Vegzelma®
bevacizumab-adcd
Injection 100mg/vial & 400mg/vial

Coding and Billing Guide VEGZELMA® (bevacizumab-adcd)

Physician Office and Hospital Outpatient Department

Refer to the accompanying VEGZELMA Full Prescribing Information, including Important Safety Information on pages 10-12.

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Celltrion CONNECT® Patient Support Program

Contact Celltrion CONNECT® if you have questions about coding, coverage, and access for VEGZELMA® (bevacizumab-adcd).

Call 1-877-81CONNC (1-877-812-6662) Monday – Friday, 9 am – 8 pm ET or visit www.celltrionconnect.com for more information.

CELLTRION CONNECT
PATIENT SUPPORT PROGRAM

Whether your patient is insured, underinsured, or uninsured, Celltrion CONNECT® may be able to help them to afford VEGZELMA.

Introduction

Celltrion USA, Inc. (Celltrion USA) developed this Coding and Billing Guide as an educational reference for coding, billing, and claims submission information that may be appropriate for reporting VEGZELMA and related services in the physician office and hospital outpatient department (HOPD) sites of care. A biosimilar to Avastin® (bevacizumab),[a] VEGZELMA was approved by the United States Food and Drug Administration (FDA) in September 2022.[1]

Disclaimer

The contents of this guide are provided for informational purposes only and do not represent legal advice. Celltrion USA does not guarantee reimbursement for VEGZELMA.

For specific guidance in your area, consult your own legal, coding, and billing staff, as it remains your responsibility to ensure the claims submitted by your office or facility are accurate. The content in this guide is current as of April 2023 and is subject to change.

Overview of Coding and Billing Information Presented in This Guide

Healthcare providers (HCPs) report codes from standardized national code sets on claim forms to payers for reimbursement. A medical group, or other entity entitled to bill and receive payment for physician services, uses the Accredited Standards Committee (ASC) X12 professional claim electronic billing format 837P – or CMS-1500 Claim Form – to submit claims to payers.[2] A facility entitled to bill and receive payment for HOPD services uses the ASC X12 institutional claim electronic billing format 837I – or CMS-1450 Claim Form – to submit claims to payers.[3] The next sections describe the appropriate use of codes and their locations on professional or institutional claim forms when reporting VEGZELMA and its intravenous (IV) infusion for FDA-approved indications.

Refer to the accompanying VEGZELMA Full Prescribing Information, including Important Safety Information on pages 10-12.

Coding

ICD-10-CM codes used to report diagnoses

The International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10-CM) codes in the table below may be appropriate in the physician and HOPD sites of care when reporting the reason for an encounter for a patient prescribed VEGZELMA.

Indication[1]	Code[4]	Description	Claim Form Location
Metastatic colorectal cancer (mCRC)	**C18.0-C18.9**	Malignant neoplasm of colon	• Physician Office CMS-1500: Item 21 • HOPD CMS-1450: Form Locator (FL) 67 and FL 67A-Q
	C19	Malignant neoplasm of rectosigmoid junction	
	C20	Malignant neoplasm of rectum	
First-line non-squamous non-small cell lung cancer (NSCLC)	**C34.00-C34.92**	Malignant neoplasm of bronchus and lung	
Persistent, recurrent, or metastatic cervical cancer	**C53.0-C53.9**	Malignant neoplasm of cervix uteri	
Epithelial ovarian, fallopian tube, or primary peritoneal cancer	**C48.0-C48.8**	Malignant neoplasm of retroperitoneum and peritoneum	
	C56.1-C56.9	Malignant neoplasm of ovary	
	C57.00-C57.02	Malignant neoplasm of fallopian tube	
Metastatic renal cell carcinoma (mRCC)	**C64.1-C64.9**	Malignant neoplasm of kidney, except renal pelvis	
	C65.1-C65.9	Malignant neoplasm of renal pelvis	
Recurrent glioblastoma (GBM)	**C71.0-C71.9**	Malignant neoplasm of brain	

Other diagnosis codes may apply. Verify with payer.

ICD-10-CM codes must be reported to the highest level of specificity available. For example, if a code has a 5th character option, reporting fewer than 5 characters will render the code invalid and may cause payers to deny the claim. One or more diagnosis codes may be appropriate on claims. The sequence of codes (primary and secondary, as necessary) may vary by payer. Payers may also allow codes other than the ones listed here, depending on coverage parameters. Review payer policy requirements for additional guidance on the use of diagnosis codes. Medical record documentation must always support the codes reported on the claim.

Refer to the accompanying VEGZELMA Full Prescribing Information, including Important Safety Information on pages 10-12.

HCPCS codes used to report drugs

Healthcare Common Procedure Coding System (HCPCS) codes are used to report drugs and other supplies and services. VEGZELMA has a product-specific HCPCS code that is effective for claims with dates of service on or after April 1, 2023.

