

Corporate Medical Policy

Atezolizumab (Tecentriq) for Intravenous Use

File Name: atezolizumab_tecentriq_for_intravenous_use
Origination: 6/2016
Last CAP Review: 11/2020
Next CAP Review: 11/2021
Last Review: 11/2020

Description of Procedure or Service

Tecentriq® (atezolizumab) is an Fc-engineered, humanized, monoclonal antibody that binds to PD-L1 and blocks its interactions with both PD-1 and B7.1 receptors. This releases the PD-L1/PD-1 mediated inhibition of the immune response, including activation of the anti-tumor immune response without inducing antibody-dependent cellular cytotoxicity.

PD-L1 may be expressed on tumor cells and/or tumor-infiltrating immune cells and can contribute to the inhibition of the anti-tumor immune response in the tumor microenvironment. Binding of PD-L1 to the PD-1 and B7.1 receptors found on T cells and antigen presenting cells suppresses cytotoxic T-cell activity, T-cell proliferation and cytokine production.

Tecentriq (atezolizumab) is used for the treatment of patients with locally advanced or metastatic urothelial carcinoma (mUC) and metastatic non-small cell lung cancer who have disease progression during or following platinum-based chemotherapy, or whose disease has worsened within 12 months of receiving platinum-based chemotherapy before surgery (neoadjuvant) or after surgery (adjuvant).

Urothelial carcinoma accounts for 90% of all bladder cancers and can also be found in the renal pelvis, ureter and urethra. Metastatic urothelial cancer (mUC) is associated with a poor prognosis and limited treatment options. It is a disease that has seen no major advances for more than 30 years. UC is the ninth most common cancer worldwide, with 430,000 new cases diagnosed in 2012, and it results in approximately 145,000 deaths globally each year. Men are three times more likely to suffer from UC, compared with women, and the disease is three times more common in developed countries than in less developed countries.

The efficacy of Tecentriq (atezolizumab) was investigated in two multi-center, international, randomized, open-label trials in patients with metastatic non-small cell lung cancer (NSCLC) who progressed during or following a platinum-containing regimen (Study 2 and Study 3). Compared with docetaxel, treatment with atezolizumab in the intended patient population in the two trials resulted in a 4.2 and a 2.9 month improvement in overall survival (OS), respectively.

In both studies, eligible patients were stratified by PD-L1 expression status in tumor-infiltrating immune cells (IC), by the number of prior chemotherapy regimens, and by histology. These studies excluded patients who had: a history of autoimmune disease, had active or corticosteroid-dependent brain metastases, administration of a live, attenuated vaccine within 28 days prior to enrollment, administration of systemic immunostimulatory agents within 4 weeks or systemic immunosuppressive medications within 2 weeks prior to enrollment. The major efficacy outcome measure of Study 2 was overall survival (OS) in the primary analysis population (first 850 randomized patients). The major efficacy outcome measure of Study 3 was overall survival (OS).

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*****Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.**

Policy

BCBSNC will provide coverage for Atezolizumab (Tecentriq) for intravenous use when it is determined to be medically necessary because the medical criteria and guidelines noted below are met.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

When Atezolizumab (Tecentriq) is covered

Atezolizumab (Tecentriq) may be considered medically necessary for the treatment of patients with:

1. Locally advanced or metastatic urothelial carcinoma, as monotherapy, who:
 - Have documented disease progression during or following platinum-containing chemotherapy; **OR**
 - Have documented disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy; **OR**
 - Are not eligible for cisplatin-containing chemotherapy and whose tumors express PD-L1 (PD-L1 stained tumor-infiltrating immune cells [IC] covering $\geq 5\%$ of the tumor area), as determined by an FDA-approved test; **OR**
 - Are not eligible for any platinum-containing chemotherapy regardless of PD-L1 status;

