Atezolizumab: Drug information

(For additional information see "Atezolizumab: Patient drug information")

For abbreviations and symbols that may be used in Lexicomp (show table)

Brand Names: US

Tecentriq

Pharmacologic Category

Antineoplastic Agent, Anti-PD-L1 Monoclonal Antibody; Antineoplastic Agent, Monoclonal Antibody

Dosing: Adult

Non-small cell lung cancer, metastatic: IV: 1,200 mg every 3 weeks (Fehrenbacher 2016; Rittmeyer 2017); continue until disease progression or unacceptable toxicity

Urothelial carcinoma, locally advanced or metastatic: IV: 1,200 mg every 3 weeks (Balar 2017; Rosenberg 2016); continue until disease progression or unacceptable toxicity

Dosing: Geriatric

Refer to adult dosing.

Dosing: Renal Impairment

No dosage adjustment is necessary (the effect on atezolizumab pharmacokinetics in patients with estimated glomerular filtration rate 15 to 29 mL/minute has not been studied and is unknown).

Dosing: Hepatic Impairment

Hepatic impairment prior to treatment:

Mild impairment (bilirubin ≤ upper limit of normal (ULN) and AST > ULN or bilirubin <1 times ULN and any AST): No dosage adjustment is necessary.

Moderate to severe impairment (bilirubin > ULN and AST > ULN or bilirubin ≥1 to 1.5 times ULN and any AST): There are no dosage adjustments provided in the manufacturer's labeling (has not been studied).

Hepatotoxicity during treatment:

AST or ALT >3 to 5 times ULN or total bilirubin >1.5 to 3 times ULN: Withhold treatment.

AST or ALT >5 times ULN or total bilirubin >3 times ULN: Discontinue permanently.

Immune-mediated hepatitis:

Grade 2 or greater transaminase elevations (with or without total bilirubin elevations): Withhold treatment and initiate high-dose systemic corticosteroids (prednisone 1 to 2 mg/kg daily or

equivalent, followed by a taper)

Severe (grade 3) or life-threatening (grade 4): Permanently discontinue treatment and initiate high-dose systemic corticosteroids (prednisone 1 to 2 mg/kg daily or equivalent, followed by a taper)

Dosing: Adjustment for Toxicity

Dosage reductions are not recommended for toxicities. Treatment is withheld or permanently discontinued. If therapy is withheld, may resume if toxicity recovers to grade 0 or 1.

Dermatologic toxicity:

Rash, grade 3: Withhold treatment.

Rash, grade 4: Discontinue permanently.

Endocrinopathies:

Adrenal insufficiency (symptomatic): Withhold treatment. Administer IV methylprednisolone 1 to 2 mg/kg/day and convert to oral prednisone 1 to 2 mg/kg/day or equivalent upon improvement in symptoms. When symptoms improve to grade 1 or lower, begin to taper steroids over at least 1 month. Resume atezolizumab treatment if symptoms improve to grade 0 or 1 within 12 weeks, and corticosteroids have been reduced to oral prednisone ≤10 mg/day (or equivalent) and patient is stable on adrenal replacement therapy (if needed).

Hyperglycemia, grade 3 or 4: Withhold treatment. May require insulin treatment.

Hyperthyroidism or hypothyroidism: Withhold treatment. May require additional treatment for symptomatic hypo- or hyperthyroidism.

Hypophysitis (symptomatic): Withhold treatment. Administer corticosteroids and hormone replacement as clinically necessary.

Hypophysitis, grade 4: Discontinue permanently. Administer corticosteroids and hormone replacement as clinically necessary.

Gastrointestinal toxicity:

Amylase or lipase elevations, grade 3 or 4 (>2 times ULN): Withhold treatment. Administer IV methylprednisolone 1 to 2 mg/kg/day and convert to oral corticosteroids (prednisone 1 to 2 mg/kg/day or equivalent) upon improvement in symptoms. Resume atezolizumab if amylase and lipase levels improve to grade 1 or lower within 12 weeks and corticosteroids have been reduced to oral prednisone ≤10 mg/day (or equivalent).

Diarrhea or colitis, grade 2 or 3: Withhold treatment. For grade 2 diarrhea or colitis, if symptoms persist for >5 days or recur, administer systemic corticosteroids (1 to 2 mg/kg/day prednisone or equivalent). For grade 3 diarrhea or colitis, administer IV methylprednisolone 1 to 2 mg/kg/day and convert to oral corticosteroids upon improvement in symptoms. If grade 2 and 3 symptoms improve to grade 0 or 1, taper corticosteroids over at least 1 month. Resume atezolizumab treatment if improves to grade 0 or 1 within 12 weeks and corticosteroids have been reduced to oral prednisone ≤10 mg/day (or equivalent).

