Portrazza®
necitumumab injection
800 mg/50 mL vial

Effective January 1, 2017, J-code for Portrazza: J9295, Injection, necitumumab, 1 mg

SAMPLE CLAIM FORM CMS-1450 (UB-04)

INDICATION

Portrazza® (necitumumab) is an epidermal growth factor receptor (EGFR) antagonist indicated, in combination with gemcitabine and cisplatin, for first-line treatment of patients with metastatic squamous non-small cell lung cancer (NSCLC).

LIMITATION OF USE

Portrazza is not indicated for the treatment of nonsquamous NSCLC.

WARNING: CARDIOPULMONARY ARREST AND HYPOMAGNESEMIA

Cardiopulmonary arrest and/or sudden death occurred in 3% of patients treated with Portrazza in combination with gemcitabine and cisplatin. Closely monitor serum electrolytes, including serum magnesium, potassium, and calcium, with aggressive replacement when warranted during and after Portrazza administration.

Hypomagnesemia occurred in 83% of patients receiving Portrazza in combination with gemcitabine and cisplatin, and was severe in 20% of patients. Monitor patients for hypomagnesemia, hypocalcemia, and hypokalemia prior to each dose of Portrazza during treatment and for at least 8 weeks following completion of Portrazza. Withhold Portrazza for grade 3 or 4 electrolyte abnormalities. Replete electrolytes as medically appropriate.

The following information is presented for informational purposes only and is not intended to provide reimbursement or legal advice. Laws, regulations, and policies concerning reimbursement are complex and are updated frequently. Individual coding decisions should be based upon diagnosis and treatment of individual patients. While we have made an effort to be current as of the issue date of this document, the information may not be as current or comprehensive when you view it. Providers are encouraged to contact third-party payers for specific information on their coverage, coding, and payment policies. Please consult with your legal counsel or reimbursement specialist for any reimbursement or billing questions. For more information, please call the Lilly PatientOne Program at 1-866-472-8663.

Please see Important Safety Information, including Boxed Warnings for cardiopulmonary arrest and hypomagnesemia, on pages 4-6 and full Prescribing Information for Portrazza.

Lilly

Sample Claim Form CMS-1450 (UB-04) (Hospital Outpatient)

All coding and documentation requirements for drugs should be confirmed with each payer.

FL 42 & 43: REVENUE CODES AND DESCRIPTION

Enter the revenue codes that correspond to HCPCS or CPT® codes outlined in FL 44. Payers may vary on revenue code requirements for each procedure/service performed.

FL 44: PRODUCT AND PROCEDURE CODING

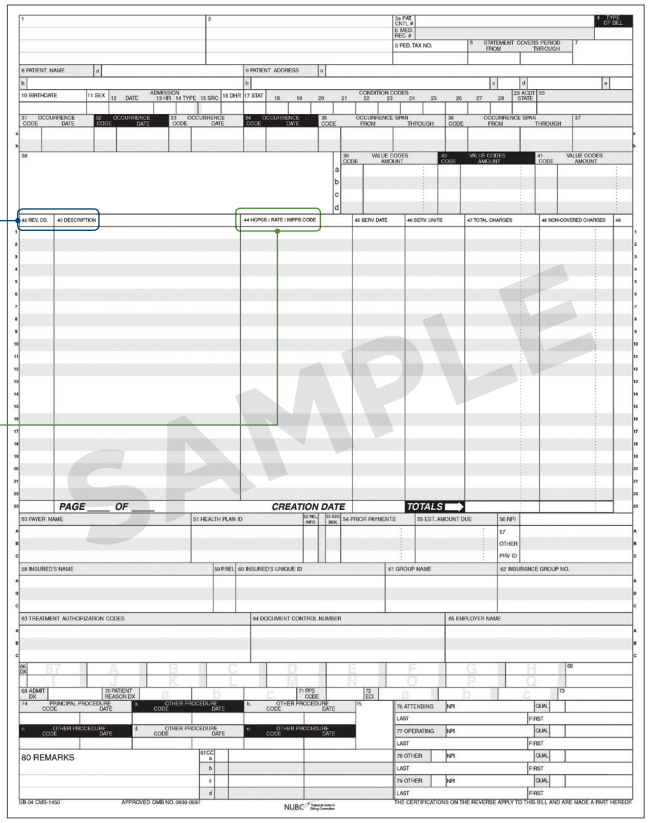
Enter the HCPCS drug code and CPT code for the administration of Portrazza.