Code[5]	Description	Claim Form Location
Q5129	Injection, bevacizumab-adcd (vegzelma), biosimilar, 10 mg	• Physician Office CMS-1500: Item 24D • HOPD CMS-1450: FL 44

When billing Q5129 for VEGZELMA, 10 mg is equal to 1 billing unit.

- Report 10 billing units when using a 100 mg single-dose vial (SDV)
- Report 40 billing units when using a 400 mg SDV

Billing units are reported as follows on claim forms:

- Professional claims CMS-1500, Item 24G
- Institutional claims CMS-1450, FL 46

HCPCS modifiers used to report drug amounts discarded or not discarded (required by Medicare)

Most payers allow HCPs to bill the entire amount of medication taken from an SDV, even if some of the drug was discarded after the patient received a clinically appropriate dosage. Add the -JW modifier to the HCPCS code to specify the amount of drug that was discarded. The amounts administered to a patient and discarded from an SDV should also be documented in the patient's medical chart.

Code Modifier[5]	Description	Comments	Claim Form Location
-JW	Drug amount discarded/not administered to any patient	Use to report the amount of drug discarded. Report on its own claim line, separate from the line reporting the amount of drug administered	**Append to HCPCS code:** • Physician Office CMS-1500: Item 24D • HOPD CMS-1450: FL 44

- Report Q5129 with the units for the amount of VEGZELMA administered on 1 line of the claim form
- Report Q5129 -JW with the units for the amount of VEGZELMA discarded on a second line of the claim form

For most payers, the amount of drug eligible for reimbursement is up to the total quantity listed on the SDV.

Medicare requires HCPs to report modifier -JZ in cases when no amount of drug is discarded from an SDV. Non-Medicare payers may vary with the use of this modifier.

Code Modifier[5]	Description	Comments	Claim Form Location
-JZ	Zero drug amount discarded/not administered to any patient	Use to attest that no amount of drug was discarded	**Append to HCPCS code:** • Physician Office CMS-1500: Item 24D • HOPD CMS-1450: FL 44

Modifier -JZ is effective January 1, 2023. For Medicare, it is required on claims with dates of service on or after July 1, 2023, when appropriate.

Refer to the accompanying VEGZELMA Full Prescribing Information, including Important Safety Information on pages 10-12.

NDCs used to report drugs

National Drug Codes (NDCs) are 3-segment universal product identifiers that describe drugs by the manufacturer, dose, formulation, and package size. Payers commonly require that HCPs report the NDC in combination with the appropriate HCPCS code on claim forms to help identify the product. While the Prescribing Information lists a 10-digit NDC, the 11-digit format is used on claims[6-8]:

11-Digit NDC[1]	Descriptor	Claim Form Location
72606-0011-01	100 mg/4 mL SDV	• Physician Office CMS-1500: Item 24A (shaded area) • HOPD CMS-1450: FL 43
72606-0012-01	400 mg/16 mL SDV	

When required, payers may request the following types of information along with the NDC[6-8]:

Segment	Comments	Examples
NDC qualifier: "N4"	Placing the N4 qualifier in front of 11-digit NDC signals to the payer that the NDC will follow	**4 mL/100 mg vial:** The amounts discarded and administered together should total the full quantity of 4 mL when using the 100 mg SDV: **N472606001101 ML4** **16 mL/400 mg vial:** The amounts discarded and administered together should total the full quantity of 16 mL when using the 400 mg SDV: **N472606001201 ML16**
11-digit NDC	Do not include hyphens or other punctuation marks	
Put a single space after the NDC		
Unit of measure qualifier: "ML"	The ML unit of measure qualifier informs the payer that the product is in liquid format	
Quantity	• The quantity immediately follows the unit of measure qualifier • Adjust the quantity based on the amount administered and any amount discarded. Use 2 claim lines for this purpose, if needed	

Refer to the accompanying VEGZELMA Full Prescribing Information, including Important Safety Information on pages 10-12.

CPT codes used to report the administration procedure

Current Procedural Terminology (CPT®[a]) codes are used on claim forms to report the administration procedure for VEGZELMA in the physician and HOPD settings.

Code[9]	Description	Comments	Claim Form Location
96413	Chemotherapy administration, intravenous infusion technique; up to 1 hour, single or initial substance/drug	Use to report VEGZELMA IV infusion lasting up to 90 minutes when the primary reason for the encounter is to administer VEGZELMA	• Physician Office CMS-1500: Item 24D • HOPD CMS-1450: FL 44
96415	Chemotherapy administration, intravenous infusion technique; each additional hour (List separately in addition to code for primary procedure)	Use in addition to 96413 or 96417 to report a VEGZELMA IV infusion that lasts longer than 90 minutes*	
96417	Chemotherapy administration, intravenous infusion technique; each additional sequential infusion (different substance/drug), up to 1 hour (List separately in addition to code for primary procedure)	Use to report VEGZELMA IV infusion lasting up to 90 minutes when the primary reason for the encounter is not to administer VEGZELMA (eg, in combination therapy when another drug is primary, based on documentation)	

* Report add-on code 96415 in addition to the primary code (96413 or 96417) only if the total infusion time exceeds 90 minutes. Shorter infusions totaling 16-90 minutes should be reported using only the primary code.

