Medical Policy

Healthcare Services Department

Policy Name	Policy Number	Scope
Tislelizumab-jsgr (Tevimbra®)	MP-RX-FP-155-24	☒ MMM MA ☒ MMM Multihealth

Service Category

☐ Anesthesia
☐ Surgery
☐ Radiology Procedures
☐ Pathology and Laboratory Procedures
☐ Medicine Services and Procedures
☐ Evaluation and Management Services
☐ DME/Prosthetics or Supplies
☒ Part B Drugs

Service Description

This document addresses the use of Tislelizumab-jsgr (Tevimbra®), a programmed death receptor-1 (PD-1)–blocking antibody approved by the Food and Drug Administration (FDA) for the treatment of adult patients with unresectable or metastatic esophageal squamous cell carcinoma (ESCC) after prior systemic chemotherapy that did not include a PD-(L)1 inhibitor.

Background Information

The FDA approved Tevimbra based on the results of the RATIONALE 302 trial, a multicenter, international, randomized, open-label, phase III study that included 512 patients. This study assessed the efficacy and safety of tislelizumab compared to the investigator's choice of chemotherapy as a second-line treatment for unresectable, locally advanced, or metastatic esophageal squamous cell carcinoma.

RATIONALE 302 demonstrated a statistically significant and clinically meaningful improvement in survival for patients treated with tislelizumab over those receiving chemotherapy. In the Intention to Treat population, the median overall survival for the tislelizumab group was 8.6 months (95% confidence interval [CI] = 7.5–10.4 months) compared to 6.3 months (95% CI = 5.3–7.0 months) for the chemotherapy group (P = .0001; hazard ratio = 0.70, 95% CI = 0.57–0.85).

Regarding safety, tislelizumab showed a more favorable profile than chemotherapy. The most common adverse events reported in the trial included increased glucose levels, decreased hemoglobin, decreased lymphocytes, decreased sodium, decreased albumin, increased alkaline phosphatase, anemia, fatigue, elevated AST, musculoskeletal pain, weight loss, increased ALT, and cough. The prescribing information for Tevimbra also includes warnings and precautions related to immune-mediated adverse reactions, infusion-related reactions, complications of allogeneic hematopoietic stem cell transplantation, and embryo-fetal toxicity.

According to NCCN, Tevimbra has a Category 1 recommendation as palliative therapy for patients who are not surgical candidates or have unresectable locally advanced, recurrent, or metastatic disease and Karnofsky performance score ≥60% or ECOG performance score ≤2 as preferred second-line therapy as a single agent for esophageal squamous cell carcinoma (ESCC) (if prior therapy for a locally advanced or metastatic ESCC did not contain checkpoint inhibitor(s)).

Tevimbra is supplied as a 100mg/10mL solution in a single-dose vial and is administered via intravenous infusion once every three weeks. Dosage adjustments may be necessary to manage adverse reactions.

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Additionally, the FDA is currently reviewing a biologics license applications for tislelizumab as a first-line treatment for patients with unresectable, recurrent, locally advanced, or metastatic esophageal squamous cell carcinoma (ESCC) and for those with locally advanced unresectable or metastatic gastric or gastroesophageal junction adenocarcinoma. The expected decision dates for these applications are set for July and December 2024, respectively.

Definitions and Measures

- ECOG or Eastern Cooperative Oncology Group Performance Status: A scale and criteria used by doctors and researchers to assess how an individual's disease is progressing, assess how the disease affects the daily living abilities of the individual, and determine appropriate treatment and prognosis. This scale may also be referred to as the WHO (World Health Organization) or Zubrod score which is based on the following scale:
  - 0 = Fully active, able to carry on all pre-disease performance without restriction
  - 1 = Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, for example, light house work, office work
  - 2 = Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours
  - 3 = Capable of only limited self-care, confined to bed or chair more than 50% of waking hours
  - 4 = Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair
  - 5 = Dead
- Karnofsky Performance Status: A scale and criteria used by doctors and researchers to assess an individual's prognosis, measure changes in their function and abilities, and determine their ability to tolerate therapies. The lower the score (from 0-100), the worse the likelihood of survival.
  - 100 = Normal, no complaints
  - 90 = Able to carry on normal activities
  - 80 = Normal activity with effort
  - 70 = Care for self. Unable to carry on normal activity or to do active work
  - 60 = Requires occasional assistance, but able to care for most of his needs
  - 50 = Requires considerable assistance and frequent medical care
  - 40 = Disabled. Requires special care and assistance
  - 30 = Severely disabled. Hospitalization indicated though death nonimminent
  - 20 = Very sick. Hospitalization necessary. Active supportive treatment necessary
  - 10 = Moribund
  - 0 = Dead
- Line of Therapy:
  - First-line therapy: The first or primary treatment for the diagnosis, which may include surgery, chemotherapy, radiation therapy or a combination of these therapies.
  - Second-line therapy: Treatment given when initial treatment (first-line therapy) is not effective or there is disease progression.

