CLINICAL GUIDELINES FOR MEDICAL NECESSITY

MEDICAL POLICY

Toripalimab-tpzi (Loqtorzi®)

Version: 1.0

EFFECTIVE DATE: 6/27/2025

NantHealth® | Eviti®

Please note the following:

For Medicare members/enrollees, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Please refer to the CMS website at http://www.cms.gov for additional information.

For Medicaid members/enrollees, circumstances when state Medicaid coverage provisions conflict with the coverage provisions within this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

Toripalimab-tpzi (Loqtorzi®)

Discussion

Toripalimab-tpzi is a humanized immunoglobulin G4 (IgG4) monoclonal antibody that binds to the PD-1 receptor and blocks its interaction with PD-L1 and PD-L2, releasing PD-1 pathway-mediated inhibition of the immune response, including the anti-tumor immune response. Binding of the PD-1 ligands, PD-L1 and PD-L2, to the PD-1 receptor found on T cells inhibits T cell proliferation and cytokine production. Upregulation of PD-1 ligands occurs in some tumors, and signaling through this pathway can inhibit active T-cell immune surveillance of tumors.[1,2]

Toripalimab-tpzi is associated with adverse reactions, including severe and fatal immune-mediated reactions, infusion-related reactions, and complications of allogeneic HSCT. When toripalimab-tpzi is used in combination with cisplatin and gemcitabine, the most common adverse reactions (≥ 20%) are nausea, vomiting, decreased appetite, constipation, hypothyroidism, rash, pyrexia, diarrhea, peripheral neuropathy, cough, musculoskeletal pain, upper respiratory infection, insomnia, dizziness, and malaise.[2]

Toripalimab-tpzi is approved by the Food and Drug Administration (FDA) for nasopharyngeal cancer.[8] The National Comprehensive Cancer Network (NCCN) endorses toripalimab-tpzi for the following cancer types: anal, colon, head and neck, rectal, and small bowel.[3,4,5,6,7]

Definitions

- **Food and Drug Administration (FDA)** - The FDA is responsible for protecting the public health by assuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices, our nation's food supply, cosmetics, and products that emit radiation.[8]
- **National Comprehensive Cancer Network (NCCN)** - An alliance of more than 30 leading cancer centers devoted to patient care, research, and education. The NCCN guidelines are utilized for Radiation Therapy and Medical Oncology standards. NCCN consensus clinical standards are periodically updated and NantHealth, Inc. reviews these and updates its policies within a timely manner.[9]
- **Programmed cell death protein 1 (PD-1)/Programmed cell death-ligand 1 (PD-L1)** - Checkpoint proteins, such as PD-L1 on tumor cells and PD-1 on T cells, help keep immune responses in check. The binding of PD-L1 to PD-1 keeps T cells from killing tumor cells in the body. Blocking the binding of PD-L1 to PD-1 with an immune checkpoint inhibitor (anti-PD-L1 or anti-PD-1) allows the T cells to kill tumor cells.[10]

Policy

Coverage will be considered for FDA approved indications and for NCCN category 1, 2A, or 2B recommendations when the following criteria are met:

Anal Carcinoma

1. At least 18 years of age; AND

2. Prescribed by or in consultation with an oncologist; AND

For **NCCN** required criteria coverage:

3. Single agent before proceeding to abdominoperineal resection for locally recurrent, progressive disease; OR
4. Second-line and subsequent therapy as a single agent for metastatic disease if no prior immunotherapy has been received.[3]

Colon Cancer

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For **NCCN** required criteria coverage:

