacement as clinically indicated and withhold IMFINZI until clinically stable for Grade 2 or higher hypophysitis. Hypopituitarism leading to adrenal insufficiency and diabetes insipidus occurred in <0.1% of 1889 patients with various cancers who received IMFINZI.

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. Administer corticosteroids as clinically indicated. Withhold IMFINZI for creatinine greater than 1.5 to 3 times the ULN; permanently discontinue IMFINZI and administer corticosteroids in patients with creatinine greater than 3 times the ULN.

In clinical studies enrolling 1889 patients with various cancers who received IMFINZI, 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 the patients including Grade 3 (1.1%), Grade 4 (0.2%), and Grade 5 (0.1%) nephritis. IMFINZI was discontinued in 0.3% of the 1889 patients.

Please read additional Important Safety Information on pages 1, 5, and 6 and accompanying complete Prescribing Information including Medication Guide.

IMPORTANT SAFETY INFORMATION (Cont'd)

Immune-Mediated Dermatologic Reactions
IMFINZI can cause immune-mediated rash. Stevens Johnson Syndrome (SJS)/toxic epidermal necrolysis (TEN) has occurred with other products in this class. Administer corticosteroids for Grade 2 rash or dermatitis lasting for more than 1 week or for Grade 3 or 4 rash or dermatitis. Withhold IMFINZI for Grade 2 rash or dermatitis lasting longer than 1 week or Grade 3 rash or dermatitis; permanently discontinue IMFINZI in patients with Grade 4 rash or dermatitis.

In clinical studies enrolling 1889 patients with various cancers who received IMFINZI, 26% of patients developed rash or dermatitis and 0.4% of the patients developed vitiligo. Rash or dermatitis led to discontinuation of IMFINZI in 0.1% of the 1889 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 immune-mediated adverse reactions, exclude other causes and initiate corticosteroids as clinically indicated. Withhold IMFINZI for Grade 3 immune-mediated adverse reactions, unless clinical judgment indicates discontinuation; permanently discontinue IMFINZI for Grade 4 adverse reactions.

The following clinically significant, immune-mediated adverse reactions occurred at an incidence of less than 1% each in 1889 patients who received IMFINZI: aseptic meningitis, hemolytic anemia, immune thrombocytopenic purpura, myocarditis, myositis, and ocular inflammatory toxicity, including uveitis and keratitis. In patients who received IMFINZI in clinical studies outside of the pooled dataset, myasthenia gravis occurred at an incidence of less than 0.1%. Permanently discontinue IMFINZI if myasthenia gravis does not resolve to ≤ Grade 1 within 30 days or if there are signs of respiratory and/or autonomic insufficiency. Additional clinically significant immune-mediated adverse reactions have been seen with other products in this class (see Warnings and Precautions Section 5.7 of IMFINZI full Prescribing Information).

Infection
IMFINZI can cause serious infections, including fatal cases. Monitor patients for signs and symptoms of infection and treat as clinically indicated. Withhold IMFINZI for Grade 3 or 4 infection, until clinically stable.

In clinical studies enrolling 1889 patients with various cancers who received IMFINZI, infections occurred in 43% of patients, including Grade 3 (8%), Grade 4 (1.9%), and Grade 5 (1.0%). The overall incidence of infections in IMFINZI treated patients in the PACIFIC study (56%) was higher compared to patients in other clinical studies (38%) in which radiation therapy was generally not administered immediately prior to initiation of IMFINZI. In patients with UC in Study 1108 (n=182), the most common Grade 3 or higher infection was urinary tract infections, which occurred in 4% of patients. In patients with Stage III NSCLC in the PACIFIC study, the most common Grade 3 or higher infection was pneumonia, which occurred in 5% of patients.

Infusion-Related Reactions
IMFINZI can cause severe or life-threatening infusion-related reactions. Monitor patients for signs and symptoms of an infusion-related reaction. Interrupt or slow the rate of infusion for Grades 1–2 infusion-related reactions; permanently discontinue for Grades 3–4 infusion-related reactions.

In clinical studies enrolling 1889 patients with various cancers who received IMFINZI, infusion-related reactions occurred in 2.2% of patients, including Grade 3 (0.3%).