Diarrhea or colitis, grade 4: Discontinue permanently. Administer IV methylprednisolone 1 to 2 mg/kg/day and convert to oral corticosteroids upon improvement in symptoms.

Pancreatitis, grade 2 or 3: Withhold treatment. Administer IV methylprednisolone 1 to 2 mg/kg/day and convert to oral corticosteroids (prednisone 1 to 2 mg/kg/day or equivalent) upon improvement in symptoms. Resume atezolizumab if pancreatitis symptoms have resolved and corticosteroids have been reduced to oral prednisone ≤10 mg/day (or equivalent).

Pancreatitis, grade 4: Discontinue permanently. Administer IV methylprednisolone 1 to 2 mg/kg/day and convert to oral corticosteroids (prednisone 1 to 2 mg/kg/day or equivalent) upon improvement in symptoms.

Pancreatitis, recurrent (any grade): Discontinue permanently. Administer IV methylprednisolone 1 to 2 mg/kg/day and convert to oral corticosteroids (prednisone 1 to 2 mg/kg/day or equivalent) upon improvement in symptoms.

Ophthalmic disorders:

Ocular inflammatory toxicity, grade 2: Withhold treatment.

Ocular inflammatory toxicity, grade 3 or 4: Discontinue permanently.

Pulmonary toxicities:

Pneumonitis, grade 2: Withhold treatment. Administer high-dose systemic corticosteroids (prednisone 1 to 2 mg/kg daily or equivalent) followed by a corticosteroid taper.

Pneumonitis, grade 3 or 4: Discontinue permanently. Administer high-dose systemic corticosteroids (prednisone 1 to 2 mg/kg daily or equivalent) followed by a corticosteroid taper.

Other/miscellaneous toxicities:

Guillain-Barre, any grade: Discontinue permanently.

Infection, grade 3 or 4: Withhold treatment.

Infusion-related reactions, grade 2 or mild to moderate: Withhold treatment or slow the rate of infusion.

Infusion-related reactions, grade 3 or 4: Discontinue permanently.

Meningoencephalitis, any grade: Discontinue permanently. Administer IV corticosteroids (methylprednisolone 1 to 2 mg/kg/day) and convert to oral therapy (prednisone 60 mg/day or equivalent) upon improvement; when symptoms improve to grade 1 or lower, taper corticosteroids over at least 1 month.

Myasthenic syndrome/myasthenia gravis: Discontinue permanently. Consider systemic corticosteroids (prednisone 1 to 2 mg/kg/day).

Dosage Forms

Excipient information presented when available (limited, particularly for generics); consult specific product labeling.

Solution, Intravenous [preservative free]:

Tecentriq: 1200 mg/20 mL (20 mL)

Generic Equivalent Available (US) No

Medication Guide and/or Vaccine Information Statement (VIS) An FDA-approved patient medication guide, which is available with the product information and as follows, must be dispensed with this medication:

Tecentriq: https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/761034s001lbl.pdf#page=25

Administration IV: Infuse the initial dose over 60 minutes, if tolerated, may infuse subsequent doses over 30 minutes. May be infused with or without a 0.2- to 0.22-micron sterile, non-pyrogenic, low-protein binding in-line filter. Do not administer as an IV push or bolus. Do not administer other medications at the same time through the same IV line. Monitor for infusion reactions.

Use

Non-small cell lung cancer, metastatic: Treatment of metastatic non-small cell lung cancer (NSCLC) in patients with disease progression during or following platinum-containing chemotherapy. Patients should have disease progression on approved therapy for EGFR or ALK genomic tumor mutations (if present) prior to receiving atezolizumab.

Urothelial carcinoma, locally advanced or metastatic: Treatment of locally advanced or metastatic urothelial carcinoma in patients who are not eligible for cisplatin-containing chemotherapy, have disease progression during or following platinum-containing chemotherapy, or have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy

Medication Safety Issues

Sound-alike/look-alike issues:

Atezolizumab may be confused with alemtuzumab, avelumab, nivolumab, pembrolizumab

High alert medication:

This medication is in a class the Institute for Safe Medication Practices (ISMP) includes among its list of drug classes which have a heightened risk of causing significant patient harm when used in error.