3. Single agent (deficient mismatch repair/microsatellite instability-high [dMMR/MSI-H] or polymerase epsilon/delta [POLE/POLD1] mutation with ultra-hypermutated phenotype [eg, TMB >50 mut/Mb]) (candidate for immunotherapy and no prior immunotherapy received) for one of the following:
   a) Locally unresectable or medically inoperable disease
   b) Primary treatment for synchronous abdominal/peritoneal metastases that are nonobstructing, or following local therapy for patients with existing or imminent obstruction
   c) Synchronous unresectable metastases
   d) Unresectable metachronous metastases; OR
4. Single agent (dMMR/MSI-H) or (POLE/POLD1) mutation with ultra-hypermutated phenotype (e.g., TMB >50 mut/Mb) for one of the following:
   a) Neoadjuvant therapy in clinical T4b or bulky nodal disease
   b) Neoadjuvant therapy for resectable synchronous liver and/or lung metastases (if no previous treatment with a checkpoint inhibitor)
   c) Initial treatment for resectable metachronous metastases if no previous immunotherapy; OR

Appendiceal Adenocarcinoma

5. Systemic therapy for advanced or metastatic disease (dMMR/MSI-H) or (POLE/POLD1) mutation with ultra-hypermutated phenotype (e.g., TMB >50 mut/Mb) as a single agent if the patient is a candidate for immunotherapy and has not received prior immunotherapy.[4]

Head and Neck Cancers

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

Nasopharyngeal

For **FDA** required criteria coverage:

3. First-line treatment of metastatic or recurrent locally advanced disease in combination with cisplatin and gemcitabine; OR
4. Single agent for the treatment of recurrent unresectable or metastatic disease with disease progression on or after a platinum-containing chemotherapy;[8] OR

Nasopharynx

For **NCCN** required criteria coverage:

5. First-line systemic therapy in combination with cisplatin and gemcitabine for T1-4, N0-3, M1 for one of the following:
   a) Oligometastatic disease and performance status (PS) 0-2
   b) Widely metastatic disease and good PS (0-2); OR
6. Subsequent-line systemic therapy (if not previously used) in combination with cisplatin and gemcitabine for T1-4, N0-3, M1 for one of the following:
   a) Oligometastatic disease and performance status (PS) 0-2
   b) Widely metastatic disease and good PS (0-2); OR
7. Subsequent-line single agent systemic therapy if disease progression on or after platinum-containing therapy for T1-4, N0-3, M1
   a) Oligometastatic disease and performance status (PS) 0-2
   b) Widely metastatic disease and good PS (0-2); OR

Very Advanced Head and Neck Cancer

8. Systemic therapy as a first-line or subsequent-line (if not previously used) option in patients with nasopharyngeal cancer and performance status (PS) 0-1 for one of the following:
   a) Unresectable locoregional recurrence with prior radiation therapy (RT)
   b) Unresectable second primary with prior RT
   c) Unresectable persistent disease with prior RT
   d) Recurrent/persistent disease with distant metastases in combination with cisplatin and gemcitabine; OR
9. Systemic therapy as an alternate single agent subsequent-line option if disease progression on or after platinum-containing therapy for nasopharyngeal cancer and performance status (PS) of 0-3 for one of the following:
   a) Unresectable locoregional recurrence with prior radiation therapy (RT)
   b) Unresectable second primary with prior RT
   c) Unresectable persistent disease with prior RT
   d) Recurrent/persistent disease with distant metastases.[5]

Rectal Cancer

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For **NCCN** required criteria coverage:

3. Single agent in patients (deficient mismatch repair/microsatellite instability-high [dMMR/MSI-H] or polymerase epsilon/delta [POLE/POLD1] mutation with ultra-

hypermutated phenotype [eg, TMB >50 mut/Mb]) if candidate for immunotherapy and no prior immunotherapy received for primary treatment for one of the following:
   a) Synchronous abdominal/peritoneal metastases that are nonobstructing, or following local therapy for patients with existing or imminent obstruction
   b) Synchronous unresectable metastases
   c) Potentially resectable or unresectable isolated pelvic/anastomotic recurrence
   d) Unresectable metachronous metastases; OR
4. Single agent for patients (deficient mismatch repair/microsatellite instability-high [dMMR/MSI-H] or polymerase epsilon/delta [POLE/POLD1] mutation with ultra-hypermutated phenotype [eg, TMB >50 mut/Mb]) for one of the following:
   a) Neoadjuvant treatment for resectable synchronous liver only and/or lung only metastases (no previous treatment with a checkpoint inhibitor)
   b) Initial treatment for resectable metachronous metastases and no previous immunotherapy.[6]

