Portrazza™ (necitumumab)
(Intravenous)

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Document Number: MODA-0475

Last Review Date: 05/03/2021
Date of Origin: 07/01/2019
Dates Reviewed: 07/2019, 05/2020, 05/2021

I. Length of Authorization

Coverage will be provided for six months and may be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- 2 vials per 21 days

B. Max Units (per dose and over time) [HCPCS Unit]:

- 800 billable units Day 1 and 8 every 21 days

III. Initial Approval Criteria[1]

Coverage is provided in the following conditions:

Patient must be at least 18 years old; **AND**

Non-Small Cell Lung Cancer (NSCLC) [1,2,3,4,10,11] †

- Patient must have metastatic disease; **AND**
- Disease must have squamous cell histology; **AND**
- Must be used in combination with BOTH gemcitabine and cisplatin; **AND**
- Patient must have a performance status of 0-2; **AND**
- Must be used as first-line therapy

Preferred therapies and recommendations are determined by review of clinical evidence. NCCN category of recommendation is taken into account as a component of this review. Regimens deemed equally efficacious (i.e., those having the same NCCN categorization) are considered to be therapeutically equivalent.

† FDA Approved Indication(s)

IV. Renewal Criteria[1]

Coverage can be renewed based upon the following criteria:

- Patient continues to meet indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: cardiopulmonary arrest, hypomagnesemia, severe dermatologic toxicity, severe infusion reactions and venous/arterial thromboembolic events.

V. Dosage/Administration[1]

Indication	Dose
Squamous NSCLC	Administer 800 mg intravenously on Days 1 and 8 of each 3-week cycle prior to gemcitabine and cisplatin infusion. Given until disease progression or unacceptable toxicity.

VI. Billing Code/Availability Information

HCPCS Code:

- J9295 - Injection, necitumumab, 1 mg; 1 billable unit = 1 mg

NDC:

- Portrazza 800 mg/50 mL: 00002-7716-xx

VII. References (STANDARD)

1. Portrazza [package insert]. Indianapolis, IN; Eli Lilly and Company; November 2015. Accessed April 2021.
2. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Non-Small Cell Lung Cancer, Version 4.2021. National Comprehensive Cancer Network, 2021. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed April 2021.
3. 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. Epub 2015 Jun 1.

4. Paz-Ares L, Mezger J, Ciuleanu TE, et al INSPIRE Investigators. 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. Epub 2015 Feb 18.

VIII. References (ENHANCED)

5. Socinski MA, Bondarenko I, Karaseva NA, et al. Weekly nab-paclitaxel in combination with carboplatin versus solvent-based paclitaxel plus carboplatin as first-line therapy in patients with advanced non-small-cell lung cancer: final results of a phase III trial. J Clin Oncol. 2012 Jun 10;30(17):2055-62.
6. Reck M, Rodríguez-Abreu D, Robinson AG, et al. Pembrolizumab versus Chemotherapy for PD-L1-Positive Non-Small-Cell Lung Cancer. N Engl J Med. 2016 Nov 10;375(19):1823-1833.
7. Paz-Ares L, Luft A, Vicente D, et al. Pembrolizumab plus Chemotherapy for Squamous Non-Small-Cell Lung Cancer. N Engl J Med. 2018 Nov 22;379(21):2040-2051.
8. Scagliotti GV, Parikh P, von Pawel J, et al. Phase III study comparing cisplatin plus gemcitabine with cisplatin plus pemetrexed in chemotherapy-naive patients with advanced-stage non-small-cell lung cancer. J Clin Oncol. 2008 Jul 20;26(21):3543-51.
9. Danson S, Middleton MR, O'Byrne KJ, et al. Phase III trial of gemcitabine and carboplatin versus mitomycin, ifosfamide, and cisplatin or mitomycin, vinblastine, and cisplatin in patients with advanced nonsmall cell lung carcinoma. Cancer. 2003 Aug 1;98(3):542-53.
10. Ohe Y, Ohashi Y, Kubota K, et al. Randomized phase III study of cisplatin plus irinotecan versus carboplatin plus paclitaxel, cisplatin plus gemcitabine, and cisplatin plus vinorelbine for advanced non-small-cell lung cancer: Four-Arm Cooperative Study in Japan. Ann Oncol. 2007 Feb;18(2):317-23.
11. Fossella F, Pereira JR, von Pawel J, et al. Randomized, multinational, phase III study of docetaxel plus platinum combinations versus vinorelbine plus cisplatin for advanced non-small-cell lung cancer: the TAX 326 study group. J Clin Oncol. 2003 Aug 15;21(16):3016-24.
12. Pujol JL, Breton JL, Gervais R, et al. Gemcitabine-docetaxel versus cisplatin-vinorelbine in advanced or metastatic non-small-cell lung cancer: a phase III study addressing the case for cisplatin. Ann Oncol. 2005 Apr;16(4):602-10.
13. Magellan Health, Magellan Rx Management. Portrazza Clinical Literature Review Analysis. Last updated April 2021. Accessed April 2021.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C33	Malignant neoplasm of trachea
C34.00	Malignant neoplasm of unspecified main bronchus
C34.01	Malignant neoplasm of right main bronchus
C34.02	Malignant neoplasm of left main bronchus

