Atezolizumab

DESCRIPTION

Atezolizumab is a monoclonal antibody that binds to programmed death-ligand 1 (PD-L1), a transmembrane protein which may be expressed on tumor cells and/or tumor-infiltrating immune cells and are often increased. By binding to the receptors on PD-L1, atezolizumab prevents its binding to the PD-1 and B7.1 receptors found on T cells and antigen presenting cells. This releases the PD-L1/PD-1 mediated inhibition of the immune response and activates

The proposal is to add text/statements in red and to delete text/statements with strikethrough:

POLICY

- Atezolizumab is considered ***medically necessary*** for the treatment of the following if the medical appropriateness criteria are met. **(See Medical Appropriateness below.)**
  - ~~Bladder Cancer~~/Urothelial Carcinoma (Bladder Cancer)
  - Breast Cancer [Triple Negative (TNBC)]
  - Hepatocellular Adenocarcinoma
  - Melanoma, cutaneous
  - Non-Small Cell Lung Cancer (NSCLC)
  - Small Cell Lung Cancer (SCLC)

- Atezolizumab for the treatment of other conditions/diseases is considered ***investigational.***

MEDICAL APPROPRIATENESS

INITIAL APPROVAL

- Atezolizumab is considered **medically appropriate** if **ALL** of the following:
  - Individual is 18 years of age or older
  - Individual has not received previous therapy with a programmed death (PD-1/PD-L1)-directed therapy (e.g., cemiplimab, nivolumab, pembrolizumab, durvalumab, avelumab, etc.) unless otherwise specified
  - Diagnosis of **ANY ONE** of the following:
    - Breast Cancer and **ALL** of the following:
      - Used in combination with albumin-bound paclitaxel
      - Individual has unresectable locally advanced, recurrent or metastatic triple-negative disease (TNBC)
      - Individual has a PD-L1 expression (PD-L1 stained tumor-infiltrating immune cells [IC] of any intensity covering ≥ 1% of the tumor area) as determined by an FDA-approved or CLIA compliant test *(If confirmed using an FDA approved assay– http://www.fda.gov/companiondiagnostics)*
    - Hepatocellular Carcinoma and **ALL** of the following:
      - Used as first-line therapy in combination with bevacizumab
      - Individual has Child-Pugh Class A disease
      - Individual has locally advanced, unresectable, inoperable, or metastatic disease
    - Melanoma, cutaneous and **ALL** of the following:
      - Individual is BRAF V600 mutation positive as detected by FDA approved or CLIA compliant test *(If confirmed using an FDA approved assay– http://www.fda.gov/companiondiagnostics)*
      - Individual has unresectable or metastatic disease
      - Used as first-line therapy in combination with cobimetinib and vemurafenib
    - Non-small cell lung cancer (NSCLC) and **ALL** of the following:

- Individual has recurrent, advanced, or metastatic disease ~~-~~(excluding locoregional recurrence or symptomatic local disease without evidence of disseminated disease) or mediastinal lymph node recurrence with prior radiation therapy ~~and~~
- Used as **ANY ONE** of the following:
  - First-line therapy and **ANY ONE** of the following:
    - Used for EGFR, ALK, ROS1, BRAF, MET exon 14 skipping mutation, and RET rearrangement negative* tumors and PD-L1 ≥50% (PD-L1 stained ≥ 50% of tumor cells [TC ≥ 50%] or PD-L1 stained tumor-infiltrating immune cells [IC] covering ≥ 10% of the tumor area [IC ≥ 10%]), as determined by an FDA-approved test or CLIA-compliant test *(If confirmed using approved assay– http://www.fda.gov/companiondiagnostics)* and used as a single agent
    - Used for non-squamous disease in combination with carboplatin, paclitaxel, and bevacizumab OR in combination with carboplatin and albumin-bound paclitaxel for **ANY ONE** of the following:
      - Used in individuals with PS 0-1 for EGFR, ALK, ROS1, BRAF, MET exon 14 skipping mutation, and RET rearrangement negative* tumors and PD-L1 <1% (TC or IC <1%)
      - Used in individuals with PS 0-2 for EGFR, ALK, ROS1, BRAF, MET exon 14 skipping mutation, and RET rearrangement negative* tumors and PD-L1 ≥1% (TC or IC ≥1%)
      - Used in individuals with PS 0-1 for BRAF V600E-mutation, NTRK gene fusion, MET exon-14 skipping mutation, or RET rearrangement positive tumors
  - ~~o~~ Subsequent therapy and **ANY ONE** of the following:
    - Used as a single agent
    - Used for non-squamous disease in combination with carboplatin, paclitaxel, and bevacizumab OR in combination with carboplatin and albumin-bound paclitaxel as **ANY ONE** of the following:
      - Used in individuals with PS 0-1 for BRAF V600E-mutation, NTRK gene fusion, MET exon-14 skipping mutation, or RET rearrangement positive tumors
      - Used in individuals with PS 0-1 EGFR, ALK, or ROS1 positive tumors ~~positive~~ and prior targeted therapy**
  - Continuation maintenance therapy in individuals who have achieved a tumor response or stable disease following initial therapy and **ANY ONE** of the following:
    - Used in combination with bevacizumab following a first-line regimen with atezolizumab, carboplatin, paclitaxel, and bevacizumab for non-squamous histology
    - Used as a single agent following a first-line regimen with atezolizumab, carboplatin, and albumin-bound paclitaxel regimen for non-squamous histology
    - Used as a single agent following a first-line regimen with single agent atezolizumab