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    - Third-line therapy: Treatment given when both initial (first-line therapy) and subsequent treatment (second- line therapy) are not effective or there is disease progression.
- Metastasis: The spread of cancer from one part of the body to another; a metastatic tumor contains cells that are like those in the original (primary) tumor and have spread.
- Programmed death (PD)-1: PD-1 proteins are found on T-cells and attach to PD ligands (PD-L1) found on normal (and cancer) cells (see immune checkpoint inhibitor above). Normally, this process keeps T-cells from attacking other cells in the body. Examples of FDA approved PD-1 inhibitors include Keytruda (pembrolizumab), Opdivo (nivolumab), and Libtayo (cemiplimab).
- Programmed death ligand (PD-L)-1: The ligands found on normal (and cancer) cells to which the PD-1 proteins attach (see immune checkpoint inhibitor above). Cancer cells can have large amounts of PD-L1 on their surface, which helps them to avoid immune attacks. Examples of FDA approved PD-L1 inhibitors include Bavencio (avelumab), Tecentriq (atezolizumab), and Imfinzi (durvalumab).
- Unresectable: Unable to be removed with surgery.

Approved Indications

Tislelizumab-jsgr (Tevimbra®) is approved by the FDA for the treatment of adult patients with unresectable or metastatic esophageal squamous cell carcinoma (ESCC) after prior systemic chemotherapy that did not include a PD-(L)1 inhibitor.

Other Uses

None

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Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS	Description
J9329	Injection, tislelizumab-jsgr, 1mg [Tevimbra]

ICD-10	Description
C15.3	Malignant neoplasm of upper third of esophagus
C15.4	Malignant neoplasm of middle third of esophagus
C15.5	Malignant neoplasm of lower third of esophagus
C15.8	Malignant neoplasm of overlapping sites of esophagus
C15.9	Malignant neoplasm of esophagus, unspecified
C16.0	Malignant neoplasm of cardia
D37.8	Neoplasm of uncertain behavior of other specified digestive organs
D37.9	Neoplasm of uncertain behavior of digestive organ, unspecified
Z85.00	Personal history of malignant neoplasm of unspecified digestive organ
Z85.01	Personal history of malignant neoplasm of esophagus

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Medical Necessity Guidelines

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Tislelizumab-jsgr (Tevimbra®)

A. **Criteria For Initial Approval** (*Provider must submit documentation [such as office chart notes, lab results, pathology reports, imaging studies, and any other pertinent clinical information] supporting the patient's diagnosis for the drug and confirming that the patient has met **all** approval criteria.)*

i. Individual has a diagnosis of metastatic esophageal squamous cell carcinoma (ESCC); (Label); **AND**
ii. Individual has a current Eastern Cooperative Oncology Group (ECOG) performance status of 0-1; **AND**
iii. II. Individual is using Tevimbra (tislelizumab-jsgr) in combination with platinum-containing chemotherapy as first line of therapy.

OR

iv. Individual has a diagnosis of metastatic esophageal squamous cell carcinoma (ESCC); (Label); **AND**
v. Disease has progressed during or after first-line treatment for advanced unresectable/metastatic ESCC; **AND**
vi. Individual has a current Eastern Cooperative Oncology Group (ECOG) performance status of 0-1; **AND**
vii. Individual is using as a single agent.