Adverse Reactions

>10%:

Cardiovascular: Peripheral edema (18%)

Central nervous system: Fatigue (52%), insomnia (NSCLC: 14%)

Dermatologic: Skin rash (15%), pruritus (13%)

Endocrine & metabolic: Hypoalbuminemia (NSCLC: 48%), hyponatremia (NSCLC: 48%),

hypokalemia (NSCLC: 18%), hypercalcemia (NSCLC: 13%)

Gastrointestinal: Decreased appetite (26%), nausea (25%), constipation (21%), colitis (19% to 20%), diarrhea (18% to 20%), abdominal pain (17%), vomiting (17%)

Genitourinary: Urinary tract infection (22%), hematuria (14%)

Hematologic & oncologic: Lymphocytopenia

Hepatic: Increased serum alkaline phosphatase (NSCLC: 42%), increased serum AST (NSCLC: 33%), increased serum ALT (NSCLC: 31%), increased serum bilirubin (NSCLC: 11%)

Immunologic: Antibody development (42%; no clinically significant impact on pharmacokinetics, safety, or efficacy)

Infection: Infection (38%)

Neuromuscular & skeletal: Musculoskeletal pain (NSCLC: 22%), back pain (≤15%), neck pain (≤15%), arthralgia (14%)

Renal: Increased serum creatinine (NSCLC: 19%)

Respiratory: Pneumonia (NSCLC: 18%), dyspnea (16%), cough (14%)

Miscellaneous: Fever (21%)

1% to 10%:

Cardiovascular: Venous thromboembolism

Central nervous system: Guillain-Barre syndrome (≤1%), meningoencephalitis (≤1%), myasthenia (≤1%), myasthenia gravis (≤1%), confusion

Endocrine & metabolic: Hypothyroidism (3% to 4%), hyperthyroidism (≤1%), hyperglycemia

Gastrointestinal: Increased serum amylase (≤1%), increased serum lipase (≤1%), pancreatitis (≤1%), dysphagia (NSCLC), intestinal obstruction

Genitourinary: Urinary tract obstruction

Hematologic & oncologic: Anemia

Hepatic: Hepatitis (≤1%)

Infection: Sepsis

Ophthalmic: Intraocular inflammation (≤1%)

Renal: Acute renal failure

Respiratory: Pneumonitis (≤4%), pleural effusion (NSCLC: >2%), hypoxia (NSCLC)

Miscellaneous: Infusion related reaction (severe: 1% to 2%)

<1%, postmarketing, and/or case reports: Adrenocortical insufficiency, diabetes mellitus (with ketoacidosis), hypophysitis

Contraindications

There are no contraindications listed in the manufacturer's labeling.

Warnings/Precautions

Concerns related to adverse effects:

• Adrenal insufficiency: Grades 1 to 3 adrenal insufficiency have been reported. For symptomatic adrenal insufficiency, withhold atezolizumab treatment and administer IV methylprednisolone 1 to 2 mg/kg/day and convert to oral prednisone 1 to 2 mg/kg/day or equivalent upon improvement in symptoms. When symptoms improve to grade 1 or lower, begin to taper steroids over at least 1 month. Resume atezolizumab treatment if symptoms improves to grade 0 or 1 within 12 weeks and corticosteroids have been reduced to oral prednisone ≤10 mg/day and patient is stable on adrenal replacement therapy (if needed).

• Diabetes mellitus: New-onset diabetes with ketoacidosis has been observed with atezolizumab. For type 1 diabetes, initiate insulin treatment. For grade 3 or higher hyperglycemia (fasting blood glucose >250 to 500 mg/dL), withhold atezolizumab; resume when metabolic control is achieved on insulin therapy.

• Gastrointestinal toxicity: Immune-mediated colitis or diarrhea (defined as requiring corticosteroids and with no clear alternative etiology) has occurred in nearly one-fifth of patients receiving atezolizumab, some events included grade 3 and 4 diarrhea. The median onset for some patients was 21 days to 1.7 months (range: 12 days to 3.4 months). Monitor for signs/symptoms of colitis and diarrhea. Withhold treatment for grade 2 or 3 diarrhea or colitis. For grade 2 diarrhea or colitis, if symptoms persist for >5 days or recur, administer systemic corticosteroids (1 to 2 mg/kg/day prednisone equivalent). For grade 3 diarrhea or colitis, administer IV methylprednisolone 1 to 2 mg/kg/day and convert to oral corticosteroids upon improvement in symptoms. If grade 2 and 3 symptoms improve to grade 0 or 1, taper corticosteroids over at least 1 month. Resume atezolizumab treatment if improves to grade 0 or 1 within 12 weeks and corticosteroids have been reduced to oral prednisone ≤10 mg/day. Discontinue permanently for grade 4 diarrhea or colitis. Pancreatitis, increases in amylase and lipase levels, and symptomatic pancreatitis (without other etiology) have occurred with atezolizumab. Monitor for signs/symptoms of acute pancreatitis. Discontinue permanently for grade 4 or any grade recurrent pancreatitis. Withhold treatment for grade 3 or higher serum amylase or lipase increases, or for grade 2 or 3 pancreatitis. Administer IV methylprednisolone 1 to 2 mg/kg/day and convert to oral corticosteroids (prednisone 1 to 2 mg/kg/day or equivalent) upon improvement in symptoms. Resume atezolizumab if amylase and lipase levels improve to grade 1 or lower within 12 weeks, pancreatitis symptoms have resolved, and corticosteroids have been reduced to oral prednisone ≤10 mg/day.

