TECENTRIQ™ (atezolizumab) IN PREVIOUSLY TREATED LOCALLY ADVANCED OR METASTATIC UROTHELIAL CARCINOMA

TECENTRIQ™
atezolizumab INJECTION FOR INTRAVENOUS USE 1200 mg

About TECENTRIQ

TECENTRIQ (atezolizumab) is a monoclonal antibody used to treat a type of bladder cancer called locally advanced or metastatic urothelial carcinoma (mUC). TECENTRIQ may be used: when your bladder cancer has spread (metastatic) and/or cannot be removed by surgery (advanced urothelial carcinoma) **and**, you have tried chemotherapy that contains platinum, and it did not work or is no longer working. It is not known if TECENTRIQ is safe and effective in children. The U.S. Food and Drug Administration (FDA) granted accelerated approval for this indication 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.[1]

FIRST AND ONLY

anti-PDL1 medicine approved by the FDA.[2,3,4]

FIRST AND ONLY

cancer immunotherapy approved for people with locally advanced or metastatic bladder cancer previously treated with platinum-based chemotherapy.[2,3,4]

FIRST

FDA-approved treatment for people with a specific type of bladder cancer in more than 30 years.[2,3,4]

Important Safety Information

What is the most important information about TECENTRIQ?

TECENTRIQ can cause the immune system to attack normal organs and tissues in many areas of the body and can affect the way they work. These problems can sometimes become serious or life-threatening and can lead to death.

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Please see the following pages and TECENTRIQ full Prescribing Information including Most Serious Side Effects for Important Safety Information.

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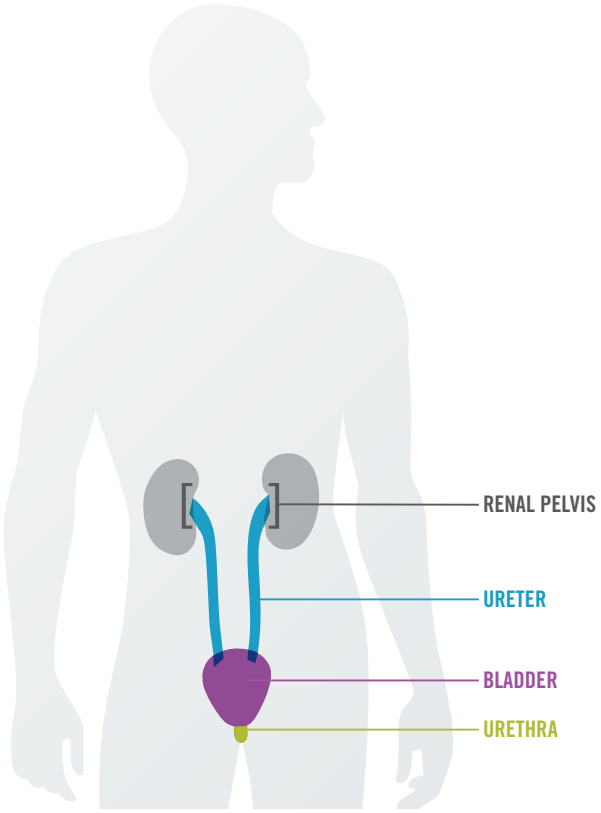
What is metastatic urothelial carcinoma?

Urothelial carcinoma is a type of bladder cancer that can also be found in the **renal pelvis, ureter and urethra.**[5] Metastatic cancer is cancer that has spread from the place where it first started to another place in the body.[6]

APPROXIMATELY
76,000
people in the U.S. will be diagnosed with bladder cancer in 2016.[7]

11%
new diagnoses are made when bladder cancer is in advanced stages.[8]



What is cancer immunotherapy?[9]

Cancer immunotherapy is a class of medicine designed to work with the body's own immune system. Immunotherapy may also affect normal cells.