HCPCS:

- **J9295: Injection, necitumumab, 1 mg** — **Effective January 1, 2017**
- C9475: Injection, necitumumab, 1 mg — Effective until December 31, 2016
- J9999: Not otherwise classified, antineoplastic drugs
- J3490: Unclassified drugs
- J3590: Unclassified biologics

CPT:

- 96413: Chemotherapy administration, intravenous infusion technique; up to 1 hour, single or initial substance/drug
- 96365: Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); initial, up to 1 hour



HCPCS=Healthcare Common Procedure Coding System; CPT=Current Procedural Terminology.

CPT is a registered trademark of the American Medical Association.

Please see additional CMS-1450 claim form information on page 3.

SELECT IMPORTANT SAFETY INFORMATION

Cardiopulmonary Arrest

- Cardiopulmonary arrest or sudden death occurred in 15 (3%) of 538 patients treated with Portrazza plus gemcitabine and cisplatin as compared to 3 (0.6%) of 541 patients treated with gemcitabine and cisplatin alone in study 1. Twelve of the 15 patients died within 30 days of the last dose of Portrazza and had comorbid conditions including history of coronary artery disease (n=3), hypomagnesemia (n=4), chronic obstructive pulmonary disease (n=7), and hypertension (n=5). Eleven of the 12 patients had an unwitnessed death. Patients with significant coronary artery disease, myocardial infarction within 6 months, uncontrolled hypertension, and uncontrolled congestive heart failure were not enrolled in study 1. The incremental risk of cardiopulmonary arrest or sudden death in patients with a history of coronary artery disease, congestive heart failure, or arrhythmias as compared to those without these comorbid conditions is not known. Closely monitor serum electrolytes, including serum magnesium, potassium, and calcium prior to each infusion of Portrazza during treatment and after Portrazza administration for at least 8 weeks after the last dose. Withhold Portrazza for grade 3 or 4 electrolyte abnormalities; subsequent cycles of Portrazza may be administered in these patients once electrolyte abnormalities have improved to grade ≤2. Replete electrolytes as medically appropriate.

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Sample Claim Form CMS-1450 (UB-04) (Hospital Outpatient), Continued

All coding and documentation requirements for drugs should be confirmed with each payer.

FL 46: SERVICE UNITS

Specify the appropriate number of service units as designated by individual payers. Check to confirm the unit of use established by other payers, as there may be variation.

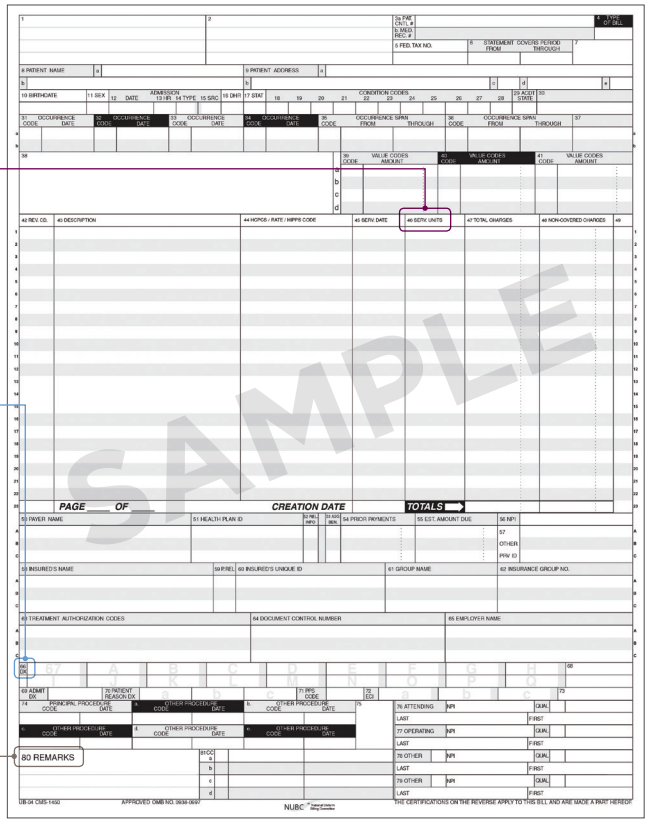
FL 66: DIAGNOSIS CODES

Enter the appropriate ICD diagnosis code(s) that correspond(s) to the type and location of the disease with which the patient has been diagnosed.