OR

2. Metastatic non-small cell lung cancer, as monotherapy, who:
 - Have disease progression during or following platinum-containing chemotherapy, **AND**
 - Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy targeting alterations in EGFR/ALK prior to receiving atezolizumab; **OR**
 - Have no EGFR or ALK genomic tumor aberrations and whose tumors have high PD-L1 expression (PD-L1 stained $\geq 50\%$ of tumor cells or PD-L1 stained tumor-infiltrating immune cells covering $\geq 10\%$ of the tumor area), as determined by an FDA-approved test, and are receiving atezolizumab as first-line treatment;

OR

3. Metastatic non-small cell lung cancer who:
 - Have no EGFR or ALK genomic tumor aberrations, and are receiving atezolizumab as first-line treatment in combination with bevacizumab, paclitaxel, and carboplatin; **OR**
 - Have no EGFR or ALK genomic tumor aberrations, and are receiving atezolizumab as first-line treatment in combination with paclitaxel protein-bound and carboplatin;

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OR

4. Triple-Negative Breast Cancer (TNBC) who:

- Have unresectable locally advanced or metastatic disease with tumors expressing PD-L1 (PD-L1 stained tumor-infiltrating immune cells [IC] of any intensity covering $\geq 1\%$ of the tumor area), as determined by an FDA-approved test, and are receiving atezolizumab in combination with paclitaxel protein-bound;

OR

5. Small Cell Lung Cancer (SCLC) who:

- Have extensive-stage disease, and are receiving atezolizumab as first-line treatment in combination with carboplatin and etoposide;

OR

6. Hepatocellular Carcinoma who:

- Have unresectable or metastatic disease and have not received prior systemic chemotherapy, and are receiving atezolizumab in combination with bevacizumab;

OR

7. Melanoma who:

- Have BRAF V600 mutation-positive unresectable or metastatic disease, and are receiving atezolizumab in combination with cobimetinib and vemurafenib.

Use of Atezolizumab (Tecentriq) may be considered medically necessary for clinical indications not listed above when the drug is prescribed for the treatment of cancer either:

- In accordance with FDA label (when clinical benefit has been established, see Policy Guidelines); **OR**
- In accordance with specific strong endorsement or support by nationally recognized compendia, when such recommendation is based on strong/high levels of evidence, and/or uniform consensus of clinical appropriateness has been reached.

When Atezolizumab (Tecentriq) is not covered

Atezolizumab (Tecentriq) is considered investigational when used for:

1. Non-cancer indications; **OR**
2. When criteria are not met regarding FDA labeling **OR** strong endorsement/support by nationally recognized compendia, as stated under “When Atezolizumab (Tecentriq) is Covered.”

Policy Guidelines

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Dosage and Administration

Administer Tecentriq as an intravenous infusion over 60 minutes. If the initial infusion is tolerated, subsequent infusions may be administered over 30 minutes.

Urothelial Carcinoma: 840mg every 2 weeks, 1200mg every 3 weeks, or 1680mg every 4 weeks.

NSCLC: For monotherapy, 840mg every 2 weeks, 1200mg every 3 weeks, or 1680mg every 4 weeks. 1200mg every 3 weeks prior to chemotherapy or other antineoplastic drugs when administered with bevacizumab and paclitaxel and carboplatin. After completion of 4-6 cycles of paclitaxel and carboplatin, and if bevacizumab is discontinued, administer as 840mg every 2 weeks, 1200mg every 3 weeks, or 1680mg every 4 weeks.

Metastatic Treatment of TNBC: 840mg followed by 100 mg/m² paclitaxel protein-bound. Administer Tecentriq on days 1 and 15, and paclitaxel protein-bound on days 1, 8, and 15 of 28 day cycles.

SCLC: 1200mg every 3 weeks prior to chemotherapy when administered with carboplatin and etoposide. After completion of 4 cycles of carboplatin and etoposide, administer as 840mg every 2 weeks, 1200mg every 3 weeks, or 1680mg every 4 weeks.

HCC: 1200mg followed by 15 mg/kg bevacizumab, every 3 weeks. If bevacizumab is discontinued, then the recommended dose is 840mg every 2 weeks, 1200mg every 3 weeks, or 1680mg every 4 weeks.