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The following codes and modifiers apply only to HOPD claims

HCPCS modifier related to drug acquired via the 340B Drug Discount Program

Medicare requires a modifier, -JG or -TB, to be added to the HCPCS code to report cases when a drug is acquired via the 340B Drug Discount Program and administered to a Medicare beneficiary in the HOPD that is paid under the Outpatient Prospective Payment System (OPPS).

Code Modifier[5]	Description	Comments	Claim Form Location
-JG	Drug or biological acquired with 340B drug pricing program discount, reported for informational purposes	Use for drugs without temporary pass-through payment status	**Append to HCPCS code:** • HOPD CMS-1450: FL 44
-TB	Drug or biological acquired with 340B drug pricing program discount, reported for informational purposes for select entities	Use for drugs with temporary pass-through payment status. VEGZELMA has temporary pass-through payment status for dates of service July 1, 2023 to June 30, 2026.[10]	

The -JG and -TB modifiers do not apply if an OPPS hospital does not acquire the drug under the 340B Drug Discount Program. Reporting informational modifiers "JG" and "TB is mandatory for OPPS providers starting in calendar year (CY) 2023 and also for non-OPPS providers starting CY 2024.[11]

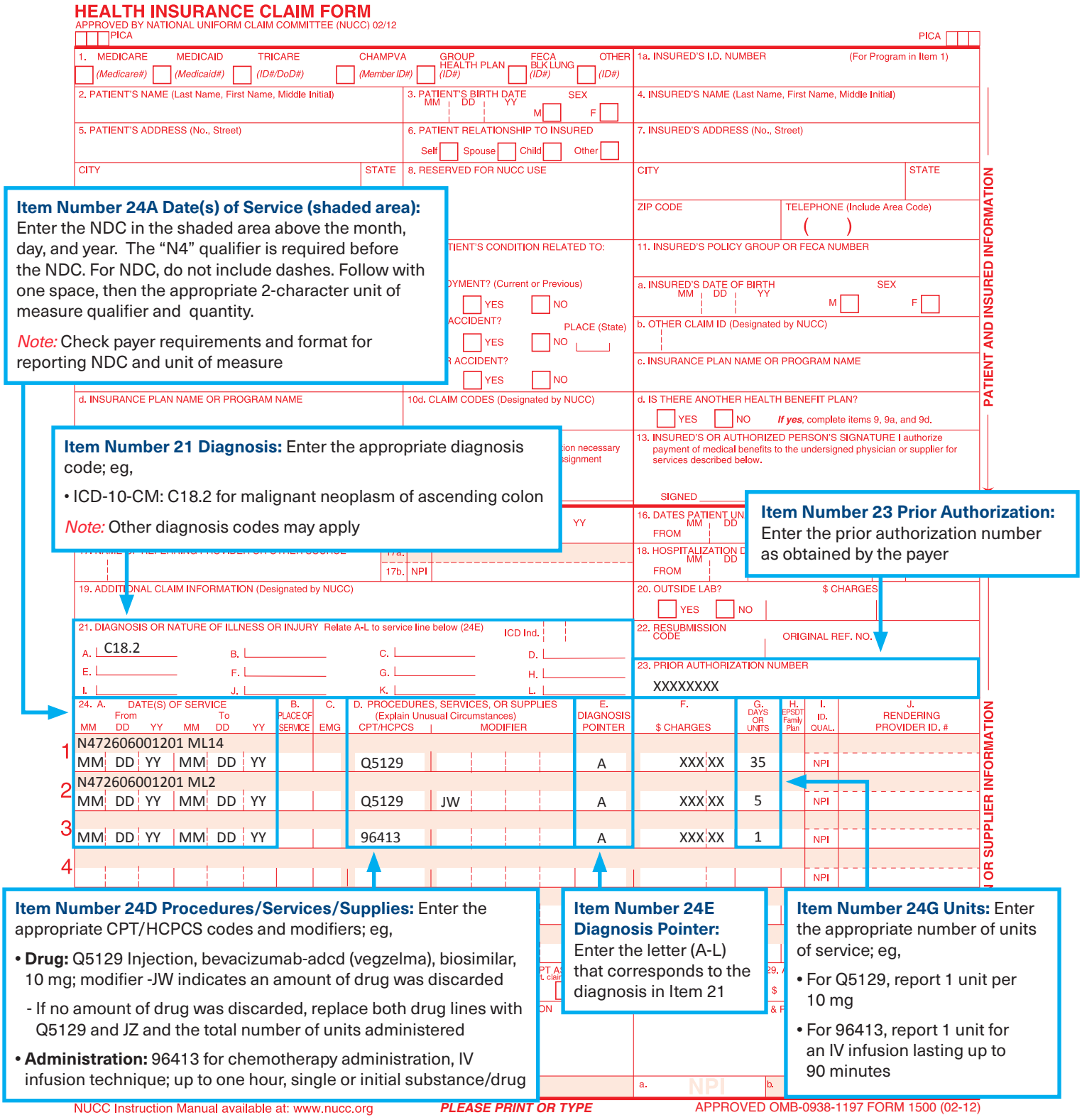
Revenue codes used to report facility cost centers

