YERVOY®
(ipilimumab)
Injection for intravenous use 5 mg/mL

Bristol Myers Squibb®
Access Support®

A REFERENCE GUIDE TO

Reimbursement and Coding YERVOY® (ipilimumab)

To view authorized distributors for YERVOY, please click here or visit www.BMSAccessSupport.com.
Please see Important Safety Information on pages 22–24 and U.S. Full Prescribing Information.

Indications

YERVOY® (ipilimumab), as a single agent or in combination with nivolumab, is indicated for the treatment of unresectable or metastatic melanoma in adult and pediatric patients 12 years and older.

YERVOY® (ipilimumab) is indicated for the adjuvant treatment of patients with cutaneous melanoma with pathologic involvement of regional lymph nodes of more than 1 mm who have undergone complete resection, including total lymphadenectomy.

Select Important Safety Information

Severe and Fatal Immune-Mediated Adverse Reactions

Immune-mediated adverse reactions listed herein may not be inclusive of all possible severe and fatal immune-mediated adverse reactions.

Immune-mediated adverse reactions, which may be severe or fatal, can occur in any organ system or tissue. While immune-mediated adverse reactions usually manifest during treatment, they can also occur at any time after starting or discontinuing YERVOY. Early identification and management are essential to ensure safe use of YERVOY. Monitor for signs and symptoms that may be clinical manifestations of underlying immune-mediated adverse reactions. Evaluate clinical chemistries including liver enzymes, creatinine, adrenocorticotropic hormone (ACTH) level, and thyroid function at baseline and before each dose. Institute medical management promptly, including specialty consultation as appropriate.

Withhold or permanently discontinue YERVOY depending on severity (please see section 2 Dosage and Administration in the accompanying Full Prescribing Information). In general, if YERVOY interruption or discontinuation is required, administer systemic corticosteroid therapy (1 or 2 mg/kg/day prednisone or equivalent) until improvement to Grade 1 or less. Upon improvement to Grade 1 or less, initiate corticosteroid taper and continue to taper over at least 1 month. Consider administration of other systemic immunosuppressants in patients whose immune-mediated adverse reactions are not controlled with corticosteroid therapy. Toxicity management guidelines for adverse events that do not necessarily require systemic corticosteroids (e.g., endocrinopathies) are discussed on pages 21-23.

Bristol Myers Squibb Is Committed to Helping Support Access

This brochure is designed to help appropriate patients get access to our medications by providing helpful reimbursement information for healthcare offices. Healthcare benefits vary significantly; therefore, it is important that oncology offices verify each patient's insurance coverage prior to initiating therapy.

Table of Contents

Healthcare providers should code healthcare claims based upon the service that is rendered, the patient's medical record, the coding requirements of each health insurer, and the best coding practices. The accurate completion of reimbursement or coverage-related documentation is the responsibility of the healthcare provider and the patient. Bristol Myers Squibb and its agents make no guarantee regarding reimbursement for any service or item.

Metastatic Melanoma: ICD-10-CM Codes for YERVOY® (ipilimumab)

ICD-10-CM codes are used to identify a patient's diagnosis. On October 1, 2015, the newest version of these codes, ICD-10-CM, was implemented throughout the United States. This version replaces the previous version, ICD-9-CM.

- The ICD-10-CM diagnosis codes contain **categories**, **subcategories**, and **codes**. Characters for categories, subcategories, and codes may be letters or numerals
- **All categories** are 3 characters
- **Subcategories** are either 4 or 5 characters
- **Codes** may be 3, 4, 5, 6, or 7 characters
- The ICD-10-CM codes for the labeled indications for YERVOY are provided below by Bristol Myers Squibb and should be verified with the payer. Some health plan and Medicare insurers may specify which codes are covered under their policies. Please code to the level of specificity documented in the medical record. For additional coding questions, call BMS Access Support® at **1-800-861-0048** or visit **www.BMSAccessSupport.com**.

ICD-10-CM Codes for YERVOY[1]	
C43	Malignant melanoma of skin
C43.0	Malignant melanoma of lip
C43.1	Malignant melanoma of eyelid, including canthus*
C43.10	Malignant melanoma of unspecified eyelid, including canthus
C43.11	Malignant melanoma of right eyelid, including canthus*
C43.111	Malignant melanoma of right upper eyelid, including canthus
C43.112	Malignant melanoma of right lower eyelid, including canthus
C43.12	Malignant melanoma of left eyelid, including canthus*
C43.121	Malignant melanoma of left upper eyelid, including canthus
C43.122	Malignant melanoma of left lower eyelid, including canthus

*This is a category code and is invalid for stand-alone use. Please select one of the expanded codes listed below.

(more C43 codes on the next page)

Note: If infusion for antineoplastic immunotherapy is the only reason for the patient encounter, physicians and hospitals may report the code below as the primary diagnosis[1]:

Z51.12 Encounter for antineoplastic immunotherapy

The accurate completion of reimbursement or coverage-related documentation is the responsibility of the healthcare provider and patient. Bristol Myers Squibb and its agents make no guarantee regarding reimbursement for any service or item.

Metastatic Melanoma: ICD-10-CM Codes for YERVOY® (ipilimumab) (cont'd)

ICD-10-CM Codes for YERVOY[1]	
C43.2	Malignant melanoma of ear and external auricular canal*
C43.20	Malignant melanoma of unspecified ear and external auricular canal
C43.21	Malignant melanoma of right ear and external auricular canal
C43.22	Malignant melanoma of left ear and external auricular canal
C43.3	Malignant melanoma of other and unspecified parts of face*
C43.30	Malignant melanoma of unspecified part of face
C43.31	Malignant melanoma of nose
C43.39	Malignant melanoma of other parts of face
C43.4	Malignant melanoma of scalp and neck
C43.5	Malignant melanoma of trunk*
C43.51	Malignant melanoma of anal skin
C43.52	Malignant melanoma of skin of breast
C43.59	Malignant melanoma of other part of trunk
C43.6	Malignant melanoma of upper limb, including shoulder*
C43.60	Malignant melanoma of unspecified upper limb, including shoulder

*This is a category code and is invalid for stand-alone use. Please select one of the expanded codes listed below.