• Hepatotoxicity: Immune-mediated hepatitis (defined as requiring corticosteroids and with no clear alternative etiology), including fatal cases, has occurred with atezolizumab. Liver test abnormalities have been reported, including grade 3 and 4 events. The median time to onset was ~1 month (range: 0.4 to 7.7 months). Monitor for signs/symptoms of hepatitis; monitor liver function tests (AST, ALT, and bilirubin) prior to treatment initiation and periodically throughout therapy. Administer systemic corticosteroids (1 to 2 mg/kg/day prednisone or equivalent) followed by a taper for grade 2 or higher transaminase elevations (with or without elevated bilirubin). Withhold treatment until resolution for grade 2 and permanently discontinue for grade 3 or 4 immune-mediated hepatitis. Patients with treatment interruption for immune-mediated hepatitis did not have recurrence upon resuming treatment.

• Hypophysitis: Hypophysitis has occurred in patients receiving atezolizumab (rare). Monitor for signs/symptoms of hypophysitis. Administer corticosteroids and hormone replacement as indicated. Withhold treatment for grade 2 or 3 hypophysitis; discontinue permanently for grade 4 hypophysitis.

• Infection: Infections occurred in over 1/3 of patients receiving atezolizumab. Grade 3 and 4 infections have occurred, with urinary tract infection and pneumonia being the most common causes of grade 3 or higher infection in patients with urothelial carcinoma and non-small cell lung cancer, respectively. There have been case reports of fatal infections. Serious infections, including sepsis, herpes encephalitis, and mycobacterial infection leading to retroperitoneal hemorrhage have been reported. Monitor for signs/symptoms of infection. Manage suspected and confirmed bacterial infections with antibiotics. Withhold treatment for grade 3 or higher infections.

• Infusion-related reactions: Severe infusion reactions have been reported in clinical trials. Interrupt or slow the infusion rate in patients with mild to moderate infusion reactions. Permanently discontinue for grade 3 or 4 infusion reactions.

• Pulmonary toxicity: Immune-mediated pneumonitis and interstitial lung disease (defined as requiring corticosteroids and with no clear alternative etiology), including fatal cases, have been reported in patients receiving atezolizumab. The median time to onset was 2.6 to 3.3 months (range: 3 days to 18.7 months) and the median duration was 15 days to 1.4 months (range: up to 12.6 months or longer). Monitor for signs (with radiographic imaging) and symptoms of pneumonitis. Administer systemic corticosteroids (1 to 2 mg/kg/day prednisone or equivalent) followed by a taper for grade 2 or higher pneumonitis. Withhold treatment until resolution for grade 2 pneumonitis; permanently discontinue for grade 3 or 4 pneumonitis.

• Thyroid disorders: Hypothyroidism occurred in patients who received atezolizumab (including grades 1, 2, and 3 events), with a median time to first onset of 4.8 to 5.4 months (range: 15 days to 31 months). Hyperthyroidism was also reported, including grades 1 and 2 events, with a median onset of 3.2 to 4.9 months (range: 21 days to 31 months). Monitor thyroid function prior to and periodically during treatment. Patients with abnormal thyroid function tests who are asymptomatic can receive atezolizumab treatment. For symptomatic hypothyroidism, withhold atezolizumab treatment and initiate thyroid replacement therapy as needed. Isolated hypothyroidism should be managed with replacement therapy and without corticosteroids. For symptomatic hyperthyroidism, withhold atezolizumab and initiate antithyroid medications as needed. Resume atezolizumab treatment when symptoms of hypo- or hyperthyroidism are controlled and thyroid function is improving.