OR

viii. Individual has a diagnosis of gastric cancer (gastric or gastroesophageal junction adenocarcinoma) (Label); **AND**
ix. Individual has either unresectable or metastatic HER2-negative disease; **AND**
x. Individual has a tumor which expresses PD-L1 (≥1); **AND**
xi. Individual is using as first-line therapy; **AND**
xii. Individual has not received another anti-PD-1 or anti-PD-L1 agent or any other antibody or drug specifically targeting T-cell co-stimulation or checkpoint pathways; **AND**
xiii. Individual is using in combination with platinum and fluoropyrimidine-based chemotherapy; **AND**
xiv. Individual has a current ECOG performance status of 0-1;

OR

xv. Individual is using for Chronic lymphocytic leukemia/Small lymphocytic leukemia (CLL/SLL) with 17p deletion (NCCN 2A); **AND**
xvi. Individual is using Tevimbra (tislelizumab-jsgr) in combination with Brukinsa (zanubrutinib).

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B. **Criteria For Continuation of Therapy**

i. MMM considers continuation of Tislelizumab-jsgr (Tevimbra®) therapy medically necessary in members requesting reauthorization for an indication listed in Section A above (Criteria for Initial Approval) when there is no evidence of unacceptable toxicity or disease progression while on the current regimen. The following information should be submitted for reauthorization:

A. A current oncology note documenting the patient's response to treatment showing no progression of disease.

B. Current imaging studies and other objective measures, as appropriate, showing no progression of disease when compared with previous results.

C. **Authorization Duration**

i. Initial Approval Duration: Up to 6 months

ii. Reauthorization Approval Duration: Up to 6 months

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D. **Conditions Not Covered**

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):

When using for ESCC:

I. Individual has used two or more prior systemic treatments for advanced/metastatic unresectable ESCC; **OR**
II. Individual has uncontrollable pleural effusion, pericardial effusion, or ascites requiring frequent drainage; **OR**
III. Individual received prior therapies targeting programmed death 1 (PD-1) or programmed death ligand 1 (PD- L1); **OR**
IV. Individual has active brain or leptomeningeal metastasis; **OR**
V. Individual has active autoimmune disease or history of autoimmune disease at high risk for relapse; **OR**
VI. Individual has known history of, or any evidence of interstitial lung disease, non-infectious pneumonitis, pulmonary fibrosis diagnosed based on imaging or clinical findings, or uncontrolled systemic diseases, including diabetes, hypertension, acute lung disease, etc; **OR**
VII. When the above criteria are not met, and for all other indications.

When using for gastric cancer:

A. Individual has squamous cell or undifferentiated or other histological type gastric cancer; **OR**
B. Individual has active leptomeningeal disease or uncontrolled brain metastasis; **OR**
C. Individual has active autoimmune disease or history of autoimmune disease, or a medical condition requiring systemic corticosteroids or immunosuppressants;

Limits or Restrictions

A. Therapeutic Alternatives

The list below includes preferred alternative therapies recommended in the approval criteria and may be subject to prior authorization.

i. N/A

B. Quantity Limitations

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. The chart below includes dosing recommendations as per the FDA-approved prescribing information.

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Drug	Recommended Dosing Schedule
Tislelizumab-jsgr (Tevimbra®)	200 mg (two single dose vials of 100 mg/10 mL) once every 3 weeks.
Exceptions	
None	

Reference Information

1. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.: 2024. URL: http://www.clinicalpharmacology.com. Updated periodically.
2. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Updated periodically
3. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
4. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2024; Updated periodically.
5. NCCN Clinical Practice Guidelines in Oncology™. © 2024 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website: http://www.nccn.org/index.asp. Accessed on July 1, 2024.
    a. Esophageal and Esophagogastric Junction Cancers. V4.2024. Revised May 9, 2024.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.

Policy History

Revision Type	Summary of Changes	P&T Approval Date	UM/CMPC Approval Date
Annual Review 6/16/2025	Coding changes: J3590 and J9999 removed. Indication for the first line therapy of ESCC in combination with platinum containing chemotherapy added. Indication for the first line treatment of unresectable or metastatic HER2- negative gastric or gastroesophageal junction adenocarcinoma whose tumors express PD-L1, in combination with platinum and fluoropyrimidine-based chemotherapy.	7/17/2025	8/8/2025

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	Use in combination with Brukinsa (zanubrutinib) for the treatmen of CLL/SLL with 17p deletion (CIT is not preferred), added to NCCN as a 2A recommendation.		
Policy Inception	New Medical Policy creation	7/29/2024	8/7/2024

Revised: 07/01/2024