(more C43 codes on the next page)

Note: If infusion for antineoplastic immunotherapy is the only reason for the patient encounter, physicians and hospitals may report the code below as the primary diagnosis[1]:

Z51.12 Encounter for antineoplastic immunotherapy

The accurate completion of reimbursement or coverage-related documentation is the responsibility of the healthcare provider and patient. Bristol Myers Squibb and its agents make no guarantee regarding reimbursement for any service or item.

Metastatic Melanoma: ICD-10-CM Codes for YERVOY® (ipilimumab) (cont'd)

ICD-10-CM Codes for YERVOY[1]	
C43.61	Malignant melanoma of right upper limb, including shoulder
C43.62	Malignant melanoma of left upper limb, including shoulder
C43.7	Malignant melanoma of lower limb, including hip*
C43.70	Malignant melanoma of unspecified lower limb, including hip
C43.71	Malignant melanoma of right lower limb, including hip
C43.72	Malignant melanoma of left lower limb, including hip
C43.8	Malignant melanoma of overlapping sites of skin
C43.9	Malignant melanoma of skin, unspecified

*This is a category code and is invalid for stand-alone use. Please select one of the expanded codes listed below.

The code C43 has an Excludes 2 note under it. Per **ICD-10-CM** official guidelines, an Excludes 2 note under a code represents "Not included here." An Excludes 2 note indicates that the condition excluded is not part of the condition represented by the code, but a patient may have both conditions at the same time. When an Excludes 2 note appears under a code, it is acceptable to use both the code and the excluded code together, when appropriate.[1]

Under code C43, the Excludes 2 note lists the following[1]:

- Malignant melanoma of skin of genital organs (C51, C52, C60, C63)
- Merkel cell carcinoma (C4A)
- Sites other than skin – code to malignant neoplasm of the site

Note: If infusion for antineoplastic immunotherapy is the only reason for the patient encounter, physicians and hospitals may report the code below as the primary diagnosis[1]:

Z51.12 Encounter for antineoplastic immunotherapy

The accurate completion of reimbursement or coverage-related documentation is the responsibility of the healthcare provider and patient. Bristol Myers Squibb and its agents make no guarantee regarding reimbursement for any service or item.

Metastatic Melanoma: ICD-10-CM Codes for YERVOY® (ipilimumab) (cont'd)

For sites other than category C43, code to the malignant neoplasm of the site.[1] Some sites where melanoma is commonly seen are shown below and on the next page.

ICD-10-CM Codes for YERVOY[1]	
C21 Malignant neoplasm of anus and anal canal	
C21.0	Malignant neoplasm of anus, unspecified
C21.1	Malignant neoplasm of anal canal
C51 Malignant neoplasm of vulva	
C51.0	Malignant neoplasm of labium majus
C51.1	Malignant neoplasm of labium minus
C51.2	Malignant neoplasm of clitoris
C51.9	Malignant neoplasm of vulva, unspecified
C52 Malignant neoplasm of vagina	
C57 Malignant neoplasm of other and unspecified female genital organs	
C57.7	Malignant neoplasm of other specified female genital organs
C57.8	Malignant neoplasm of overlapping sites of female genital organs
C57.9	Malignant neoplasm of female genital organ, unspecified

Note: If infusion for antineoplastic immunotherapy is the only reason for the patient encounter, physicians and hospitals may report the code below as the primary diagnosis[1]:

Z51.12 Encounter for antineoplastic immunotherapy

The accurate completion of reimbursement or coverage-related documentation is the responsibility of the healthcare provider and patient. Bristol Myers Squibb and its agents make no guarantee regarding reimbursement for any service or item.

Metastatic Melanoma: ICD-10-CM Codes for YERVOY® (ipilimumab) (cont'd)

ICD-10-CM Codes for YERVOY[1]	
C60	Malignant neoplasm of penis
C60.0	Malignant neoplasm of prepuce
C60.1	Malignant neoplasm of glans penis
C60.8	Malignant neoplasm of overlapping sites of penis
C60.9	Malignant neoplasm of penis, unspecified
C63	Malignant neoplasm of other and unspecified male genital organs
C63.0	Malignant neoplasm of epididymis*
C63.00	Malignant neoplasm of unspecified epididymis
C63.01	Malignant neoplasm of right epididymis
C63.02	Malignant neoplasm of left epididymis
C63.1	Malignant neoplasm of spermatic cord*
C63.10	Malignant neoplasm of unspecified spermatic cord
C63.11	Malignant neoplasm of right spermatic cord
C63.12	Malignant neoplasm of left spermatic cord
C63.2	Malignant neoplasm of scrotum
C63.7	Malignant neoplasm of other specified male genital organs
C63.8	Malignant neoplasm of overlapping sites of male genital organs
C63.9	Malignant neoplasm of male genital organ, unspecified

*This is a category code and is invalid for stand-alone use. Please select one of the expanded codes listed below.

Note: If infusion for antineoplastic immunotherapy is the only reason for the patient encounter, physicians and hospitals may report the code below as the primary diagnosis[1]:

Z51.12 Encounter for antineoplastic immunotherapy

The accurate completion of reimbursement or coverage-related documentation is the responsibility of the healthcare provider and patient. Bristol Myers Squibb and its agents make no guarantee regarding reimbursement for any service or item.