** Note: If there is insufficient tissue to allow testing for all of the RET, MET, EGFR, ALK, ROS1, and BRAF, repeat biopsy and/or plasma testing should be done. If these are not feasible, treatment is guided by available results and, if unknown, these patients are treated as though they do not have driver oncogenes*

- Small Cell Lung Cancer (SCLC) and ~~**ALL of the following:**~~ individual has extensive stage disease (ES-SCLC) (excluding individuals with poor PS 3-4 not due to SCLC) and **ANY ONE** of the following:
  - Used as first-line therapy in combination with etoposide and carboplatin
  - Used as single-agent maintenance therapy after initial therapy with etoposide and carboplatin
- ~~Must not be used for relapsed disease in individuals on maintenance therapy with atezolizumab or durvalumab at the time relapse *(NOTE: If relapse occurred >6 months after atezolizumab or durvalumab maintenance therapy, individual should be re-treated with carboplatin + etoposide alone or cisplatin + etoposide alone).*~~
- Urothelial Carcinoma (Bladder Cancer) with **ALL** of the following:
  - Used as a single agent
  - Individual is further diagnosed as **ANY ONE** of the following:

- Locally advanced or metastatic urothelial carcinoma
- Local bladder cancer recurrence or persistent disease in a preserved bladder
- Local or metastatic bladder cancer recurrence post-cystectomy
- Primary carcinoma of the urethra and **ANY ONE** of the following:
  - Used for recurrent (excluding recurrence of stage T3-4 disease or palpable inguinal lymph nodes) or metastatic disease
  - Used for stage T3-4, cN1-2 disease or cN1-2 palpable inguinal lymph nodes (first-line therapy only)
- Metastatic upper genitourinary (GU) tract tumors
- Metastatic urothelial carcinoma of the prostate

- Used as **ANY ONE** of the following:
  - Subsequent therapy after previous platinum treatment*
  - First-line therapy in cisplatin-ineligible individuals* and **ANY ONE** of the following:
    - Individual is carboplatin-ineligible*
    - Individual has a PD-L1 expression of ≥5% (PD-L1 stained tumor-infiltrating immune cells [IC] covering ≥ 5% of the tumor area) as determined by an FDA-approved or CLIA-compliant test (*If confirmed using an FDA approved assay–* http://www.fda.gov/companiondiagnostics)

**If platinum treatment occurred greater than 12 months ago, the individual should be re-treated with platinum-based therapy if the individual is still platinum eligible (see below for cisplatin- or carboplatin-ineligible comorbidities).*

- *Cisplatin-ineligible comorbidities may include the following: GFR < 60 mL/min, PS ≥ 2, hearing loss of ≥ 25 decibels (dB) at two contiguous frequencies, or grades ≥ 2 peripheral neuropathy. Carboplatin may be substituted for cisplatin particularly in those individuals with a GFR <60 mL/min or a PS of 2.*
- *Carboplatin-ineligible comorbidities may include the following: CrCl < 30 mL/min, PS ≥ 3, grade ≥ 3 peripheral neuropathy, or NYHA class ≥ 3, etc.*

**Genomic Aberration/Mutational Driver Targeted Therapies (*not all inclusive, refer to guidelines for appropriate use*)
Sensitizing *EGFR* mutation-positive tumors • Afatinib • Dacomitinib • Erlotinib • Gefitinib • Osimertinib
ALK rearrangement-positive tumors • Alectinib • Brigatinib • Ceritinib • Crizotinib • Lorlatinib
ROS1 rearrangement-positive tumors • Ceritinib • Crizotinib • Entrectinib