ICD-10	ICD-10 Description
C34.10	Malignant neoplasm of upper lobe, unspecified bronchus or lung
C34.11	Malignant neoplasm of upper lobe, right bronchus or lung
C34.12	Malignant neoplasm of upper lobe, left bronchus or lung
C34.2	Malignant neoplasm of middle lobe, bronchus or lung
C34.30	Malignant neoplasm of lower lobe, unspecified bronchus or lung
C34.31	Malignant neoplasm of lower lobe, right bronchus or lung
C34.32	Malignant neoplasm of lower lobe, left bronchus or lung
C34.80	Malignant neoplasm of overlapping sites of unspecified bronchus and lung
C34.81	Malignant neoplasm of overlapping sites of right bronchus and lung
C34.82	Malignant neoplasm of overlapping sites of left bronchus and lung
C34.90	Malignant neoplasm of unspecified part of unspecified bronchus or lung
C34.91	Malignant neoplasm of unspecified part of right bronchus or lung
C34.92	Malignant neoplasm of unspecified part of left bronchus or lung
Z85.118	Personal history of other malignant neoplasm of bronchus and lung

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs) may exist and compliance with these policies is required where applicable. They can be found at: http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC

Appendix 3 – CLINICAL LITERATURE REVIEW

OS = overall survival; PFS = progression-free survival; ORR = objective response rate; CR = complete response; PR = partial response; DoR = duration of response; TTP = time to progression; FFS = failure-free survival; EFS = event-free survival; PFR = progression free rate; AE = adverse events

Non-Small Cell Lung Cancer (NSCLC)

Squamous cell, Metastatic disease, First-line Therapy							
Regimen	**NCCN Category**	**FDA Approved**	**Trial Design**	**Comparator**	**Primary End-Point**	**Line of Therapy**	**Conclusion**
Necitumumab + cisplatin + gemcitabine	Not recommended	Yes	Phase 3 (SQUIRE), randomized open-label	Cisplatin + gemcitabine	OS	First line	• The addition of necitumumab to cisplatin and gemcitabine chemotherapy improved overall survival by 1.6 months in patients with advanced squamous NSCLC however, resulted in 10% more adverse events.
Carboplatin + nab-paclitaxel	1 (for PS 0-1) 2A (for PS 2)	Yes (for patients who are not candidates for curative surgery or radiation)	Phase 3, randomized (1:1)	Paclitaxel + carboplatin	ORR	First-line	• Nab-paclitaxel resulted in a significantly improved ORR versus paclitaxel • No significant difference was observed in PFS or OS • Nab-paclitaxel also produced less grade ≥ 3 adverse events than paclitaxel.
Pembrolizumab	1 preferred	Yes	Phase 3 (KEYNOTE-024), open-label, randomized	Platinum-based chemotherapy	PFS	First-line	• In patients with advanced NSCLC and PD-L1 expression on at least 50% of tumor cells, pembrolizumab was associated with significantly longer progression-free and overall survival and with fewer adverse events than was platinum-based chemotherapy. (
Pembrolizumab + carboplatin + paclitaxel or nab-paclitaxel	1 preferred	Yes	Phase 3 (KEYNOTE-407), double-	Placebo + carboplatin + paclitaxel or nab-paclitaxel	OS PFS	First line	• In patients with previously untreated metastatic, squamous NSCLC, the addition of pembrolizumab to chemotherapy with carboplatin plus paclitaxel or nab-paclitaxel resulted in significantly longer

			blind, randomized,				overall survival and progression-free survival than chemotherapy alone.
Cisplatin + gemcitabine	1 (for PS 0-1)	Yes	Phase 3, randomized	Cisplatin + pemetrexed	OS	First-line	• Cisplatin + pemetrexed provides similar efficacy to cisplatin + gemcitabine, with better tolerability
Carboplatin + gemcitabine	1 (for PS 0-1) 2A (for PS 2)	No	Phase 3, randomized	Mitomycin + ifosfamide + cisplatin (MIC) or mitomycin + vinblastine + cisplatin (MVP)	OS	First-line	• The results of the current study failed to demonstrate any difference in efficacy between the newer regimen of GC and the older regimens of MIC and MVP
Carboplatin + paclitaxel (TC)	1 (for PS 0-1) 2A (for PS 2)	No	Phase 3, randomized	Cisplatin + irinotecan (IP) vs. cisplatin + gemcitabine (GP) vs. cisplatin + vinorelbine (NP)	OS	First-line	• The four regimens have similar efficacy and different toxicity profiles, and they can be used to treat advanced NSCLC patients.
Carboplatin + docetaxel (DCb) or Cisplatin + docetaxel (DC)	1 (for PS 0-1) 2A (for PS 2)	No	Phase 3 (TAX 326), randomized, multinational	Cisplatin + vinorelbine (VC)	----------	First-line	• DC resulted in a more favorable ORR and OS rate than VC. Both DC and DCb were better tolerated and provided patients with consistently improved QoL compared with VC. These findings demonstrate that a docetaxel plus platinum combination is an effective treatment option with a favorable therapeutic index for first-line treatment of advanced or metastatic NSCLC.
Gemcitabine + docetaxel (GD)	1 (for PS 0-1) 2A (for PS 2)	No	Phase 3, multicenter, randomized	Cisplatin + vinorelbine (CV)	PFS	First-line	• There was no advantage in PFS with GD compared with CV; however, the CV regimen had higher rate of toxic events, mainly myelosuppression