Healthcare Common Procedure Coding System (HCPCS) and Revenue Codes for YERVOY® (ipilimumab)

Recommended HCPCS Code for YERVOY[2]		
HCPCS Code	Description	Billing Units
J9228	Injection, ipilimumab, 1 mg	1 mg = 1 billing unit

Use the following claim formats when YERVOY is administered to patients on an outpatient basis and billed to health plans:

- Physician office: CMS-1500 (paper format) or ASC 837P (electronic format)
- Hospital outpatient: UB-04 (CMS-1450) [paper format] or ASC 837I (electronic format)
- **JW modifier** – Providers and suppliers are required to report the JW modifier on Part B drug claims for discarded drugs and biologicals. Also, providers and suppliers must document the amount of discarded drugs or biologicals in Medicare beneficiaries' medical records[3]
- **JZ modifier** – Starting no later than July 1, 2023, providers and suppliers are required to attest if there were not discarded amounts of drugs and biologicals[3]
- **JG modifier** – To be used by hospital outpatient to identify if the drug was obtained through 340B pricing. Note that use of this modifier will not trigger any differentiated payment[3]

All the coding information presented is applicable to outpatient procedures only. Please see pages 14-15 for more information.

Revenue Codes[5] (for Use in the Hospital Outpatient Setting)	
Revenue Code	Description
0636	Drugs requiring detailed coding
0335	Chemotherapy administration, IV
0260	IV therapy

The accurate completion of reimbursement or coverage-related documentation is the responsibility of the healthcare provider and patient. Bristol Myers Squibb and its agents make no guarantee regarding reimbursement for any service or item.

Current Procedural Terminology (CPT®)* Codes for YERVOY® (ipilimumab)

The CPT codes that may be appropriate when administering YERVOY appear in the table below.

Recommended CPT Codes for YERVOY[6]	
CPT Code	**Description**
96413	Chemotherapy administration, intravenous infusion technique; up to 1 hour, single or initial substance/drug
96415	Chemotherapy administration, intravenous infusion technique; each additional hour • List separately in addition to code for primary procedure • Use 96415 in conjunction with 96413 • Report 96415 for infusion intervals of greater than 30 minutes beyond 1-hour increments
96417	Chemotherapy administration, IV infusion; each additional sequential infusion (different substance/drug), up to 1 hour (list separately in addition to code for primary procedure). (Use 96417 in conjunction with 96413) Report only once per sequential infusion. Report 96415 for additional hour(s) of sequential infusion

Please contact the payer or BMS Access Support® for additional coding information regarding YERVOY.

*CPT codes and descriptions only are ©2019 by American Medical Association (AMA). All rights reserved. The AMA assumes no liability for data contained or not contained herein. CPT is a registered trademark of the American Medical Association.

The accurate completion of reimbursement or coverage-related documentation is the responsibility of the healthcare provider and patient. Bristol Myers Squibb and its agents make no guarantee regarding reimbursement for any service or item.

Authorized Distributors

Physician Offices

Specialty Distributor	Phone Orders	Fax Orders and Website
Cardinal Health Specialty PharmaceuticalDistribution	1-877-453-3972	https://specialtyonline.cardinalhealth.com
CuraScript Specialty Distribution	1-877-599-7748	https://www.curascriptsd.com
HyGen Pharmaceuticals Specialty Division	877-630-9198	https://hygenpharma.com/#contactus
McKesson Specialty Health	1-800-482-6700	https://mscs.mckesson.com
Morris & Dickson Specialty	1-800-710-6100	Fax: 1-318-524-3096 https://www.mdspecialtydist.com
Oncology Supply	1-800-633-7555	https://www.oncologysupply.com

For offices that prefer to use the services of a specialty pharmacy, specialty pharmacies can obtain YERVOY from the distributors listed above.

Hospitals and Infusion Centers

Specialty Distributor	Phone Orders	Fax Orders and Website
AD Healthcare	1-800-746-6273	Fax: 1-800-547-9413 https://www.asdhealthcare.com
Cardinal Health Specialty Pharmaceutical Distribution	1-866-677-4844	Fax: 1-614-553-6301 https://orderexpress.cardinalhealth.com
DMS Pharmaceutical Group, Inc.	1-877-788-1100	Fax: 1-847-518-1105 https://www.dmspharma.com
HyGen Pharmaceuticals Specialty Division	877-630-9198	https://hygenpharma.com/#contactus
McKesson Plasma and Biologics	1-877-625-2566	Fax: 1-888-752-7626 https://connect.mckesson.com
Morris & Dickson Specialty	1-800-710-6100	Fax: 1-318-524-3096 https://www.mdspecialtydist.com

National Drug Codes (NDCs) Information for YERVOY® (ipilimumab)

The NDCs for YERVOY, listed below, are often necessary in addition to the appropriate J-code when filing a claim for reimbursement.

NDCs for YERVOY[7]

One 200-mg (5-mg/mL), single-use vial

200-mg vial = 200 billable units

0003-2328-22

One 50-mg (5-mg/mL), single-use vial

50-mg vial = 50 billable units

0003-2327-11

Storage Information

Store under refrigeration at 2°C to 8°C (36°F to 46°F). Protect from light by storing in the original package until time of use. Do not freeze or shake.

The accurate completion of reimbursement or coverage-related documentation is the responsibility of the healthcare provider and patient. Bristol Myers Squibb and its agents make no guarantee regarding reimbursement for any service or item.

5010 Electronic Transaction Coding for YERVOY® (ipilimumab)

- For electronic transactions, including 837P and 837I, the NDC is to be preceded by the qualifier N4 and followed immediately by the 11-digit NDC code for payers that require it[7]
- This is typically followed by the quantity qualifier, such as: UN (units), F2 (international units), GR (gram), or mL (milliliter), and the quantity administered[7]

5010 Transaction Coding for YERVOY[7,8]

How Supplied	11-digit NDC	NDC Qualifier	NDC Basis of Measurement	Sample NDC 5010 Format
50-mg/10-mL (5 mg/mL) single-use vial	00003-2327-11	N4	mL	N400003232711ML10
200-mg/40-mL (5 mg/mL) single-use vial	00003-2328-22	N4	mL	N400003232822ML40