Revenue codes are used on institutional CMS-1450 Claim Form to map a specific charge to a cost center. For VEGZELMA, revenue code 0636 is required to allow payment that is separate from that of the administration service. Revenue codes for other services may vary by facility. In addition to the revenue code, the HOPD typically enters a narrative description or standard abbreviation specific to each revenue code. Examples of revenue codes that an HOPD may use to track costs for services associated with VEGZELMA are provided below.

Service	Code[12]	Description	Claim Form Location
Drug	**0636**	Drugs requiring detailed coding	• HOPD CMS-1450: FL 42
IV infusion	**0260**	IV therapy, general	
	0510	Clinic, general	

Claim Forms

Sample CMS-1500 Claim Form (Physician Office)



HEALTH INSURANCE CLAIM FORM

APPROVED BY NATIONAL UNIFORM CLAIM COMMITTEE (NUCC) 02/12

PICA

1. MEDICARE (Medicare#) MEDICAID (Medicaid#) TRICARE (ID#/DoD#) CHAMPVA (Member ID#) GROUP HEALTH PLAN (ID#) FECA BLK LUNG (ID#) OTHER (ID#)

1a. INSURED'S I.D. NUMBER (For Program in Item 1)

2. PATIENT'S NAME (Last Name, First Name, Middle Initial)

3. PATIENT'S BIRTH DATE MM DD YY SEX M F

4. INSURED'S NAME (Last Name, First Name, Middle Initial)

5. PATIENT'S ADDRESS (No., Street)

6. PATIENT RELATIONSHIP TO INSURED Self Spouse Child Other

7. INSURED'S ADDRESS (No., Street)

CITY STATE

8. RESERVED FOR NUCC USE

CITY STATE

ZIP CODE TELEPHONE (Include Area Code) ( )

TIENT'S CONDITION RELATED TO:

11. INSURED'S POLICY GROUP OR FECA NUMBER

OYMENT? (Current or Previous) YES NO

a. INSURED'S DATE OF BIRTH MM DD YY SEX M F

ACCIDENT? YES NO PLACE (State)

b. OTHER CLAIM ID (Designated by NUCC)

R ACCIDENT? YES NO

c. INSURANCE PLAN NAME OR PROGRAM NAME

d. INSURANCE PLAN NAME OR PROGRAM NAME

10d. CLAIM CODES (Designated by NUCC)

d. IS THERE ANOTHER HEALTH BENEFIT PLAN? YES NO *If yes*, complete items 9, 9a, and 9d.

ion necessary signment

13. INSURED'S OR AUTHORIZED PERSON'S SIGNATURE I authorize payment of medical benefits to the undersigned physician or supplier for services described below.

SIGNED

YY

16. DATES PATIENT UN MM DD FROM

17a.

17b. NPI

18. HOSPITALIZATION D MM DD FROM

19. ADDITIONAL CLAIM INFORMATION (Designated by NUCC)

20. OUTSIDE LAB? YES NO $ CHARGES

21. DIAGNOSIS OR NATURE OF ILLNESS OR INJURY Relate A-L to service line below (24E) ICD Ind.

A. C18.2 B. C. D.

E. F. G. H.

I. J. K. L.

22. RESUBMISSION CODE ORIGINAL REF. NO.

23. PRIOR AUTHORIZATION NUMBER XXXXXXXX

24. A. DATE(S) OF SERVICE From MM DD YY To MM DD YY	B. PLACE OF SERVICE	C. EMG	D. PROCEDURES, SERVICES, OR SUPPLIES (Explain Unusual Circumstances) CPT/HCPCS	MODIFIER	E. DIAGNOSIS POINTER	F. $ CHARGES	G. DAYS OR UNITS	H. EPSDT Family Plan	I. ID. QUAL.	J. RENDERING PROVIDER ID. #
1 N472606001201 ML14 MM DD YY MM DD YY			Q5129		A	XXX XX	35		NPI	
2 N472606001201 ML2 MM DD YY MM DD YY			Q5129	JW	A	XXX XX	5		NPI	
3 MM DD YY MM DD YY			96413		A	XXX XX	1		NPI	
4									NPI	

PATIENT AND INSURED INFORMATION

OR SUPPLIER INFORMATION

a. NPI b.