Small Bowel Adenocarcinoma

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For **NCCN** required criteria coverage:

3. Single agent as primary treatment for locally unresectable or medically inoperable disease (deficient mismatch repair/microsatellite instability-high [dMMR/MSI-H] or polymerase epsilon/delta [POLE/POLD1] mutation with ultra-hypermutated phenotype [e.g., tumor mutational burden (TMB) > 50 mut/Mb]); OR
4. Single agent for advanced or metastatic disease (dMMR/MSI-H or POLE/POLD1 mutation with ultra-hypermutated phenotype [e.g., TMB > 50 mut/Mb]), if there is no previous treatment with a checkpoint inhibitor, for any line of therapy.[7]

Authorization Period and Renewal Criteria

1. Initial Authorization Period: 12 months
2. Renewal Criteria: No evidence of disease progression or unacceptable toxicity
3. Renewal Authorization Period: 12 months

Coding (CPT®, ICD-10, and HCPCS)

Procedure codes appearing in medical policy documents are only included as a general reference. This list may not be all-inclusive and is subject to updates. In addition, the codes listed are not a guarantee of payment. CPT codes are available through the AMA.

Code	Description
C11	Malignant neoplasm of nasopharynx

C17	Malignant neoplasm of small intestine
C18	Malignant neoplasm of colon
C18.1	Malignant neoplasm of appendix
C20	Malignant neoplasm of rectum
C21	Malignant neoplasm of anus and anal canal
C30.0	Malignant neoplasm of nasal cavity
J3263	Injection, toripalimab-tpzi

Revision and Review History

No.	Description	Date(s)
1	Original Effective Date:	6/27/2025
2	Policy Annual Review Dates:	
3	Department Owner:	Medical Affairs
4	NH Advisory Committee Approval Dates:	6/27/2025
5	Revision Changes:	

References

[1] Rajasekaran N, Wang X, Ravindranathan S, et al. Toripalimab, a therapeutic monoclonal anti-PD-1 antibody with high binding affinity to PD-1 and enhanced potency to activate human T cells. Cancer Immunol Immunother. 2024;73(3):60. Published 2024 Feb 24. https://pubmed.ncbi.nlm.nih.gov/38400933/. Accessed June 9, 2025.

[2] Loqtorzi (Toripalimab-tpzi) [package insert]. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/761240Orig1s002lbl.pdf. Accessed June 9, 2025.

[3] National Comprehensive Cancer Network. NCCN Guidelines: Anal Carcinoma. https://www.nccn.org/professionals/physician_gls/pdf/anal.pdf. Accessed June 9, 2025.

[4] National Comprehensive Cancer Network. NCCN Guidelines: pMMR/MSS Colon Cancer. https://www.nccn.org/professionals/physician_gls/pdf/colon.pdf. Accessed June 9, 2025.

[5] National Comprehensive Cancer Network. NCCN Guidelines: Head and Neck Cancers. https://www.nccn.org/professionals/physician_gls/pdf/head-and-neck.pdf. Accessed June 9, 2025.

[6] National Comprehensive Cancer Network. NCCN Guidelines: Rectal Cancer. https://www.nccn.org/professionals/physician_gls/pdf/rectal.pdf. Accessed June 9, 2025.

[7] National Comprehensive Cancer Network. NCCN Guidelines: Small Bowel Adenocarcinoma. https://www.nccn.org/professionals/physician_gls/pdf/small_bowel.pdf. Accessed June 9, 2025.

[8] U.S. Food & Drug Administration. https://www.fda.gov/about-fda/what-we-do. Accessed April 23, 2025.

[9] National Comprehensive Cancer Network. https://www.nccn.org/home. Accessed April 23, 2025.

[10] Immune checkpoint inhibitors. National Cancer Institute. https://www.cancer.gov/about-cancer/treatment/types/immunotherapy/checkpoint-inhibitors. Accessed June 9, 2025.