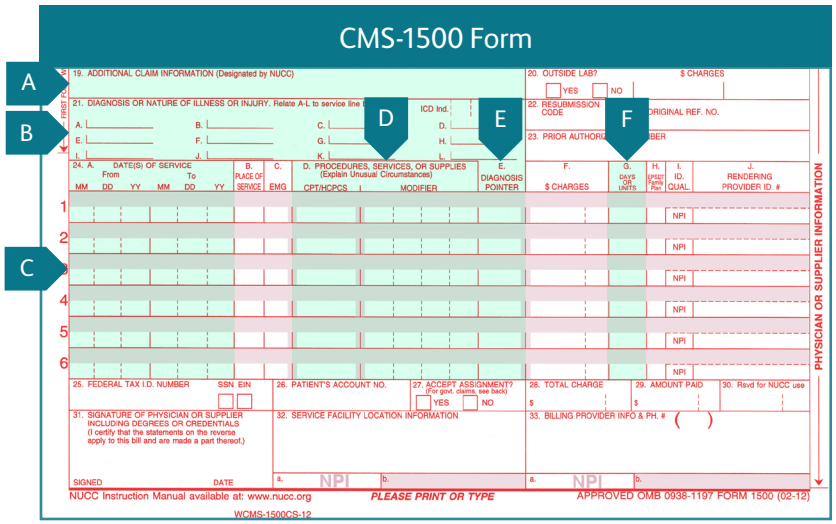
The example given in the far right column above demonstrates NDC quantity reporting for 1 vial of YERVOY. The actual amount of drug used can vary based on factors such as indication or patient weight. Currently, reporting NDC quantity varies from payer to payer, so the provider should consult each specific payer to determine the required format.

The accurate completion of reimbursement or coverage-related documentation is the responsibility of the healthcare provider and patient. Bristol Myers Squibb and its agents make no guarantee regarding reimbursement for any service or item.

Coding and Billing Units for YERVOY® (ipilimumab)

Please contact the payer or BMS Access Support® for additional information on coding and billing units

CMS-1500 Form



Physician Office

A **Item 19:** Many payers require detailed information about the drug in Box 19.[8] Typically, payers require the drug name, total dosage and strength, method of administration, 11-digit NDC, and basis of measurement

B **Item 21:** Enter the site-specific ICD-10-CM codes in priority order[8]

C **Item 24A:** NDC information is required in the shaded area above the line on which a drug is reported in 24D.[8] The 11-digit NDC is preceded by the qualifier N4 and followed by the quantity qualifier (ML) and the quantity administered.[8] For example, enter "N400003232711ML10" for the 50-mg/10-mL vial or "N400003232822ML40" for the 200-mg/40-mL vial[7]

D **Item 24D:** Enter HCPCS code J9228, CPT code 96413, and CPT codes 96415 and 96417 (if needed) for time of treatment infusion.[2,6] In addition, it is required that you enter J9288-JW on next line to record waste.[3] Alternatively, if no wastage enter J9288-JZ to attest there were no discarded amounts[3]

E **Item 24E:** Enter the diagnosis code reference letter or number from Box 21 that relates to the date of service and the services or procedures performed that are entered on that same line under 24D[8]

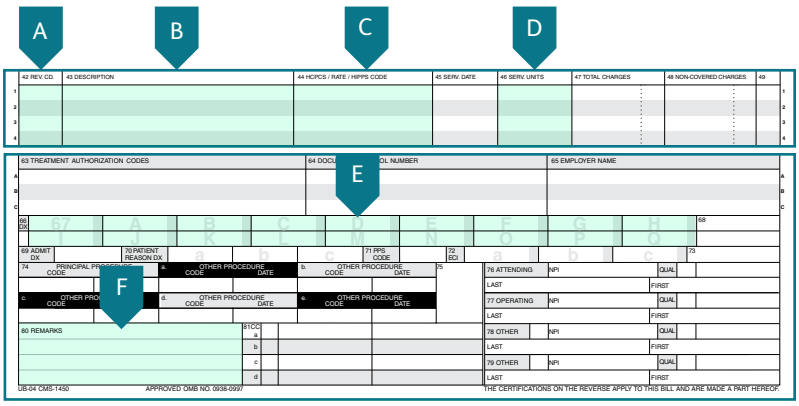
F **Item 24G:** Billing units are reported here[8]
1 mg = 1 billing unit

This sample form is for informational purposes only.

The accurate completion of reimbursement or coverage-related documentation is the responsibility of the healthcare provider and patient. Bristol Myers Squibb and its agents make no guarantee regarding reimbursement for any service or item.

Coding and Billing Units for YERVOY® (ipilimumab) (cont'd)

UB-04 Form



This sample form is for informational purposes only.

Outpatient Hospital

A **Form Locator (FL) 42:** Enter a 4-digit revenue code that best describes the service provided, in accordance with hospital billing policy.[9] For chemotherapy administration, revenue codes 0260 (IV therapy) or 0335 (radiology–therapeutic: chemotherapy-IV) could be used.[5] CMS recommends using revenue code 0636 (drugs requiring detailed coding)[5,10]

B **FL 43:** Enter the qualifier "N4" followed by the 11-digit NDC in positions 01-13.[9] Additionally, report the quantity qualifier (ML) followed by the quantity administered (50 mg/10 mL or 200 mg/40 mL) beginning in position 14.[7,9] For example, use "N400003232711ML10" for the 50-mg/10-mL vial or "N400003232822ML40" for the 200-mg/40-mL vial[7]

C **FL 44:** Enter HCPCS code J9228, CPT code 96413, and CPT code 96415 (if needed) for time of treatment infusion.[2,6] In addition, it is required that you enter J9228-JW on next line to record waste[3] Alternatively, if no wastage, enter J9228-JZ to attest there were no discarded amounts. Include the JG modifier if the drug was obtained using 340B pricing[3]

D **FL 46:** Billing units are called service units and are placed here.[9] 1 mg = 1 billing unit

E **FL 67A-67Q:** Enter the site-specific ICD-10-CM diagnosis codes for the malignancy being treated[9]

F **FL 80:** Some payers require detailed information about the drug in FL 80.[8,9] Typically, payers require the drug name, total dosage and strength, method of administration, 11-digit NDC, and basis of measurement

The accurate completion of reimbursement or coverage-related documentation is the responsibility of the healthcare provider and patient. Bristol Myers Squibb and its agents make no guarantee regarding reimbursement for any service or item.