NUCC Instruction Manual available at: www.nucc.org **PLEASE PRINT OR TYPE** APPROVED OMB-0938-1197 FORM 1500 (02-12)

Item Number 24A Date(s) of Service (shaded area): Enter the NDC in the shaded area above the month, day, and year. The "N4" qualifier is required before the NDC. For NDC, do not include dashes. Follow with one space, then the appropriate 2-character unit of measure qualifier and quantity.

Note: Check payer requirements and format for reporting NDC and unit of measure

Item Number 21 Diagnosis: Enter the appropriate diagnosis code; eg,

- ICD-10-CM: C18.2 for malignant neoplasm of ascending colon

Note: Other diagnosis codes may apply

Item Number 23 Prior Authorization: Enter the prior authorization number as obtained by the payer

Item Number 24D Procedures/Services/Supplies: Enter the appropriate CPT/HCPCS codes and modifiers; eg,

- **Drug:** Q5129 Injection, bevacizumab-adcd (vegzelma), biosimilar, 10 mg; modifier -JW indicates an amount of drug was discarded
  - If no amount of drug was discarded, replace both drug lines with Q5129 and JZ and the total number of units administered
- **Administration:** 96413 for chemotherapy administration, IV infusion technique; up to one hour, single or initial substance/drug

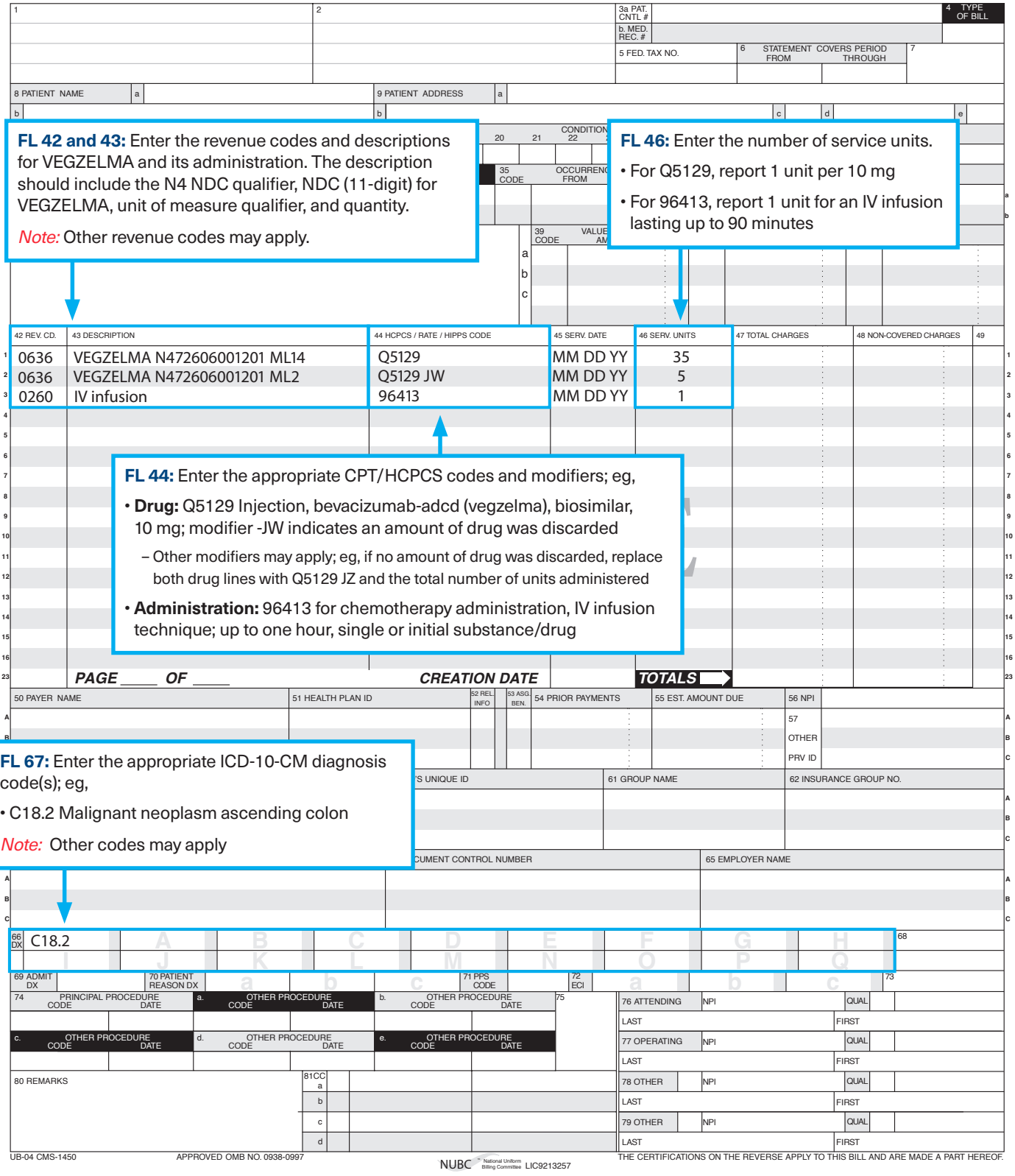
Item Number 24E Diagnosis Pointer: Enter the letter (A-L) that corresponds to the diagnosis in Item 21