Melanoma: Prior to initiating atezolizumab, a 28-day cycle of cobimetinib and vemurafenib should be administered. The recommended dose of atezolizumab is 840mg every 2 weeks, when administered with cobimetinib 60mg daily (21 days on, 7 days off) and vemurafenib 720mg twice daily.

The most common adverse reactions ($\geq 20\%$) in patients with locally advanced or metastatic urothelial carcinoma were fatigue, decreased appetite, nausea, urinary tract infection, pyrexia, and constipation. The most common adverse reactions ($\geq 20\%$) in patients with metastatic non-small cell lung cancer were fatigue, decreased appetite, dyspnea, cough, nausea, musculoskeletal pain, and constipation. Clinically significant immune-related adverse events for patients receiving atezolizumab included pneumonitis, hepatitis, colitis, and thyroid disease.

Drugs prescribed for treatment of cancer in accordance with FDA label may be considered medically necessary when clinical benefit has been established, and should not be determined to be investigational as defined in Corporate Medical Policy (CMP), “Investigational (Experimental) Services.”

Please refer to CMP “Investigational (Experimental) Services” for a summary of evidence standards from nationally recognized compendia.

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcsnc.com. They are listed in the Category Search on the Medical Policy search page.

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Applicable service codes: J9022, S0353, S0354

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources

Food and Drug Administration (FDA) Prescribing Information.

http://www.accessdata.fda.gov/drugsatfda_docs/label/2016/761034Orig1s000lbl.pdf

MedLine https://www.nlm.nih.gov/medlineplus/news/fullstory_158937.html

<http://www.roche.com/media/store/releases/med-cor-2016-05-19.htm>

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Food and Drug Administration (FDA) Prescribing Information.

http://www.accessdata.fda.gov/drugsatfda_docs/label/2016/761041lbl.pdf

Medical Director review 10/2016

Specialty Matched Consultant Advisory Panel 11/2016

Medical Director review 1/2017

Specialty Matched Consultant Advisory Panel 11/2017

Food and Drug Administration (FDA) Prescribing Information.

https://www.gene.com/download/pdf/tecentriq_prescribing.pdf

Specialty Matched Consultant Advisory Panel 11/2018

Genentech, Inc. Tecentriq (atezolizumab) injection, for intravenous use. Highlights of prescribing information. May 2019. Available at:

https://www.gene.com/download/pdf/tecentriq_prescribing.pdf. Last accessed October 2019.

Specialty Matched Consultant Advisory Panel 11/2019

Medical Director review 11/2019

Genentech, Inc. Tecentriq (atezolizumab) injection, for intravenous use. Highlights of prescribing information. July 2020. Available at: https://www.gene.com/download/pdf/tecentriq_prescribing.pdf.

Last accessed November 2020.

Specialty Matched Consultant Advisory Panel 11/2020

Policy Implementation/Update Information

7/1/16 New policy developed. Atezolizumab (Tecentriq) may be considered medically necessary for the following clinical conditions: 1. Locally advanced or metastatic urothelial carcinoma and Tecentriq is used as monotherapy; AND 2. Documented disease progression during or following platinum-containing chemotherapy; OR 3.