BRAF V600E-mutation positive tumors • Dabrafenib/Trametinib • Vemurafenib
NTRK Gene Fusion positive tumors • Larotrectinib • Entrectinib
PD-1/PD-L1 expression-positive tumors (≥1%) • Pembrolizumab • Atezolizumab • Nivolumab ± ipilimumab
MET Exon-14 skipping mutations • Capmatinib • Crizotinib
RET rearrangement-positive tumors • Cabozantinib • Selpercatinib • Vandetanib

RENEWAL CRITERIA

- Atezolizumab is considered **medically appropriate** for renewal therapy if **ALL** of the following criteria are met:
  - Individual continues to meet initial approval criteria (not including prerequisite therapy)
  - Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread
  - Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: ~~severe infusion reactions,~~ immune-mediated adverse reactions (such as pneumonitis, hepatitis, colitis, endocrinopathies, etc.), severe infections, severe infusion related reactions, etc.
  - Continuation Maintenance Therapy for NSCLC or SCLC and individual continues to meet initial approval criteria

INDICATION(S)	DOSAGE & ADMINISTRATION
Triple negative Breast Cancer- (TNBC)	Administer 840 mg intravenously on days 1 and 15 of a 28-day cycle until disease progression or unacceptable toxicity
Urothelial Carcinoma (UC)	The recommended dosage is administered intravenously until disease progression or unacceptable toxicity: • 840 mg every 2 weeks or • 1200 mg every 3 weeks or • 1680 mg every 4 weeks
Non-Small Cell Lung Cancer (NSCLC)	Single Agent The recommended dosage is administered intravenously until disease progression or unacceptable toxicity: • 840 mg every 2 weeks or • 1200 mg every 3 weeks or • 1680 mg every 4 weeks Combination Therapy The recommended dosage is administered intravenously

	• 1200 mg every 3 weeks; then revert to single-agent therapy dosing after completion of 4-6 cycles of combination therapy
Small Cell Lung Cancer (SCLC)	Combination Therapy with carboplatin and etoposide The recommended dosage is administered intravenously • 1200 mg every 3 weeks; then revert to single-agent therapy dosing after completion of 4 cycles of carboplatin and etoposide Single Agent Maintenance Therapy The recommended dosage is administered intravenously until disease progression or unacceptable toxicity: • 840 mg every 2 weeks or • 1200 mg every 3 weeks or • 1680 mg every 4 weeks
Hepatocellular Adenocarcinoma (HCC)	Administer 1200 mg intravenously every 3 weeks until disease progression or unacceptable toxicity
Cutaneous Melanoma	Administer 840 mg intravenously every 2 weeks until disease progression or unacceptable toxicity. **Prior to initiating TECENTRIQ, patients should receive a 28 day treatment cycle of cobimetinib 60 mg orally once daily (21 days on and 7 days off) and vemurafenib 960 mg orally twice daily from Days 1-21 and vemurafenib 720 mg orally twice daily from Days 22-28.*

LENGTH OF AUTHORIZATION

Coverage will be provided for six months and may be renewed

Refer to **DOSAGE LIMITS** below

APPLICABLE TENNESSEE STATE MANDATE REQUIREMENTS

BlueCross BlueShield of Tennessee's Medical Policy complies with Tennessee Code Annotated Section 56-7-2352 regarding coverage of off-label indications of Food and Drug Administration (FDA) approved drugs when the off-label use is recognized in one of the statutorily recognized standard reference compendia or in the published peer-reviewed medical literature.

IMPORTANT REMINDER

We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member's health plan must be reviewed. If there is a conflict between the Medical Policy and a health plan, the express terms of the health plan will govern.

ADDITIONAL INFORMATION

For appropriate chemotherapy regimens, dosage information, contraindications, precautions, warnings, and monitoring information, please refer to one of the standard reference compendia (e.g., the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) published by the National Comprehensive Cancer Network®, Drugdex

Evaluations of Micromedex Solutions at Truven Health, or The American Hospital Formulary Service Drug Information).

SOURCES

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U. S. Food and Drug Administration. (2020, November). Center for Drug Evaluation and Research. *Tecentriq® (atezolizumab) injection, for intravenous use.* Retrieved December 17, 2020 from https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/761034s001lbl.pdf.

EFFECTIVE DATE

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