Item Number 24G Units: Enter the appropriate number of units of service; eg,

- For Q5129, report 1 unit per 10 mg
- For 96413, report 1 unit for an IV infusion lasting up to 90 minutes

Refer to the accompanying VEGZELMA Full Prescribing Information, including Important Safety Information on pages 10-12.

Sample CMS-1450 Claim Form (HOPD)



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Indications for Use[1]

Metastatic Colorectal Cancer (mCRC)

VEGZELMA, in combination with intravenous fluorouracil-based chemotherapy, is indicated for the first- or second-line treatment of patients with mCRC

VEGZELMA, in combination with fluoropyrimidine-irinotecan- or fluoropyrimidine-oxaliplatin-based chemotherapy, is indicated for the second-line treatment of patients with mCRC who have progressed on a first-line bevacizumab product-containing regimen

Limitations of Use: VEGZELMA is not indicated for adjuvant treatment of colon cancer.

First-Line Non-Squamous Non-Small Cell Lung Cancer (NSCLC)

VEGZELMA, in combination with carboplatin and paclitaxel, is indicated for the first-line treatment of patients with unresectable, locally advanced, recurrent, or metastatic non-squamous NSCLC.

Recurrent Glioblastoma (GBM)

VEGZELMA is indicated for the treatment of recurrent GBM in adults.

Metastatic Renal Cell Carcinoma (mRCC)

VEGZELMA, in combination with interferon alfa, is indicated for the treatment of mRCC.

Persistent, Recurrent, or Metastatic Cervical Cancer

VEGZELMA, in combination with paclitaxel and cisplatin or paclitaxel and topotecan, is indicated for the treatment of patients with persistent, recurrent, or metastatic cervical cancer.

Epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Cancer

VEGZELMA, in combination with carboplatin and paclitaxel, followed by VEGZELMA as a single agent, is indicated for the treatment of patients with stage III or IV epithelial ovarian, fallopian tube, or primary peritoneal cancer following initial surgical resection. VEGZELMA, in combination with paclitaxel, pegylated liposomal doxorubicin, or topotecan, is indicated for the treatment of patients with platinum-resistant recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who received no more than 2 prior chemotherapy regimens. VEGZELMA, in combination with carboplatin and paclitaxel, or with carboplatin and gemcitabine, followed by VEGZELMA as a single agent, is indicated for the treatment of patients with platinum-sensitive recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer.

Important Safety Information

WARNINGS AND PRECAUTIONS

Gastrointestinal Perforations and Fistulae: Serious, and sometimes fatal, gastrointestinal perforation occurred at a higher incidence in patients receiving bevacizumab products vs chemotherapy. The incidence ranged from 0.3% to 3% across clinical studies, with the highest incidence in patients with a history of prior pelvic radiation. Serious fistulae ranged from <1% to 1.8% across clinical studies, with the highest incidence in patients with cervical cancer. Avoid VEGZELMA in patients with ovarian cancer who have evidence of recto-sigmoid involvement by pelvic examination or bowel involvement on CT scan or clinical symptoms of bowel obstruction. Discontinue in patients who develop gastrointestinal perforation, tracheoesophageal fistula, or any Grade 4 fistula. Discontinue in patients with fistula formation involving any internal organ.

Surgery and Wound Healing Complications: The incidence of surgery and wound healing complications, including serious and fatal complications, was increased in patients receiving bevacizumab products. In patients who experience wound healing complications during treatment, withhold VEGZELMA until adequate wound healing. Discontinue VEGZELMA in patients who develop necrotizing fasciitis.

Hemorrhage: Severe or fatal hemorrhage occurred up to 5-fold more frequently in patients receiving bevacizumab products vs chemotherapy alone. Discontinue VEGZELMA in patients who develop a Grades 3-4 hemorrhage.

Arterial Thromboembolic Events: Serious, sometimes fatal, arterial thromboembolic events (ATE) occurred at a higher incidence in patients receiving bevacizumab vs chemotherapy. Discontinue VEGZELMA in patients who develop a severe ATE. The safety of reinitiating bevacizumab products after an ATE is resolved is not known.