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- Documented disease progression with 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy. Medical director review 6/2016. (lpr)
- 8/30/16 Deleted HCPCS code C9399 and added C9483 to Billing/Coding section for 10/1/16 effective date. (lpr)
- 12/30/16 Added covered indication for metastatic non-small cell lung cancer to “When Covered” section. Medical Director review 10/2016. Specialty Matched Consultant Advisory Panel review 11/30/2016. Reference added. (lpr)
- 1/6/17 Clarified and renumbered covered indications under “When Covered” section to reflect that the drug is approved for either cancer #1 (metastatic urothelial carcinoma) or #2 (metastatic non-small cell lung cancer). Medical director review 1/4/17. (lpr)
- 1/27/17 Added the following statement to “When Covered” section: “Use of Atezolizumab (Tecentriq) may be considered medically necessary for clinical indications not listed above when the drug is prescribed for the treatment of cancer either: In accordance with FDA label (when clinical benefit has been established, see Policy Guidelines); OR In accordance with specific strong endorsement or support by nationally recognized compendia, when such recommendation is based on strong/high levels of evidence, and/or uniform consensus of clinical appropriateness has been reached”. Under When Not Covered section added the following statement: Atezolizumab (Tecentriq) is considered investigational when used for; 1) Non-cancer indications; OR 2) When criteria are not met regarding FDA labeling or strong endorsement/ support by nationally recognized compendia, as stated under “When Atezolizumab (Tecentriq) is Covered.” Added the following statements under “Policy Guidelines” section: 1) Drugs prescribed for treatment of cancer in accordance with FDA label may be considered medically necessary when clinical benefit has been established, and should not be determined to be investigational as defined in Corporate Medical Policy, Investigational (Experimental) Services.” 2) Please refer to CMP “Investigational (Experimental) Services” for a summary of evidence standards from nationally recognized compendia. Medical Director review 1/2017. (lpr)
- 12/29/17 Specialty Matched Consultant Advisory Panel review 11/29/2017. Relocated the words “Atezolizumab (Tecentriq) is used as a monotherapy” to the medically necessary statement prior to bullets #1 and #2 under “When Covered” section. No change to policy statement. Added CPT codes J9022, S0353, S0354 to the Billing/Coding section; removed unlisted CPT codes J3490, J3590, J9999 and C9483. (lpr)
- 1/15/19 Added the following indications to “When Covered” section for locally advanced or metastatic urothelial carcinoma: “are not eligible for cisplatin-containing chemotherapy and whose tumors express PD-L1 (PD-L1 stained tumor-infiltrating immune cells [IC] covering $\geq 5\%$ of the tumor area), as determined by an FDA-approved; OR are not eligible for any platinum-containing chemotherapy regardless of PD-L1 status.” References added. Specialty Matched Consultant Advisory Panel review 11/28/2018. (krc)
- 12/10/19 Updated “When Covered” section with the following indications: Metastatic Non-Small Cell Lung Cancer (NSCLC) who have no EGFR or ALK genomic tumor aberrations, and are receiving atezolizumab as first-line treatment in combination with bevacizumab, paclitaxel, and carboplatin; Triple-Negative Breast Cancer (TNBC) who have unresectable locally advanced or metastatic disease with tumors expressing PD-L1 (PD-L1 stained tumor-infiltrating immune cells [IC] of any intensity covering $\geq 1\%$ of the tumor area), as determined by an FDA-approved test, and are receiving atezolizumab in combination with paclitaxel protein-bound; and Small Cell Lung Cancer (SCLC) who have extensive-stage disease, and are receiving atezolizumab as first-line treatment in combination with carboplatin and etoposide. Under “When Covered” for metastatic NSCLC monotherapy, added the following: “targeting alterations in EGFR/ALK” to

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further clarify type of FDA-approved therapy. Updated Policy Guidelines with appropriate dosing by indication. Minor edits made throughout policy for clarity. References added. Specialty Matched Consultant Advisory Panel review 11/20/2019. Medical Director review 11/2019. (krc)

- 1/12/21 Updated “When Covered” section with the following indications: metastatic NSCLC with no EGFR or ALK genomic tumor aberrations and whose tumors have high PD-L1 expression as determined by an FDA-approved test, and are receiving atezolizumab as first-line treatment; metastatic NSCLC with no EGFR or ALK genomic tumor aberrations, and are receiving atezolizumab as first-line treatment in combination with paclitaxel protein-bound and carboplatin; unresectable or metastatic HCC with no prior systemic chemotherapy; and BRAF V600 mutation-positive unresectable or metastatic melanoma. Updated Policy Guidelines with appropriate dosing by indication. Minor edits made throughout policy for clarity. Reference added. Specialty Matched Consultant Advisory Panel review 11/18/2020. (krc)

Medical policy is not an authorization, certification, explanation of benefits or a contract. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the group contract and subscriber certificate that is in effect at the time services are rendered. This document is solely provided for informational purposes only and is based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. Medical practices and knowledge are constantly changing and BCBSNC reserves the right to review and revise its medical policies periodically.