Medical Policy

Healthcare Services Department

Policy Name	Policy Number	Scope
Necitumumab (Portrazza®)	MP-RX-FP-131-24	☒ 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 *Necitumumab (Portrazza®),* an epidermal growth factor receptor (EGFR) antagonist approved by the Food and Drug Administration (FDA) in combination with gemcitabine and cisplatin, for first-line treatment of patients with metastatic squamous non-small cell lung cancer.

The National Comprehensive Cancer Network (NCCN) Guidelines for Non-Small Cell Lung Cancer (Version 1.2024) does not include necitumumab as part of its recommendations for patients with metastatic squamous cell NSCLC. The panel of experts involved in the decision concluded that adding necitumumab to the cisplatin/gemcitabine regimen did not provide significant benefits in terms of efficacy, considering the toxicity, cost, and limited improvement observed when compared to cisplatin/gemcitabine alone.

Background Information

Necitumumab (Portrazza®) is a medication designed to target a protein called epidermal growth factor receptor (EGFR), which is commonly found on certain lung cancer cells. By binding to EGFR, Portrazza blocks its interaction with other molecules, thereby inhibiting the growth of cancer cells. In laboratory settings, Portrazza has been shown to cause the internalization and breakdown of EGFR, as well as trigger immune responses against EGFR-expressing cancer cells.

Necitumumab (Portrazza®) was approved by the FDA on November 24, 2015 for use alongside gemcitabine and cisplatin as a first-line treatment for metastatic squamous non-small cell lung cancer (NSCLC) based on the findings of the phase III clinical trial by Thatcher et al (2015). In the study, Portrazza was administered alongside gemcitabine (1250 mg/m2, Days 1 and 8) and cisplatin (75 mg/m2, Day 1) every 3 weeks. Gemcitabine and cisplatin were given for a maximum of 6 cycles unless there was disease progression or intolerable side effects. Portrazza (800 mg via intravenous infusion on Days 1 and 8 of each 3-week cycle) was given before gemcitabine and cisplatin. Patients with stable disease on Portrazza plus gemcitabine and cisplatin were eligible to continue Portrazza alone after completing the 6 planned cycles of chemotherapy or if chemotherapy was stopped due to side effects. In this trial, only a slight improvement in overall survival was observed (11.5 months compared to 9.9 months). Furthermore, patients receiving the Portrazza regimen experienced a higher incidence of grade 3 or higher adverse events. The National Comprehensive Cancer Network (NCCN) NSCLC Panel unanimously decided to remove the necitumumab/cisplatin/gemcitabine regimen from the NCCN Guidelines for patients with metastatic squamous cell NSCLC. This decision was made due to concerns about the regimen's toxicity, cost, and the limited improvement in efficacy compared to the cisplatin/gemcitabine regimen, according to the NCCN.

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The use of Portrazza comes with significant warnings and precautions. Clinical trials have identified risks such as cardiopulmonary arrest and hypomagnesemia (low magnesium levels) in patients treated with Portrazza in combination with other chemotherapy drugs compared to those treated with chemotherapy alone. Additionally, there is an increased risk of blood clotting events in patients receiving Portrazza, along with notable skin-related side effects such as rash and skin irritation. Infusion-related reactions are also possible, although they are uncommon.

Approved Indications

A. First-line treatment of patients with metastatic squamous non-small cell lung cancer in combination with gemcitabine and cisplatin.

Limitation of Use: Portrazza is not indicated for treatment of non-squamous non-small cell lung cancer as it did not show benefit in this setting. The INSPIRE trial, a randomized, open-label, multicenter study, determined the lack of efficacy of Portrazza in combination with pemetrexed and cisplatin for treating patients with metastatic non-squamous NSCLC. The trial was halted prematurely after enrolling 633 patients due to a higher incidence of death from any cause and thromboembolic events in the Portrazza group. The primary efficacy measure was overall survival (OS), with progression-free survival (PFS) and overall response rate (ORR) also evaluated. Adding Portrazza to pemetrexed and cisplatin did not result in improved OS [hazard ratio (HR)=1.01; 95% confidence interval (CI) (0.84, 1.21)], PFS [HR=0.96; 95% CI (0.8, 1.16)], or ORR (31% in the Portrazza plus pemetrexed and cisplatin group and 32% in the pemetrexed and cisplatin alone group).

Other Uses

i. 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
J9295	Injection, necitumumab, 1 mg

ICD-10	Description
C34.00 -C34.92	Malignant neoplasm of unspecified main bronchus [not covered for non-hyphensquamous small cell lung cancer]

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.

Necitumumab (Portrazza®)

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. Patient has a diagnosis of metastatic squamous non-small cell lung cancer (NSCLC); **AND**
   A. Portrazza is being prescribed as first line treatment; **AND**
   B. Portrazza is being used in combination with gemcitabine and cisplatin.

B. Criteria For Continuation of Therapy

i. MMM considers continuation of Necitumumab (Portrazza®) 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.

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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

D. Conditions Not Covered

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

i. For treatment of non-squamous NSCLC.
ii. Necitumumab (Portrazza®) may not be approved when the above criteria (Section A: Criteria for Initial Approval) are not met and for all other indications.

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.

Drug	Recommended Dosing Schedule
Necitumumab (Portrazza®) 800 mg/50 mL (16 mg/mL) SDV	800 mg (absolute dose) as an intravenous infusion over 60 minutes on Days 1 and 8 of each 3-week cycle.
Exceptions	
None	

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Reference Information

1. Eli Lilly and Company. Portrazza (necitumumab) injection, for intravenous use. Prescribing Information. Indianapolis, IN: Eli Lilly; November 2015.
2. National Comprehensive Cancer Network (NCCN). Non-small cell lung cancer. NCCN Clinical Practice Guidelines in Oncology, Version 1.2024.
3. Paz-Ares L, Mezger J, Ciuleanu TE, et al. Necitumumab plus pemetrexed and cisplatin as first-line therapy in patients with stage IV non-squamous non-small-cell lung cancer (INSPIRE): An open-label, randomised, controlled phase 3 study. Lancet Oncol. 2015;16(3):328-337.
4. Thatcher N, Hirsch FR, Luft AV, et al; SQUIRE Investigators. Necitumumab plus gemcitabine and cisplatin versus gemcitabine and cisplatin alone as first-line therapy in patients with stage IV squamous non-small-cell lung cancer (SQUIRE): An open-label, randomised, controlled phase 3 trial. Lancet Oncol. 2015;16(7):763-774.

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 12/18/2024	Add dosage form to quantity limits table. Add federal statement. Minor wording and formatting changes. Coding Reviewed: no changes.	3/20/2025	4/2/2025
Policy Inception 01/25/2024	New Medical Policy creation	4/18/2024	6/28/2024