Dosing and Administration of YERVOY® (ipilimumab)

Recommended dosing[7]

YERVOY (ipilimumab)	
DOSING & SCHEDULE*†	DURATION
Unresectable or Metastatic Melanoma	
3 mg/kg of YERVOY intravenously over 90 minutes	every 3 weeks for a maximum of 4 doses
Adjuvant Treatment of Melanoma	
10 mg/kg of YERVOY intravenously over 90 minutes	every 3 weeks for a maximum of 4 doses followed by 10 mg/kg every 12 weeks for up to 3 years

Dosing and Administration of YERVOY® (ipilimumab) (cont'd)

Recommended dosage modifications for adverse reactions[7]

No dose reduction for YERVOY is recommended. In general, withhold YERVOY for severe (Grade 3) immune-mediated adverse reactions. Permanently discontinue YERVOY for life-threatening (Grade 4) immune-mediated adverse reactions, recurrent severe (Grade 3) immune-mediated reactions that require systemic immunosuppressive treatment, persistent moderate (Grade 2) or severe (Grade 3) reactions lasting 12 weeks or longer after last YERVOY dose (excluding endocrinopathy), or an inability to reduce corticosteroid dose to 10 mg or less of prednisone or equivalent per day within 12 weeks of initiating steroids. Dosage modifications for YERVOY for adverse reactions that require management different from these general guidelines are summarized below.

Recommended Dosage Modifications for Adverse Reactions		
Adverse Reaction	**Severity***	**Dosage Modifications**
Immune-Mediated Adverse Reactions [See *Warnings and Precautions (5.1) in the U.S. Full Prescribing Information*]		
Colitis	Grade 2	Withhold[a]
	Grade 3 or 4	Permanently discontinue
Hepatitis with no tumor involvement of the liver or Hepatitis with tumor involvement of the liver/non-HCC	AST or ALT increases to more than 3 times and up to 5 times the ULN or Total bilirubin increases to more than 1.5 times and up to 3 times the ULN	Withhold[a]
	AST or ALT more than 5 times the ULN or Total bilirubin more than 3 times the ULN	Permanently discontinue
Hepatitis with tumor involvement of the liver[b]/HCC[c]	Baseline AST/ALT is more than 1 and up to 3 times ULN and increases to more than 5 and up to 10 times ULN or Baseline AST/ALT is more than 3 and up to 5 times ULN and increases to more than 8 and up to 10 times ULN	Withhold[a]
	AST/ALT increases to more than 10 times ULN or Total bilirubin increases to more than 3 times ULN	Permanently discontinue
Exfoliative Dermatologic Conditions	Suspected SJS, TEN, or DRESS	Withhold
	Confirmed SJS, TEN, or DRESS	Permanently discontinue
Endocrinopathies[d]	Grades 3 or 4	Withhold until clinically stable or permanently discontinue depending on severity

(continued on next page)

Dosing and Administration of YERVOY® (ipilimumab) (cont'd)

Recommended Dosage Modifications for Adverse Reactions (cont'd)[7]		
Adverse Reaction	**Severity***	**Dosage Modifications**
Pneumonitis	Grade 2	Withhold[a]
	Grade 3 or 4	Permanently discontinue
Nephritis with Renal Dysfunction	Grade 2 or 3 increased blood creatinine	Withhold[a]
	Grade 4 increased blood creatinine	Permanently discontinue
Neurological Toxicities	Grade 2	Withhold[a]
	Grade 3 or 4	Permanently discontinue
Myocarditis	Grade 2, 3, or 4	Permanently discontinue
Ophthalmologic	Grade 2, 3, or 4 that does not improve to Grade 1 within 2 weeks while receiving topical therapy or that requires systemic treatment	Permanently discontinue
Other Adverse Reactions		
Infusion-Related Reactions [see *Warnings and Precautions (5.2)*]	Grade 1 or 2	Interrupt or slow the rate of infusion
	Grade 3 or 4	Permanently discontinue

ALT = alanine aminotransferase, AST = aspartate aminotransferase, DRESS = Drug Rash with Eosinophilia and Systemic Symptoms, SJS = Stevens Johnson Syndrome, TEN = toxic epidermal necrolysis, ULN = upper limit of normal.

*Based on Common Terminology Criteria for Adverse Events (CTCAE), Version 4.03

[a] Resume in patients with complete or partial resolution (Grade 0 or 1) after corticosteroid taper. Permanently discontinue if no complete or partial resolution within 12 weeks of last dose or inability to reduce prednisone to 10 mg per day (or equivalent) or less within 12 weeks of initiating steroids.

[b] If AST/ALT are less than or equal to ULN at baseline, withhold or permanently discontinue YERVOY based on recommendations for hepatitis with no liver involvement.

[c] This guidance is only applicable to HCC patients who are being treated with YERVOY in combination with nivolumab.

[d] Depending on clinical severity, consider withholding for Grade 2 endocrinopathy until symptom improvement with hormone replacement. Resume once acute symptoms have resolved.

Determining Your Order for YERVOY® (ipilimumab)

Dosing for YERVOY is weight-based; therefore, the dosage of YERVOY will vary not only by indication, but by patient weight as well[7]

Example Orders			
Patient Weight Examples	YERVOY	Total Dosage Needed	Suggested Vials
Metastatic Melanoma			
50 kg (110 lbs)	3 mg/kg	150 mg	3 x 50 50 50 = 150 mg
83 kg (183 lbs)	3 mg/kg	249 mg	1 x 200 + 1 x 50 = 250 mg
Adjuvant Treatment of Melanoma			
50 kg (110 lbs)	10 mg/kg	500 mg	2 x 200 200 + 2 x 50 50 = 500 mg
83 kg (183 lbs)	10 mg/kg	830 mg	4 x 200 200 200 200 + 1 x 50 = 850 mg

How to store YERVOY[7]

- YERVOY must be stored under refrigeration between 2°C and 8°C (36°F to 46°F)
- Protect vials from light by storing in the original carton until time of use
- Do not freeze or shake

Medicare Drug Reimbursement for YERVOY® (ipilimumab)

What is the Medicare reimbursement allowable for YERVOY?