Important Safety Information (continued)

Getting medical treatment right away may help keep these problems from becoming more serious. A healthcare provider may treat a patient with corticosteroid or hormone replacement medicines. A healthcare provider may delay or completely stop treatment with TECENTRIQ if a patient has severe side effects.

Patients should call or see their healthcare provider right away if they get any symptoms of the following problems or these symptoms get worse.

TECENTRIQ can cause serious side effects, including:

- **Lung Problems (pneumonitis)** – Signs and symptoms of pneumonitis may include new or worsening cough, shortness of breath, and chest pain
- **Liver Problems (hepatitis)** – Signs and symptoms of hepatitis may include yellowing of the skin or the whites of the eyes, severe nausea or vomiting, pain on the right side of the stomach area (abdomen), drowsiness, dark urine (tea colored), bleeding or bruising more easily than normal, and feeling less hungry than usual

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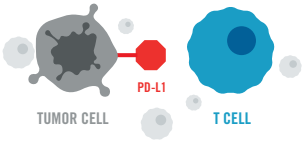
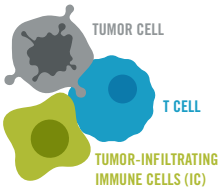
What is PD-L1?[10,11,12]

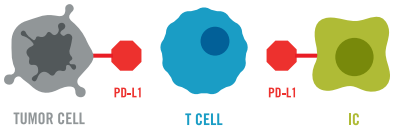
The immune system can help protect the body against cancer by sending T cells – a type of white blood cell – to attack tumor cells.



However, tumor cells can produce a protein called **programmed death ligand 1 (PD-L1)** that works like a "stop sign" to inactivate T cells.

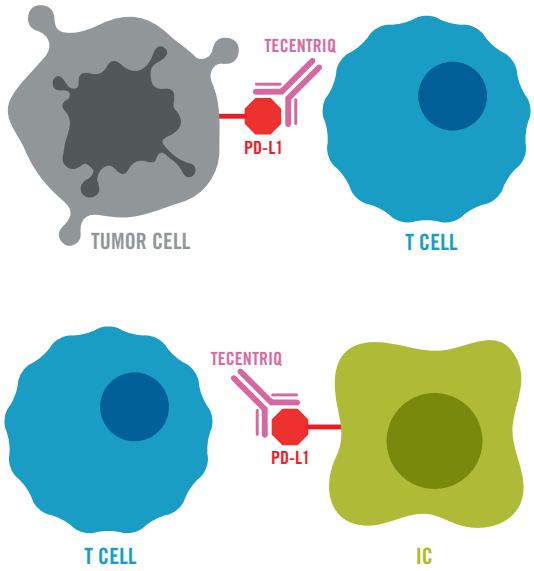


As a tumor grows, many other cells can join and interact with it.

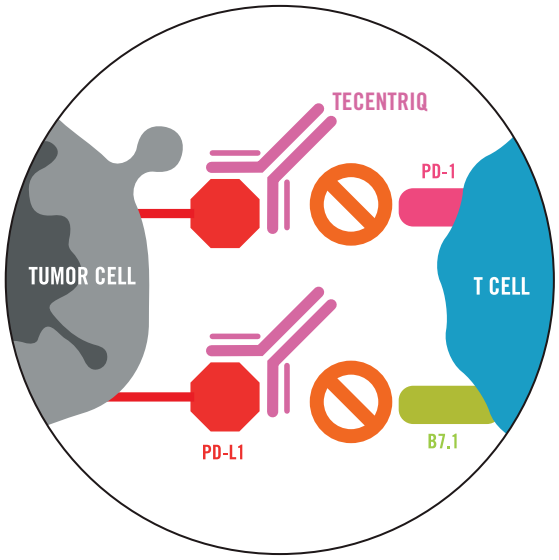


Some of these cells, called tumor-infiltrating immune cells, can also express PD-L1 and inactivate T cells.

How TECENTRIQ may work[1] (proposed mechanism of action)



TECENTRIQ is designed to bind to PD-L1 expressed on tumor cells and tumor-infiltrating immune cells. TECENTRIQ may also affect normal cells.