Venous Thromboembolic Events: An increased risk of venous thromboembolic events (VTE) was observed across clinical studies. Discontinue VEGZELMA in patients with a Grade 4 VTE, including pulmonary embolism.

Hypertension: Severe hypertension occurred at a higher incidence in patients receiving bevacizumab products vs chemotherapy alone. Monitor blood pressure every two to three weeks during treatment with VEGZELMA. Treat with appropriate anti-hypertensive therapy and monitor blood pressure regularly. Discontinue in patients who develop hypertensive crisis or hypertensive encephalopathy.

Posterior Reversible Encephalopathy Syndrome: Posterior reversible encephalopathy syndrome (PRES) was reported in <0.5% of patients across clinical studies. Discontinue VEGZELMA in patients who develop PRES.

Renal Injury and Proteinuria: The incidence and severity of proteinuria was higher in patients receiving bevacizumab products vs chemotherapy. Nephrotic syndrome occurred

in <1% of patients receiving bevacizumab products across clinical studies, in some instances with fatal outcome. Discontinue VEGZELMA in patients who develop nephrotic syndrome.

Infusion-Related Reactions: In clinical studies, infusion-related reactions with the first dose of bevacizumab products occurred in <3% of patients and severe reactions occurred in 0.4% of patients. Decrease the rate of infusion for mild, clinically insignificant infusion-related reactions. Interrupt the infusion in patients with clinically significant infusion-related reactions and consider resuming at a slower rate following resolution. Discontinue VEGZELMA in patients who develop a severe infusion-related reaction and administer appropriate medical therapy.

Embryo-Fetal Toxicity: Bevacizumab products may cause fetal harm when administered to pregnant women. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with VEGZELMA and for 6 months after the last dose.

Ovarian Failure: The incidence of ovarian failure was 34% vs 2% in premenopausal women receiving bevacizumab with chemotherapy vs chemotherapy alone for adjuvant treatment of a solid tumor. Inform females of reproductive potential of the risk of ovarian failure prior to initiating treatment with VEGZELMA.

Congestive Heart Failure (CHF): VEGZELMA is not indicated for use with anthracycline-based chemotherapy. Discontinue VEGZELMA in patients who develop CHF.

MOST COMMON ADVERSE REACTIONS

The most common adverse reactions observed in patients receiving bevacizumab products as a single agent or in combination with other anti-cancer therapies at a rate >10% were epistaxis, headache, hypertension, rhinitis, proteinuria, taste alteration, dry skin, hemorrhage, lacrimation disorder, back pain, and exfoliative dermatitis.

Across clinical studies, bevacizumab was discontinued in 8% to 22% of patients because of adverse reactions.

ADVERSE REACTIONS BY INDICATION

Metastatic colorectal cancer, in combination with intravenous fluorouracil-based chemotherapy for first- or second-line treatment

- **Study AVF2107g:** Grades 3-4 adverse reactions occurring at higher incidence (≥2%) in patients receiving bevacizumab with IFL (N=392) vs placebo with IFL (N=396) were leukopenia (37% vs 31%), neutropenia (21% vs 14%), diarrhea (34% vs 25%), abdominal pain (8% vs 5%), constipation (4% vs 2%), hypertension (12% vs 2%), deep vein thrombosis (9% vs 5%), intra-abdominal thrombosis (3% vs 1%), syncope (3% vs 1%), asthenia (10% vs 7%), and pain (8% vs 5%)

Metastatic colorectal cancer, in combination with fluoropyrimidine-irinotecan- or fluoropyrimidine-oxaliplatin-based chemotherapy for second-line treatment in patients who have progressed on a first-line bevacizumab product-containing regimen

- **Study E3200:** Selected Grades 3–5 (non-hematologic) and Grades 4–5 (hematologic) reactions occurring at a higher incidence (≥2%) in patients receiving bevacizumab with FOLFOX4 (N=521) vs FOLFOX4 alone were fatigue (19% vs 13%), diarrhea (18% vs 13%), sensory neuropathy (17% vs 9%), nausea (12% vs 5%), vomiting (11% vs 4%), dehydration (10% vs 5%), hypertension (9% vs 2%), abdominal pain (8% vs 5%), hemorrhage (5% vs 1%), other neurological (5% vs 3%), ileus (4% vs 1%), and headache (3% vs 0%)

Unresectable, locally advanced, recurrent or metastatic non-squamous non-small cell lung cancer, in combination with carboplatin and paclitaxel for first-line treatment