Physicians*

- The payment limit is 106% of average sales price (ASP), not including sequestration, and represents one billing unit of YERVOY, which is billed for each 1 mg[11,12†]
- The amount paid to physicians for HCPCS code J9228 is published at the beginning of each calendar quarter in "Payment Allowance Limits for Medicare Part B Drugs,"[12] which can be downloaded at https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Part-B-Drugs/McrPartBDrugAvgSalesPrice
- Medicare Part B will pay physicians 80% of the allowed price for J9228; the patient is responsible for 20% co-insurance, which may be covered by secondary insurance (private supplemental coverage, Medicaid, etc.)[13]

Hospital outpatient clinics*

Drugs paid separately under the hospital outpatient fee schedule are based on 106% of average sales price (ASP), not including sequestration, for one billing unit for the corresponding HCPCS code. This is 1 mg for J9228.[11,12†]

- The Payment Allowance Limits[12] are published each quarter at https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Part-B-Drugs/McrPartBDrugAvgSalesPrice

Hospital inpatient settings

- Reimbursement in the inpatient setting is bundled into the Medicare Diagnosis Related Groups called MS-DRGs[14,15]
- This prospective rate changes on October 1 each year and does not allow for drugs to be paid separately[16,17]

*While the statutory amount that Medicare will reimburse for a Part B Drug in a physician office will remain at ASP +6%, sequestration has resulted in a reduction to the Medicare portion of the payment to Medicare providers. Essentially, all payments from Medicare carriers to the providers (including physician offices, hospitals, etc.) will be reduced by 2%.[18]

†See The Centers for Medicare & Medicaid Services' (CMS) Internet Only Manual (IOM) Publication 100-04, Chapter 17-20.1.3.

Commercial Insurance Reimbursement for YERVOY® (ipilimumab)

Physicians

- Drug reimbursement, like service reimbursement, is usually based on a fee schedule[19]
- The fee schedules are based on the ASP or AWP, as published by a credible source,[20,21] or an average costing methodology as determined by the payer, such as usual, customary, and reasonable (UC&R)[22]

Hospital outpatient clinics

- In this setting, reimbursement is most commonly based on percentage of charges[21]
- Alternatively, some hospitals use the same ASP or AWP methodologies typically used by physician offices[21]
- Other methodologies include capitated model, cost minus submitted charges, or discount off submitted charges[21]

Hospital inpatient settings

- Inpatient rates are prospective, meaning they are predetermined per discharge[14,15]
- There are private payers that pay on a version of the DRGs[15]
- There are also payers that pay on a negotiated and fixed rate per day called a "per diem."[15] There are capitated rates for inpatients as well[15]
- New drugs may be carved out of per diems or capitated rates, if the hospital negotiates to do so[23]

Important Safety Information

Severe and Fatal Immune-Mediated Adverse Reactions

Immune-mediated adverse reactions listed herein may not be inclusive of all possible severe and fatal immune-mediated adverse reactions.

Immune-mediated adverse reactions, which may be severe or fatal, can occur in any organ system or tissue. While immune-mediated adverse reactions usually manifest during treatment, they can also occur at any time after starting or discontinuing YERVOY. Early identification and management are essential to ensure safe use of YERVOY. Monitor for signs and symptoms that may be clinical manifestations of underlying immune-mediated adverse reactions. Evaluate clinical chemistries including liver enzymes, creatinine, adrenocorticotropic hormone (ACTH) level, and thyroid function at baseline and before each dose. Institute medical management promptly, including specialty consultation as appropriate.

Withhold or permanently discontinue YERVOY depending on severity (please see section 2 Dosage and Administration in the accompanying Full Prescribing Information). In general, if YERVOY interruption or discontinuation is required, administer systemic corticosteroid therapy (1 or 2 mg/kg/day prednisone or equivalent) until improvement to Grade 1 or less. Upon improvement to Grade 1 or less, initiate corticosteroid taper and continue to taper over at least 1 month. Consider administration of other systemic immunosuppressants in patients whose immune-mediated adverse reactions are not controlled with corticosteroid therapy.

Toxicity management guidelines for adverse events that do not necessarily require systemic corticosteroids (e.g., endocrinopathies) are discussed below.

Immune-Mediated Colitis

YERVOY can cause immune-mediated colitis, which may be fatal. Cytomegalovirus (CMV) infection/reactivation has been reported in patients with corticosteroid-refractory immune-mediated colitis. In cases of corticosteroid-refractory colitis, consider repeating infectious workup to exclude alternative etiologies. Immune-mediated diarrhea/colitis occurred in 12% (62/511) of patients who received YERVOY 3 mg/kg as a single agent, including Grade 3-5 (7%) and Grade 2 (5%). Immune-mediated diarrhea/colitis occurred in 31% (144/471) of patients who received YERVOY 10 mg/kg as a single agent, including fatal (0.2%), Grade 4 (1.5%), Grade 3 (14%), and Grade 2 (14%).

Immune-Mediated Hepatitis

Immune-mediated hepatitis occurred in 4.1% (21/511) of patients who received YERVOY 3 mg/kg as a single agent, including Grade 3-5 (1.6%) and Grade 2 (2.5%). Immune-mediated hepatitis occurred in 15% (73/471) of patients who received YERVOY 10 mg/kg as a single agent, including Grade 4 (2.8%), Grade 3 (8%), and Grade 2 (5%).