Embryo-Fetal Toxicity
Based on its mechanism of action and data from animal studies, IMFINZI can cause fetal harm when administered to a pregnant woman. There are no data on the use of IMFINZI in pregnant women. Advise pregnant women of the potential risk to a fetus and advise women of reproductive potential to use effective contraception during treatment and for at least 3 months after the last dose of IMFINZI.

Lactation
There is no information regarding the presence of IMFINZI in human milk; however, because of the potential for adverse reactions in breastfed infants from IMFINZI, advise women not to breastfeed during treatment and for at least 3 months after the last dose.

Most Common Adverse Reactions

- In patients with UC in Study 1108 (n=182), the most common adverse reactions (≥15%) were fatigue (39%), musculoskeletal pain (24%), constipation (21%), decreased appetite (19%), nausea (16%), peripheral edema (15%), and

Please read additional Important Safety Information on pages 1, 4, and 6 and accompanying complete Prescribing Information including Medication Guide.

IMPORTANT SAFETY INFORMATION (Cont'd)

Most Common Adverse Reactions (Cont'd)

urinary tract infection (15%). The most common Grade 3 or 4 adverse reactions (≥3%) were fatigue, urinary tract infection, musculoskeletal pain, abdominal pain, dehydration, and general physical health deterioration

- In patients with UC in Study 1108, discontinuation due to adverse reactions occurred in 3.3% of patients. Serious adverse reactions occurred in 46% of patients. The most frequent serious adverse reactions (>2%) were acute kidney injury (4.9%), urinary tract infection (4.4%), musculoskeletal pain (4.4%), liver injury (3.3%), general physical health deterioration (3.3%), sepsis, abdominal pain, and pyrexia/tumor associated fever (2.7% each)
- In patients with Stage III NSCLC in the PACIFIC study (IMFINZI n=475), the most common adverse reactions (≥20% of patients) were cough (40%), fatigue (34%), pneumonitis or radiation pneumonitis (34%), upper respiratory tract infections (26%), dyspnea (25%), and rash (23%). The most common Grade 3 or 4 adverse reactions (≥3%) were pneumonitis/radiation pneumonitis (3.4%) and pneumonia (7%)
- In patients with Stage III NSCLC in the PACIFIC study (IMFINZI n=475), discontinuation due to adverse reactions occurred in 15% of patients in the IMFINZI arm. Serious adverse reactions occurred in 29% of patients receiving IMFINZI. The most frequent serious adverse reactions (≥2% of patients) were pneumonitis or radiation pneumonitis (7%) and pneumonia (6%). Fatal pneumonitis or radiation pneumonitis and fatal pneumonia occurred in <2% of patients and were similar across arms
- In patients with extensive-stage SCLC in the CASPIAN study (n=265), the most common adverse reactions (≥20%) were nausea, fatigue/asthenia, and alopecia. The most common Grade 3 or 4 adverse reaction (≥3%) was fatigue/asthenia (3.4%)
- In patients with extensive-stage SCLC in the CASPIAN study (n=265), IMFINZI was discontinued due to adverse reactions in 7% of the patients receiving IMFINZI plus chemotherapy. Serious adverse reactions occurred in 31% of patients receiving IMFINZI plus chemotherapy. The most frequent serious adverse reactions reported in at least 1% of patients were febrile neutropenia (4.5%), pneumonia (2.3%), anemia (1.9%), pancytopenia (1.5%), pneumonitis (1.1%), and COPD (1.1%). Fatal adverse reactions occurred in 4.9% of patients receiving IMFINZI plus chemotherapy

The safety and effectiveness of IMFINZI have not been established in pediatric patients.

Please read additional Important Safety Information on pages 1, 4, and 5 and accompanying complete Prescribing Information including Medication Guide.

You are encouraged to report negative side effects of AstraZeneca prescription drugs by calling 1-800-236-9933. If you prefer to report these to the FDA, either visit www.FDA.gov/medwatch or call 1-800-FDA-1088.

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Reference: 1. Centers for Medicare & Medicaid Services. MLN Matters No. MM9603 Revised. JW Modifier: Drug Amount Discarded/Not Administered to any Patient. https://www.cms.gov/Outreach-and-Education/Medicare-Learning-Network-MLN/MLNMattersArticles/downloads/MM9603.pdf. Accessed December 10, 2019.

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