TECENTRIQ may prevent PD-L1 from binding to other proteins called PD-1 and B7.1, which may remove the "stop sign" which signals to inactivate T-cells.

Important Safety Information (continued)

- **Intestinal Problems (colitis)** – Signs and symptoms of colitis may include diarrhea (loose stools) or more bowel movements than usual, blood in the stools or dark, tarry, sticky stools, severe stomach area (abdomen) pain or tenderness

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Please see the following pages and TECENTRIQ full Prescribing Information including Most Serious Side Effects for Important Safety Information.

TECENTRIQ efficacy and safety profile in mUC[1]

The FDA's accelerated approval of TECENTRIQ for locally advanced or mUC is based on results of the Phase II IMvigor 210 study. IMvigor 210 is an open-label, multicenter, two-cohort study that evaluated the safety and efficacy of TECENTRIQ in 310 people with locally advanced or mUC, regardless of PD-L1 expression. People in a cohort of the study whose disease had progressed during or following previous treatment with a platinum-based chemotherapy regimen or who had disease progression within 12 months of treatment with a platinum-based neoadjuvant or adjuvant chemotherapy regimen received a 1200-mg intravenous dose of TECENTRIQ on day one of 21-day cycles until unacceptable toxicity or either radiographic or clinical progression. The primary endpoint of the study was objective response rate (ORR). Secondary endpoints included duration of response. The median follow-up time for this cohort was 14.4 months.

OBJECTIVE RESPONSE RATE
(ORR, PRIMARY ENDPOINT)

DURATION OF RESPONSE
(DOR, KEY SECONDARY ENDPOINT)

ALL PATIENTS

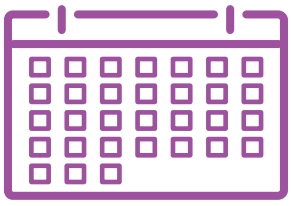
The study showed that TECENTRIQ **shrank tumors in 15% (95% CI: 11, 19)** of people with mUC whose disease worsened after initial treatment.

LOW PD-L1 EXPRESSION

The study showed that TECENTRIQ **shrank tumors in 10% (95% CI: 6, 14)** of people with mUC whose disease worsened after initial treatment and who have PD-L1 expression < 5% in tumor-infiltrating immune cells.

HIGH PD-L1 EXPRESSION

The study showed that TECENTRIQ **shrank tumors in 26% (95% CI: 18, 36)** of people with mUC whose disease worsened after initial treatment and who have PD-L1 expression ≥ 5% in tumor-infiltrating immune cells.



Median DOR was not reached in all patients and patients with high PD-L1 expression. In patients with low PD-L1 expression, median DOR was 12.7 months.

Important Safety Information (continued)

- **Hormone Gland Problems (especially the pituitary, thyroid, adrenal glands and pancreas)** – Signs and symptoms that the hormone glands are not working properly may include headaches that will not go away or unusual headaches, extreme tiredness, weight gain or weight loss, dizziness or fainting, feeling more hungry or thirsty than usual, hair loss, changes in mood or behavior (such as decreased sex drive, irritability, or forgetfulness), feeling cold, constipation, voice gets deeper, urinating more often than usual, nausea or vomiting, and stomach area (abdomen) pain
- **Nervous System Problems (neuropathies, meningoencephalitis)** – Signs of nervous system problems may include severe muscle weakness, numbness or tingling in hands and feet, fever, confusion, changes in mood or behavior, extreme sensitivity to light, and neck stiffness