Immune-Mediated Dermatologic Adverse Reactions

YERVOY can cause immune-mediated rash or dermatitis, including bullous and exfoliative dermatitis, Stevens Johnson Syndrome, toxic epidermal necrolysis (TEN), and DRESS (drug rash with eosinophilia and systemic symptoms). Topical emollients and/or topical corticosteroids may be adequate to treat mild to moderate non-bullous/exfoliative rashes. Immune-mediated rash occurred in 15% (76/511) of patients who received YERVOY 3 mg/kg as a single agent, including Grade 3-5 (2.5%) and Grade 2 (12%). Immune-mediated rash occurred in 25% (118/471) of patients who received YERVOY 10 mg/kg as a single agent, including Grade 3 (4%) and Grade 2 (21%).

(continued on next page)

Please see U.S. Full Prescribing Information.

Important Safety Information (cont'd)

Immune-Mediated Endocrinopathies

Grade 2-5 immune-mediated endocrinopathies occurred in 4% (21/511) of patients who received YERVOY 3 mg/kg as a single agent. Severe to life-threatening (Grade 3-4) endocrinopathies occurred in 9 patients (1.8%). All 9 of these patients had hypopituitarism with some patients having additional concomitant endocrinopathies, such as adrenal insufficiency, hypogonadism, and hypothyroidism. Six of the 9 patients were hospitalized for severe endocrinopathies. Moderate (Grade 2) endocrinopathy occurred in 12 patients (2.3%), including hypothyroidism, adrenal insufficiency, hypopituitarism, hyperthyroidism and Cushing's syndrome. Immune-mediated endocrinopathies occurred in 28% of patients (132/471) who received YERVOY 10 mg/kg as a single agent, including Grade 4 (0.6%), Grade 3 (8%) and Grade 2 (20%). Of the 39 patients with Grade 3 to 4 endocrinopathies, 35 patients had hypopituitarism (associated with one or more secondary endocrinopathies, e.g., adrenal insufficiency, hypogonadism, and hypothyroidism), 3 patients had hyperthyroidism, and 1 had primary hypothyroidism. Twenty-seven of the 39 patients (69%) were hospitalized for endocrinopathies. Of the 93 patients with Grade 2 endocrinopathy, 74 had primary hypopituitarism associated with one or more secondary endocrinopathy, e.g., adrenal insufficiency, hypogonadism, and hypothyroidism, 9 had primary hypothyroidism, 3 had hyperthyroidism, 3 had thyroiditis with hypo- or hyperthyroidism, 2 had hypogonadism, 1 had both hyperthyroidism and hypopituitarism, and 1 subject developed Graves' ophthalmopathy. YERVOY can cause immune-mediated hypophysitis. Hypophysitis can present with acute symptoms associated with mass effect such as headache, photophobia, or visual field cuts. Hypophysitis can cause hypopituitarism. Initiate hormone replacement as clinically indicated.

Other Immune-Mediated Adverse Reactions

Across clinical trials of YERVOY administered as a single agent or in combination with nivolumab, the following clinically significant immune-mediated adverse reactions, some with fatal outcome, occurred in <1% of patients unless otherwise specified, as shown below:

Nervous System: Autoimmune neuropathy (2%), meningitis, encephalitis, myelitis and demyelination, myasthenic syndrome/myasthenia gravis, Guillain-Barré syndrome, nerve paresis, motor dysfunction

Cardiovascular: Angiopathy, myocarditis, pericarditis, temporal arteritis, vasculitis

Ocular: Blepharitis, episcleritis, iritis, orbital myositis, scleritis, uveitis. Some cases can be associated with retinal detachment. If uveitis occurs in combination with other immune-mediated adverse reactions, consider a Vogt-Koyanagi-Harada–like syndrome, which has been observed in patients receiving YERVOY and may require treatment with systemic corticosteroids to reduce the risk of permanent vision loss.

Gastrointestinal: Duodenitis, gastritis, pancreatitis (1.3%)

Musculoskeletal and Connective Tissue: Arthritis, myositis, polymyalgia rheumatica, polymyositis, rhabdomyolysis

Other (hematologic/immune): Aplastic anemia, conjunctivitis, cytopenias (2.5%), eosinophilia (2.1%), erythema multiforme, histiocytic necrotizing lymphadenitis (Kikuchi lymphadenitis), hypersensitivity vasculitis, meningitis, neurosensory hypoacusis, psoriasis, sarcoidosis, systemic inflammatory response syndrome, and solid organ transplant rejection.

(continued on next page)

Please see U.S. Full Prescribing Information.

Important Safety Information (cont'd)

Infusion-Related Reactions

Severe infusion-related reactions can occur with YERVOY. Discontinue YERVOY in patients with severe or life-threatening (Grade 3 or 4) infusion reactions. Interrupt or slow the rate of infusion in patients with mild or moderate (Grade 1 or 2) infusion reactions. Infusion-related reactions occurred in 2.9% (28/982) of patients who received single-agent YERVOY 3 mg/kg or 10 mg/kg for the treatment of melanoma.

Complications of Allogeneic Hematopoietic Stem Cell Transplant after YERVOY

Fatal or serious graft-versus-host disease (GVHD) can occur in patients who receive YERVOY either before or after allogeneic hematopoietic stem cell transplantation (HSCT). These complications may occur despite intervening therapy between CTLA-4 receptor blocking antibody and allogeneic HSCT. Follow patients closely for evidence of GVHD and intervene promptly. Consider the benefit versus risks of treatment with YERVOY after allogeneic HSCT.

Embryo-Fetal Toxicity

Based on its mechanism of action, YERVOY can cause fetal harm when administered to a pregnant woman. The effects of YERVOY are likely to be greater during the second and third trimesters of pregnancy. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with YERVOY and for 3 months after the last dose.

Lactation

There are no data on the presence of YERVOY in human milk or its effects on the breastfed child or milk production. Because of the potential for serious adverse reactions in breastfed children, advise women not to breastfeed during treatment with YERVOY and for 3 months following the last dose.