FL 80: REMARKS

To support the review and payment of the claim, include additional information as required by respective payers. This may include NDC, total dosage, and date Portrazza was administered.

ICD=International Classification of Diseases; NDC=National Drug Code.



SELECT IMPORTANT SAFETY INFORMATION

Hypomagnesemia

- Hypomagnesemia occurred in 83% of 461/538 patients with available laboratory results treated with Portrazza as compared to 70% of 457/541 patients with available laboratory results treated with gemcitabine and cisplatin alone in study 1. Hypomagnesemia was severe (grade 3 or 4) in 20% of the patients treated with Portrazza compared to 7% of the patients treated with gemcitabine and cisplatin alone. The median time to development of hypomagnesemia and accompanying electrolyte abnormalities was 6 weeks (25th percentile 4 weeks; 75th percentile 9 weeks) after initiation of Portrazza. Monitor patients for hypomagnesemia, hypocalcemia, and hypokalemia prior to each infusion of Portrazza during treatment, and for at least 8 weeks following the completion of Portrazza. Withhold Portrazza for grade 3 or 4 electrolyte abnormalities; subsequent cycles of Portrazza may be administered in these patients once hypomagnesemia and related electrolyte abnormalities have improved to grade ≤2. Replete electrolytes as medically appropriate.

WARNING: CARDIOPULMONARY ARREST AND HYPOMAGNESEMIA

Cardiopulmonary arrest and/or sudden death occurred in 3% of patients treated with Portrazza in combination with gemcitabine and cisplatin. Closely monitor serum electrolytes, including serum magnesium, potassium, and calcium, with aggressive replacement when warranted during and after Portrazza administration.

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WARNINGS AND PRECAUTIONS

Cardiopulmonary Arrest

- Cardiopulmonary arrest or sudden death occurred in 15 (3%) of 538 patients treated with Portrazza plus gemcitabine and cisplatin as compared to 3 (0.6%) of 541 patients treated with gemcitabine and cisplatin alone in study 1. Twelve of the 15 patients died within 30 days of the last dose of Portrazza and had comorbid conditions including history of coronary artery disease (n=3), hypomagnesemia (n=4), chronic obstructive pulmonary disease (n=7), and hypertension (n=5). Eleven of the 12 patients had an unwitnessed death. Patients with significant coronary artery disease, myocardial infarction within 6 months, uncontrolled hypertension, and uncontrolled congestive heart failure were not enrolled in study 1. The incremental risk of cardiopulmonary arrest or sudden death in patients with a history of coronary artery disease, congestive heart failure, or arrhythmias as compared to those without these comorbid conditions is not known. Closely monitor serum electrolytes, including serum magnesium, potassium, and calcium prior to each infusion of Portrazza during treatment and after Portrazza administration for at least 8 weeks after the last dose. Withhold Portrazza for grade 3 or 4 electrolyte abnormalities; subsequent cycles of Portrazza may be administered in these patients once electrolyte abnormalities have improved to grade ≤2. Replete electrolytes as medically appropriate.

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Venous and Arterial Thromboembolic Events (VTE and ATE)

- VTE and ATE, some fatal, were observed with Portrazza in combination with gemcitabine and cisplatin. In study 1, the incidence of VTE was 9% in patients receiving Portrazza plus gemcitabine and cisplatin versus 5% in patients receiving gemcitabine and cisplatin alone, and the incidence of grade 3 or higher VTEs was 5% versus 3%, respectively. The incidence of fatal VTEs was similar between arms (0.2% vs 0.2%). The most common VTEs were pulmonary embolism (5%) and deep-vein thrombosis (2%).