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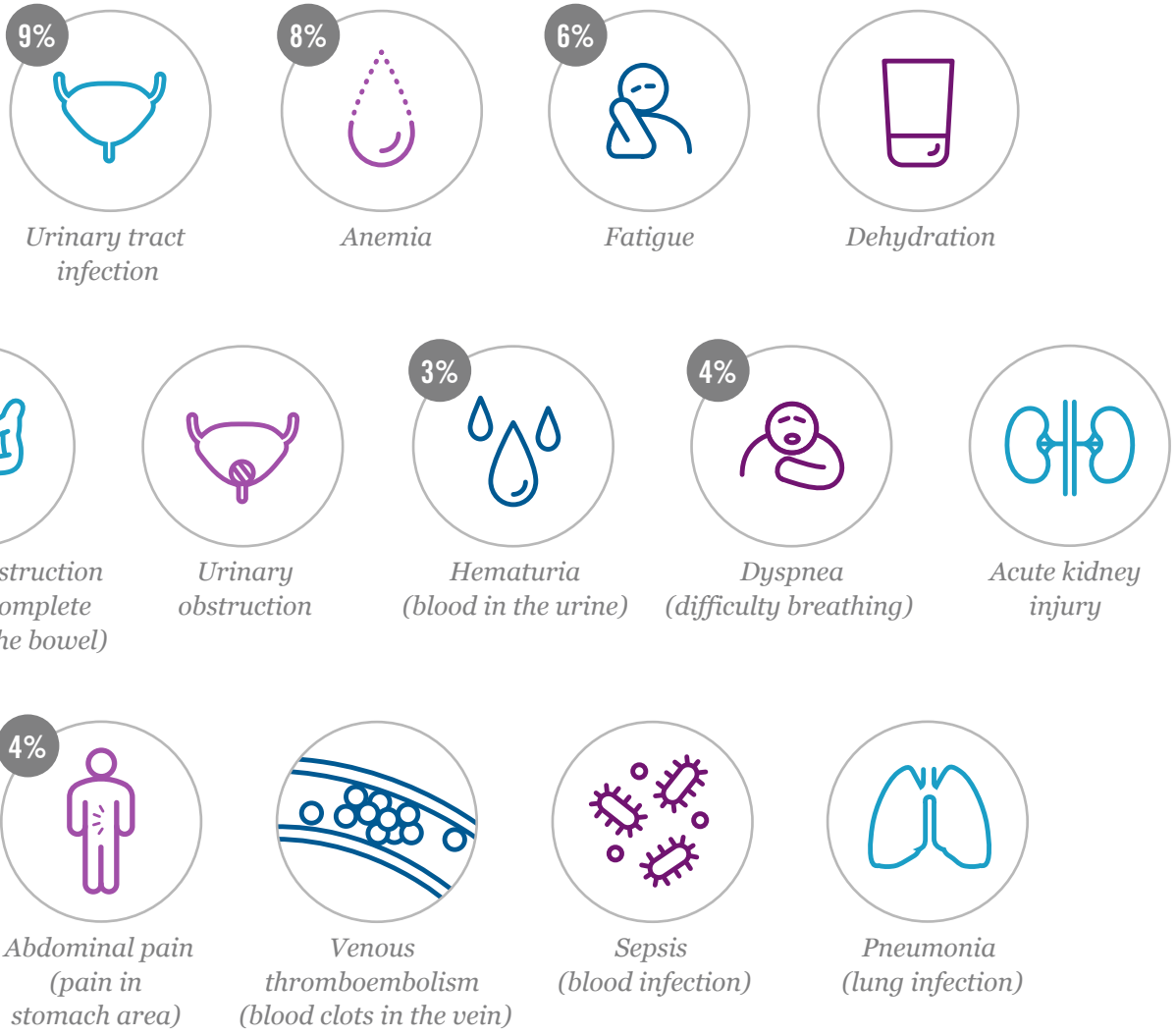
Study-specific safety

The most common Grade 3-4 adverse reactions (>2%) were:



Three people (0.9%) experienced either sepsis, pneumonitis (lung problems) or intestinal obstruction, which led to death.