- **Study E4599:** Grades 3-5 (non-hematologic) and Grades 4-5 (hematologic) adverse reactions occurring at a higher incidence (≥2%) in patients receiving bevacizumab with paclitaxel and carboplatin (N=422) vs chemotherapy alone were neutropenia (27% vs 17%), fatigue (16% vs 13%), hypertension (8% vs 0.7%), infection without neutropenia (7% vs 3%), venous thromboembolism (5% vs 3%), febrile neutropenia (5% vs 2%), pneumonitis/pulmonary infiltrates (5% vs 3%), infection with Grade 3 or 4 neutropenia (4% vs 2%), hyponatremia (4% vs 1%), headache (3% vs 1%), and proteinuria (3% vs 0%)

Recurrent glioblastoma in adults

- **Study EORTC 26101:** In the bevacizumab with lomustine arm (N=278), 22% of patients discontinued treatment due to adverse reactions vs 10% of patients in the lomustine arm. In patients receiving bevacizumab with lomustine, the adverse reaction profile was similar to that observed in other approved indications

Metastatic renal cell carcinoma in combination with interferon alfa

- **Study BO17705:** Grades 3-5 adverse reactions occurring at a higher incidence (>2%) in patients receiving bevacizumab with interferon alfa (N=337) vs placebo with interferon alfa (N=304) were fatigue (13% vs 8%), asthenia (10% vs 7%), proteinuria (7% vs 0%), hypertension (6% vs 1%; including hypertension and hypertensive crisis), and hemorrhage (3% vs 0.3%; including epistaxis, small intestinal hemorrhage, aneurysm ruptured, gastric ulcer hemorrhage, gingival bleeding, hemoptysis, hemorrhage intracranial, large intestinal hemorrhage, respiratory tract hemorrhage, and traumatic hematoma)

Important Safety Information (cont.)

WARNINGS AND PRECAUTIONS (cont.)

ADVERSE REACTIONS BY INDICATION (cont.)

Persistent, recurrent, or metastatic cervical cancer, in combination with paclitaxel and cisplatin, or paclitaxel and topotecan

- **Study GOG-0240:** Grades 3-4 adverse reactions occurring at a higher incidence (≥2%) in patients receiving bevacizumab with chemotherapy (N=218) vs chemotherapy alone (N=222) were abdominal pain (12% vs 10%), hypertension (11% vs 0.5%), thrombosis (8% vs 3%), diarrhea (6% vs 3%), anal fistula (4% vs 0%), proctalgia (3% vs 0%), urinary tract infection (8% vs 6%), cellulitis (3% vs 0.5%), fatigue (14% vs 10%), hypokalemia (7% vs 4%), hyponatremia (4% vs 1%), dehydration (4% vs 0.5%), neutropenia (8% vs 4%), lymphopenia (6% vs 3%), back pain (6% vs 3%), and pelvic pain (6% vs 1%)

Epithelial ovarian, fallopian tube, or primary peritoneal cancer in combination with carboplatin and paclitaxel, followed by VEGZELMA as a single agent, for stage III or IV disease following initial surgical resection

- **Study GOG-0218:** Grades 3-4 adverse reactions occurring at a higher incidence (≥2%) in either of the bevacizumab arms (N=608, N=607) vs control arm (N=602) were fatigue (CPB15+ - 9%, CPB15 - 6%, CPP - 6%), hypertension (CPB15+ - 10%, CPB15 - 6%, CPP - 2%), thrombocytopenia (CPB15+ - 21%, CPB15 - 20%, CPP - 15%), and leukopenia (CPB15+ - 51%, CPB15 - 53%, CPP - 50%)

Epithelial ovarian, fallopian tube, or primary peritoneal cancer in combination with paclitaxel, pegylated liposomal doxorubicin, or topotecan for platinum-resistant recurrent disease who received no more than 2 prior chemotherapy regimens

- **Study MO22224:** Grades 3-4 adverse reactions occurring at a higher incidence (≥2%) in patients receiving bevacizumab with chemotherapy (N=179) vs chemotherapy alone (N=181) were hypertension (6.7% vs 1.1%) and palmar-plantar erythrodysaesthesia syndrome (4.5% vs 1.7%)

Epithelial ovarian, fallopian tube, or primary peritoneal cancer in combination with carboplatin and paclitaxel or carboplatin and gemcitabine, followed by VEGZELMA as a single agent, for platinum-sensitive recurrent disease

- **Study AVF4095g:** Grades 3-4 adverse reactions occurring at a higher incidence (≥2%) in patients receiving bevacizumab with chemotherapy (N=247) vs placebo with chemotherapy (N=233) were thrombocytopenia (40% vs 34%), nausea (4% vs 1.3%), fatigue (6% vs 4%), headache (4% vs 0.9%), proteinuria (10% vs 0.4%), dyspnea (4% vs 1.7%), epistaxis (5% vs 0.4%), and hypertension (17% vs 0.9%)

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit **www.fda.gov/medwatch** or call **1-800-FDA-1088**.

Please see full Prescribing Information for complete information.

References

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