Please see Important Safety Information continued on pages 5-6 and full Prescribing Information for Portrazza, including Boxed Warnings for cardiopulmonary arrest and hypomagnesemia.

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WARNINGS AND PRECAUTIONS, CONTINUED

Venous and Arterial Thromboembolic Events (VTE and ATE), Continued

- The incidence of ATEs of any grade was 5% versus 4%, and the incidence of grade 3 or higher ATE was 4% versus 2% in the Portrazza-containing and gemcitabine and cisplatin arms, respectively, in study 1. The most common ATEs were cerebral stroke and ischemia (2%) and myocardial infarction (1%). In an exploratory analysis of study 1, the relative risk of VTE or ATE was approximately 3-fold higher in patients with a reported history of VTE or ATE than in patients with no reported history of VTE or ATE. Discontinue Portrazza for patients with serious or life-threatening VTE or ATE.

Dermatologic Toxicities

- Dermatologic toxicities, including rash, dermatitis acneiform, acne, dry skin, pruritus, generalized rash, skin fissures, maculo-papular rash, and erythema, occurred in 79% of patients receiving Portrazza in study 1. Skin toxicity was severe in 8% of patients. Skin toxicity usually developed within the first 2 weeks of therapy and resolved within 17 weeks after onset. For grade 3 skin reactions, modify the dose of Portrazza. Limit sun exposure. Discontinue Portrazza for severe (grade 4) skin reactions or grade 3 skin induration/fibrosis.

Infusion-Related Reactions (IRRs)

- In study 1, 1.5% of Portrazza-treated patients experienced IRRs of any severity with 0.4% grade 3 IRRs. No patients received premedication for IRR for the first dose of Portrazza in study 1. Most IRRs occurred after the first or second administration of Portrazza. Monitor patients during and following Portrazza infusion for signs and symptoms of IRR. Discontinue Portrazza for serious or life-threatening IRR.

Nonsquamous NSCLC—Increased Toxicity and Increased Mortality

- Portrazza is not indicated for the treatment of patients with nonsquamous NSCLC. In a study of Portrazza plus pemetrexed and cisplatin (PC) versus PC alone (study 2), patients treated with Portrazza and PC experienced more serious (51% vs 41%) and fatal toxicities (16% vs 10%) and cardiopulmonary arrest/sudden death within 30 days of the last study drug (3.3% vs 1.3%) compared to patients who received PC alone.

Embryofetal Toxicity

- Based on animal data and its mechanism of action, Portrazza can cause fetal harm when administered to a pregnant woman. Disruption or depletion of epidermal growth factor receptor (EGFR) in animal models results in impairment of embryofetal development, including effects on placental, lung, cardiac, skin, and neural development. The absence of EGFR signaling has resulted in embryolethality as well as postnatal death in animals. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with Portrazza and for 3 months following the final dose.

MOST COMMON ADVERSE REACTIONS

- Adverse reactions (all grades; grade 3/4) that occurred at an incidence rate of ≥5% (all grades) or a ≥2% (grade 3/4) difference between patients receiving Portrazza plus gemcitabine and cisplatin versus gemcitabine and cisplatin alone in study 1 were rash (44% vs 6%; 4% vs 0.2%), dermatitis acneiform (15% vs 0.6%; 1% vs 0%), acne (9% vs 0.6%; 0.4% vs 0%), pruritus (7% vs 0.9%; 0.2% vs 0.2%), dry skin (7% vs 1%; 0% vs 0%), skin fissures (5% vs 0%; 0.4% vs 0%), vomiting (29% vs 25%; 3% vs 0.9%), diarrhea (16% vs 11%; 2% vs 1%), stomatitis (11% vs 6%; 1% vs 0.6%), weight decreased (13% vs 6%; 0.7% vs 0.6%), hemoptysis (10% vs 5%; 1% vs 0.9%), pulmonary embolism (5% vs 2%; 4% vs 2%), headache (11% vs 6%; 0% vs 0.4%), VTE (9% vs 5%; 5% vs 3%), paronychia (7% vs 0.2%; 0.4% vs 0%), and conjunctivitis (7% vs 2%; 0.4% vs 0%).
- The most common adverse reactions (all grades) observed in Portrazza-treated patients at a rate of ≥15% and ≥2% higher than gemcitabine and cisplatin alone were rash (44% vs 6%), vomiting (29% vs 25%), diarrhea (16% vs 11%), and dermatitis acneiform (15% vs 0.6%).
- The most common severe (grade 3 or higher) adverse events that occurred at a ≥2% higher rate in Portrazza-treated patients compared to patients treated with gemcitabine and cisplatin alone were VTE (5%; including pulmonary embolism), rash (4%), and vomiting (3%).