• Other immune-mediated toxicities: Other immune-mediated adverse events have occurred, including meningoencephalitis, myasthenic syndrome/myasthenia gravis, Guillain-Barre syndrome, and ocular inflammatory toxicity. Monitor for clinical signs/symptoms of meningitis and encephalitis; discontinue permanently for any grade meningitis or encephalitis; administer IV corticosteroids (methylprednisolone 1 to 2 mg/kg/day) and convert to oral therapy (prednisone 60 mg/day or equivalent) upon improvement; when symptoms improve to grade 1 or lower, taper corticosteroids over at least 1 month. Monitor for neuropathy (motor and sensory); permanently discontinue for any grade myasthenic syndrome/myasthenia gravis or Guillain-Barre syndrome and begin appropriate medical management; consider systemic corticosteroids (prednisone 1 to 2 mg/kg/day).

Concurrent drug therapy issues:

• Drug-drug interactions: Potentially significant interactions may exist, requiring dose or frequency adjustment, additional monitoring, and/or selection of alternative therapy. Consult drug interactions

database for more detailed information.

Metabolism/Transport Effects

None known.

Drug Interactions

(For additional information: Launch drug interactions program) Lexicomp®

Belimumab: Monoclonal Antibodies may enhance the adverse/toxic effect of Belimumab. *Risk X: Avoid combination*

Pregnancy Implications

Adverse events were observed in animal reproduction studies. Based on the mechanism of action, atezolizumab is expected to cause fetal harm if used during pregnancy. Women of reproductive potential should use effective contraception during therapy and for at least 5 months after the last dose.

Breast-Feeding Considerations

It is not known if atezolizumab is present in breast milk; however, IgG immunoglobulins are found in milk. Due to the potential for serious adverse reactions in the breastfed infant, breastfeeding is not recommended by the manufacturer during therapy or for at least 5 months after the last dose.

Monitoring Parameters

Monitor liver function tests (AST, ALT, and bilirubin; at baseline and periodically during treatment), thyroid function (prior to and periodically during treatment), serum glucose. Monitor for signs/symptoms of colitis, diarrhea, endocrinopathies, hepatitis, hypophysitis, infection, infusion reactions, meningitis and encephalitis, neuropathy (motor and sensory), pancreatitis (acute), rash, and pneumonitis.

Mechanism of Action

Atezolizumab is a humanized monoclonal antibody immune checkpoint inhibitor that binds to programmed death ligand 1 (PD-L1) to selectively prevent the interaction between the programmed cell death-1 (PD-1) and B7.1 (also known as CD80) receptors, while still allowing interaction between PD-L2 and PD-1. PD-L1 is an immune check point protein expressed on tumor cells and tumor infiltrating cells and down regulates anti-tumor t-cell function by binding to PD-1 and B7.1; blocking PD-1 and B7.1 interactions restores antitumor t-cell function (Fehrenbacher 2016, Rosenberg 2016).

Pharmacodynamics/Kinetics

Distribution: V_{dss}: 6.9 L

Half-life, elimination: 27 days

Excretion: Clearance: 0.2 L/day

Pricing: US

Solution (Tecentriq Intravenous)

1200 mg/20 mL (20 mL): $10344.00

Disclaimer: The pricing data provide a representative AWP and/or AAWP price from a single manufacturer of the brand and/or generic product, respectively. The pricing data should be used for benchmarking purposes only, and as such should not be used to set or adjudicate any prices for reimbursement or purchasing

functions. Pricing data is updated monthly.

International Brand Names

Tecentriq (KR, NZ)

REFERENCES

1. *Balar AV, Galsky MD, Rosenberg JE, et al. Atezolizumab as first-line treatment in cisplatin-ineligible patients with locally advanced and metastatic urothelial carcinoma: a single-arm, multicentre, phase 2 trial. Lancet. 2017; 389(10064):67-76. [PubMed 27939400]*
2. *Fehrenbacher L, Spira A, Ballinger M, et al. Atezolizumab versus docetaxel for patients with previously treated non-small-cell lung cancer (POPLAR): a multicentre, open-label, phase 2 randomised controlled trial. Lancet. 2016;387(10030):1837-1846. [PubMed 26970723]*
3. *Rittmeyer A, Barlesi F, Waterkamp D, et al. Atezolizumab versus docetaxel in patients with previously treated non-small-cell lung cancer (OAK): a phase 3, open-label, multicentre randomised controlled trial. Lancet. 2017;389(10066):255-265. [PubMed 27979383]*
4. *Rosenberg JE, Hoffman-Censits J, Powles T, et al. Atezolizumab in patients with locally advanced and metastatic urothelial carcinoma who have progressed following treatment with platinum-based chemotherapy: a single-arm, multicentre, phase 2 trial. Lancet. 2016;387(10031):1909-1920. [PubMed 26952546]*
5. *Tecentriq (atezolizumab) [prescribing information]. South San Francisco, CA: Genentech Inc; April 2017.*

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