Common Adverse Reactions

The most common adverse reactions (≥5%) in patients who received YERVOY at 3 mg/kg were fatigue (41%), diarrhea (32%), pruritus (31%), rash (29%), and colitis (8%). The most common adverse reactions (≥5%) in patients who received YERVOY at 10 mg/kg were rash (50%), diarrhea (49%), fatigue (46%), pruritus (45%), headache (33%), weight loss (32%), nausea (25%), pyrexia (18%), colitis (16%), decreased appetite (14%), vomiting (13%), and insomnia (10%).

Please see U.S. Full Prescribing Information.

References

1. American Medical Association. *ICD-10-CM 2020: The Complete Official Codebook.* Chicago, IL: American Medical Association; 2019.
2. American Medical Association. *2019 HCPCS Level II.* Professional ed. Chicago, IL: American Medical Association; 2019.
3. Centers for Medicare & Medicaid Services. Medicare-FFS Program, Billing 340B Modifiers under the Hospital Outpatient Prospective Payment System (OPPS). Baltimore, MD. Centers for Medicare & Medicaid Services; March 3, 2023. Accessed February 26, 2024. https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/downloads/clm104c01.pdf
4. Centers for Medicare & Medicaid Services. MLN Matters, Number MM9603 Revised. https://www.cms.gov/Outreach-and-Education/Medicare-Learning-Network-MLN/MLNMattersArticles/Downloads/MM9603.pdf. Revised June 10, 2016. Accessed January 22, 2024.
5. Palmetto GBA. Medicare Part A Billing Guide. March 2017. https://www.palmettogba.com/Palmetto/Providers.Nsf/files/Part_A_Billing_Guide.pdf/$File/Part_A_Billing_Guide.pdf. Accessed January 22, 2024.
6. American Medical Association. *CPT Professional 2020.* Professional ed. Chicago, IL: American Medical Association; 2019.
7. YERVOY [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; 2023.
8. Centers for Medicare & Medicaid Services. Medicare Claims Processing Manual. Chapter 26 – Completing and Processing the Form CMS-1500 Data Set. Revision 4388. https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/downloads/clm104c26.pdf. Accessed January 22, 2024.
9. Centers for Medicare & Medicaid Services. Medicare Claims Processing Manual. Chapter 25 – Completing and Processing the Form CMS-1450 Data Set. Revision 10880, August, 6, 2021. http://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/downloads/clm104c25.pdf. Accessed January 22, 2024.
10. Centers for Medicare & Medicaid Services. Medicare Claims Processing Manual. Chapter 17 – Drugs and Biologicals. Revision 12201, August, 10, 2023. https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/clm104c17.pdf. Accessed January 22, 2024.
11. Centers for Medicare & Medicaid Services. 2020 ASP drug pricing files. Updated September 9, 2020. https://www.cms.gov/medicare/medicare-part-b-drug-average-sales-price/2020-asp-drug-pricing-files. Accessed January 22, 2024.
12. Centers for Medicare & Medicaid Services. Payment allowance limits for Medicare Part B drugs. https://www.cms.gov/apps/ama/license.asp?file=/files/zip/october-2020-asp-pricing-file.zip. Accessed January 22, 2024.
13. Centers for Medicare & Medicaid Services. Medicare & You 2020. https://www.medicare.gov/sites/default/files/2019-09/10050-medicare-and-you.pdf. Accessed January 22, 2024.
14. Centers for Medicare & Medicaid Services. Acute inpatient PPS. https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/AcuteInpatientPPS/index.html. Accessed January 22, 2024.
15. AMCP Task Force on Drug Payment Methodologies. AMCP guide to pharmaceutical payment methods, executive edition. *J Manag Care Pharm.* 2007;13(8 suppl C):S1-S39.
16. Centers for Medicare & Medicaid Services. Drug coverage under different parts of Medicare. https://www.cms.gov/outreach-and-education/outreach/partnerships/downloads/11315-p.pdf. Accessed January 22, 2024.
17. CMS.gov. MS-DRG Classifications and Software https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/AcuteInpatientPPS/MS-DRG-Classifications-and-Software. Accessed January 22, 2024.
18. Centers for Medicare & Medicaid Services. CMS Medicare FFS Provider e-news. March 8, 2013. https://www.cms.gov/Outreach-and-Education/Outreach/FFSProvPartProg/Downloads/2013-03-08-standalone.pdf. Accessed January 22, 2024.
19. Robinson JC. Insurers' strategies for managing the use and cost of biopharmaceuticals. *Health Aff (Millwood).* 2006;25(5):1205-1217
20. American Society of Clinical Oncology. Payment reform glossary. ASCO website. https://www.asco.org/sites/new-www.asco.org/files/content-files/blog-release/pdf/Payment-Reform-Glossary.pdf. Accessed January 22, 2024.
21. Magellan Rx Management. Medical Pharmacy Trend Report 2016. http://www.magellanrxinsights.com. Accessed January 22, 2024.
22. US Bureau of Labor Statistics. Definitions of health insurance terms. http://www.bls.gov/ncs/ebs/sp/healthterms.pdf. Accessed October 10, 2019.
23. Academy of Managed Care Pharmacy. Managed care glossary. AMCP website. https://www.amcp.org/about/managed-care-pharmacy-101/managed-care-glossary. Accessed January 22, 2024.

Bristol Myers Squibb®

Access Support®

Looking for support? We're here for you.

Patient access support, reimbursement resources, and financial support options may be available through **BMS Access Support®**

Call a Patient Access Specialist at **1-800-861-0048**, 8 AM to 8 PM ET, Monday - Friday

Visit **www.BMSAccessSupport.com**

Schedule a meeting with a BMS Access and Reimbursement Manager on the BMS Access Support website

BMS Access Support is dedicated to helping patients access their prescribed BMS medications. We provide benefits reviews, prior authorization and appeals support, and reimbursement information to support patient access. Additionally, we offer financial support options and educational resources to support patients throughout their treatment journey.

The accurate completion of reimbursement or coverage-related documentation is the responsibility of the healthcare provider and the patient. Bristol Myers Squibb and its agents make no guarantee regarding reimbursement for any service or item.

Bristol Myers Squibb®

731-US-2400001 02/24