Please see Important Safety Information continued on page 6 and full Prescribing Information for Portrazza, including Boxed Warnings for cardiopulmonary arrest and hypomagnesemia.

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MOST COMMON ADVERSE REACTIONS, CONTINUED

- Clinically relevant adverse reactions (all grades) reported in ≥1% and <5% of patients treated with Portrazza were dysphagia (3%), oropharyngeal pain (1%), muscle spasms (2%), phlebitis (2%), and hypersensitivity/IRRs (1.5%).
- In study 1, 12% of the patients in the Portrazza arm discontinued study treatment due to an adverse reaction. The most common Portrazza-related toxicity leading to Portrazza discontinuation was skin rash (1%).
- Electrolyte abnormalities (all grades; grade 3 or 4) according to laboratory assessment at an incidence rate of >10% and a >2% difference between arms in patients receiving Portrazza plus gemcitabine and cisplatin versus gemcitabine and cisplatin alone in study 1 included hypomagnesemia (83% vs 70%; 20% vs 7%), hypokalemia (28% vs 18%; 5% vs 3%), hypocalcemia (45% vs 30%; 6% vs 2%), albumin corrected hypocalcemia (36% vs 23%; 4% vs 2%), and hypophosphatemia (31% vs 23%; 8% vs 6%).
- The median time to onset of hypomagnesemia was 6 weeks (25th percentile 4 weeks; 75th percentile 9 weeks). Hypomagnesemia was reported as resolved in 43% of the patients who received Portrazza. In study 1, 32% of the patients in the Portrazza arm and 16% of the patients who received gemcitabine and cisplatin alone received magnesium replacement.

USE IN SPECIFIC POPULATIONS

- **Pregnancy:** Based on animal data and its mechanism of action, Portrazza can cause fetal harm when administered to a pregnant woman. Disruption or depletion of EGFR in animal models results in impairment of embryofetal development, including effects on placental, lung, cardiac, skin, and neural development. The absence of EGFR signaling has resulted in embryolethality as well as postnatal death in animals. No animal reproduction studies have been conducted with necitumumab. There are no available data for Portrazza exposure in pregnant women. Advise pregnant women of the potential risk to a fetus and the risk to postnatal development.
- **Lactation:** There is no information regarding the presence of necitumumab in human milk, the effects on the breastfed infant, or the effects on milk production. Because of the potential for serious adverse reactions in breastfed infants from Portrazza, advise a nursing woman not to breastfeed during treatment with Portrazza and for 3 months following the final dose.
- **Females of Reproductive Potential:** Based on its mechanism of action, Portrazza can cause fetal harm when administered to a pregnant woman. Advise females of reproductive potential to use effective contraception during treatment with Portrazza and for 3 months following the final dose.
- **Geriatric Use:** Of the 545 patients in the Portrazza plus gemcitabine and cisplatin arm in Study 1, 213 (39%) were 65 years and over, while 108 (20%) were 70 years and over. In an exploratory subgroup analysis of study 1, the hazard ratio for overall survival in patients 70 years or older was 1.03 (95% CI: 0.75, 1.42). Of the adverse reactions that occurred at an incidence rate of ≥5% (all grades) or a ≥2% (grade 3/4) difference between patients receiving Portrazza plus gemcitabine and cisplatin versus gemcitabine and cisplatin alone, there was a higher incidence (≥3%) of venous thromboembolic events including pulmonary embolism in patients age 70 and over compared to those who were younger than age 70.

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