Important Safety Information (continued)

- **Inflammation of the Eyes** – Symptoms may include blurry vision, double vision or other vision problems, eye pain or redness
- **Severe Infections** – Symptoms of infection may include fever, cough, frequent urination, flu-like symptoms, and pain when urinating
- **Severe Infusion Reactions** – Signs and symptoms of infusion reactions may include chills or shaking, itching or rash, flushing, shortness of breath or wheezing, dizziness, fever, feeling like passing out, back or neck pain, and facial swelling

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Important Safety Information (continued)

Before receiving TECENTRIQ, patients should tell their healthcare provider about all of their medical conditions, including if they:

- have immune system problems (such as Crohn's disease, ulcerative colitis, or lupus); have had an organ transplant; have lung or breathing problems; have liver problems; have a condition that affects your nervous system (such as Myasthenia Gravis or Guillain-Barre syndrome); or are being treated for an infection.
- are pregnant or plan to become pregnant.
  - o TECENTRIQ can harm an unborn baby.
  - o If patients are able to become pregnant, they should use an effective method of birth control during treatment and for at least 5 months after the last dose of TECENTRIQ.
- are breastfeeding or plan to breastfeed.
  - o It is not known if TECENTRIQ passes into the breastmilk.
  - o Do not breastfeed during treatment and for at least 5 months after the last dose of TECENTRIQ.

Patients should tell their healthcare provider about all of the medicines they take, including prescription and over-the-counter medicines, vitamins and herbal supplements.

The most common side effects of TECENTRIQ include:

- feeling tired
- decreased appetite
- nausea
- urinary tract infection
- fever
- constipation

These are not all the possible side effects of TECENTRIQ. Patients should ask their healthcare provider or pharmacist for more information.

Report side effects to the FDA at (800) FDA-1088, or http://www.fda.gov/medwatch. Report side effects to Genentech at (888) 835-2555.

Please visit http://www.TECENTRIQ.com for the TECENTRIQ full Prescribing Information for additional Important Safety Information.

[1] TECENTRIQ (atezolizumab) Prescribing Information. Genentech, Inc. 2016.

[2] Guancial EA, et al. Journal of Clinical Interventions in Aging. 2015;10:939-949. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4467651/. Accessed December 9, 2015.

[3] National Cancer Institute. Drugs Approved for Bladder Cancer. http://www.cancer.gov/about-cancer/treatment/drugs/bladder. Accessed December 9, 2015.

[4] CenterWatch. FDA Approved Drugs for Oncology. https://www.centerwatch.com/drug-information/fda-approved-drugs/therapeutic-area/12/oncology. Accessed December 9, 2015.

[5] American Cancer Society. What Is Bladder Cancer? http://www.cancer.org/cancer/bladdercancer/detailedguide/bladder-cancer-what-is-bladder-cancer. Accessed November 24, 2015.

[6] National Cancer Institute. Metastatic Cancer Fact Sheet. http://www.cancer.gov/about-cancer/what-is-cancer/metastatic-fact-sheet. Accessed January 8, 2016.

[7] American Cancer Society. Key Statistics For Bladder Cancer. http://www.cancer.org/cancer/bladdercancer/detailedguide/bladder-cancer-key-statistics. Accessed March 23, 2016.

[8] National Cancer Institute. SEER Stat Fact Sheets: Bladder Cancer. http://seer.cancer.gov/statfacts/html/urinb.html. Accessed May 18, 2015.

[9] American Cancer Society. Cancer Immunotherapy. http://www.cancer.org/acs/groups/cid/documents/webcontent/003013-pdf.pdf. Accessed January 8, 2016.

[10] Chen DS, et al. Molecular Pathways: Next-Generation Immunotherapy—Inhibiting Programmed Death-Ligand 1 and Programmed Death-1. Clin. Cancer Res. 2012. 18:6580-6587.

[11] Chen DS, Mellman I. Oncology Meets Immunology: The Cancer-Immunity Cycle. *Immunity.* 2013. 39:1-10.

[12] Keir ME, et al. PD-1 and Its Ligands in Tolerance and Immunity. *Annual Review of Immunology.* 2008. 26:677-704.