INDICATIONS
EMPLICITI® (elotuzumab) is indicated in combination with lenalidomide and dexamethasone for the treatment of adult patients with multiple myeloma who have received one to three prior therapies.
EMPLICITI is indicated in combination with pomalidomide and dexamethasone for the treatment of adult patients with multiple myeloma who have received at least two prior therapies including lenalidomide and a proteasome inhibitor.

SELECTED IMPORTANT SAFETY INFORMATION

Please see detailed Important Safety Information for EMPLICITI on pages 17-18 and US Full Prescribing Information for EMPLICITI at the end of this document.
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.

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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 best coding practices. 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.

Please see Important Safety Information for EMPLICITI on pages 17-18 and US Full Prescribing Information for EMPLICITI at the end of this document.

For reimbursement assistance, call BMS Access Support at 1-800-861-0048, 8 AM to 8 PM ET, Monday–Friday, or visit www.BMSAccessSupport.com.
MULTIPLE MYELOMA:
ICD-10-CM Codes for EMPLICITI® (elotuzumab)

ICD-10-CM codes are used to identify a patient’s diagnosis and inpatient procedure. 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 indication for EMPLICITI are provided below by Bristol-Myers Squibb and should be verified with the payer. Some health plans 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.

<table>
<thead>
<tr>
<th>ICD-10-CM Codes for EMPLICITI® (elotuzumab)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C90 Multiple myeloma and malignant plasma cell neoplasms</td>
</tr>
<tr>
<td>C90.0 Multiple myeloma</td>
</tr>
<tr>
<td>C90.00 Multiple myeloma not having achieved remission</td>
</tr>
<tr>
<td>C90.02 Multiple myeloma in relapse</td>
</tr>
</tbody>
</table>

**Note:** If infusion is the only reason for the patient encounter, physicians and hospitals may report the code below as the primary diagnosis:

- **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.

Please see Important Safety Information for EMPLICITI on pages 17-18 and US Full Prescribing Information for EMPLICITI at the end of this document.

For reimbursement assistance, call BMS Access Support at 1-800-861-0048, 8 AM to 8 PM ET, Monday–Friday, or visit www.BMSAccessSupport.com.
Healthcare Common Procedure Coding System (HCPCS) and Revenue Codes for EMPLICITI® (elotuzumab)

### Recommended HCPCS Code for EMPLICITI®

<table>
<thead>
<tr>
<th>HCPCS Code</th>
<th>Description</th>
<th>Billing Units</th>
</tr>
</thead>
<tbody>
<tr>
<td>J9176</td>
<td>Injection, elotuzumab, 1 mg</td>
<td>1 mg = 1 billing unit</td>
</tr>
</tbody>
</table>

Use the following claim formats when EMPLICITI 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.

All the coding information presented is applicable to outpatient procedures only. Please see pages 8-9 for more information.

### Revenue Codes⁴ (for Use in the Hospital Outpatient Setting)

<table>
<thead>
<tr>
<th>Revenue Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0636</td>
<td>Drugs requiring detailed coding</td>
</tr>
<tr>
<td>0335</td>
<td>Chemotherapy administration, IV</td>
</tr>
<tr>
<td>0260</td>
<td>IV solutions</td>
</tr>
</tbody>
</table>

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.

Please see Important Safety Information for EMPLICITI on pages 17-18 and US Full Prescribing Information for EMPLICITI at the end of this document.

For reimbursement assistance, call BMS Access Support at 1-800-861-0048, 8 AM to 8 PM ET, Monday–Friday, or visit www.BMSAccessSupport.com.

CPT® codes that may be appropriate when administering EMPLICITI appear in the table below.

<table>
<thead>
<tr>
<th>CPT Code</th>
<th>Description</th>
<th>APC*†</th>
</tr>
</thead>
<tbody>
<tr>
<td>96413</td>
<td>Chemotherapy administration, intravenous infusion technique; up to 1 hour, single or initial substance/drug</td>
<td>5695</td>
</tr>
<tr>
<td>96415</td>
<td>Each additional hour</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• List separately in addition to code for primary procedure</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Use 96415 in conjunction with 96413</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Report 96415 for infusion intervals of greater than 30 minutes beyond 1-hour increments</td>
<td>5692</td>
</tr>
</tbody>
</table>

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

* 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.

† APC=ambulatory payment classification; 5695=Level V Drug Administration; 5692=Level II Drug Administration.6,7

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.

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Please see Important Safety Information for EMPLICITI on pages 17-18 and US Full Prescribing Information for EMPLICITI at the end of this document.

For reimbursement assistance, call BMS Access Support at 1-800-861-0048, 8 AM to 8 PM ET, Monday–Friday, or visit www.BMSAccessSupport.com.
National Drug Code (NDC) Information for EMPLICITI® (elotuzumab)

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

<table>
<thead>
<tr>
<th>NDC Information for EMPLICITI®</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>00003-2291-11</td>
<td>300 mg single-dose vial</td>
</tr>
<tr>
<td>00003-4522-11</td>
<td>400 mg single-dose vial</td>
</tr>
</tbody>
</table>

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.

Please see Important Safety Information for EMPLICITI on pages 17-18 and US Full Prescribing Information for EMPLICITI at the end of this document.

For reimbursement assistance, call BMS Access Support at 1-800-861-0048, 8 AM to 8 PM ET, Monday–Friday, or visit www.BMSAccessSupport.com.
5010 Electronic Transaction Coding for EMPLICITI® (elotuzumab)

- 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.
- This is typically followed by the quantity qualifier, such as UN (units), F2 (international units), GR (gram), or ML (milliliter), and the quantity administered.

<table>
<thead>
<tr>
<th>5010 Transaction Coding for EMPLICITI®</th>
</tr>
</thead>
<tbody>
<tr>
<td>How Supplied</td>
</tr>
<tr>
<td>----------------------------------------</td>
</tr>
<tr>
<td>300 mg (lyophilized powder) single-dose vial</td>
</tr>
<tr>
<td>400 mg (lyophilized powder) single-dose vial</td>
</tr>
</tbody>
</table>

The examples given in the far-right column demonstrate NDC quantity reporting for 1 vial of EMPLICITI. The actual amount of drug used can vary based on factors such as 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.

Please see Important Safety Information for EMPLICITI on pages 17-18 and US Full Prescribing Information for EMPLICITI at the end of this document.

For reimbursement assistance, call BMS Access Support at 1-800-861-0048, 8 AM to 8 PM ET, Monday–Friday, or visit www.BMSAccessSupport.com.
Coding and Billing Units for EMPLICITI® (elotuzumab)

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

Physician Office

**Item 19:** Many payers require detailed information about the drug in Box 19. Typically, payers require the drug name, total dosage and strength, and a concise description of an “unlisted procedure code” or a “Not Otherwise Classified” NDC code.

**Item 21:** Enter the appropriate ICD-10-CM diagnosis codes for the type of multiple myeloma being treated.

**Item 24A:** NDC information is required in the shaded area above the line on which a drug is reported in 24D. The NDC is preceded by the qualifier N4 and followed by the quantity qualifier (UN) and the quantity administered. For example, use “N400003229111UN1” for the 300-milligram (mg) vial or “N400003452211UN1” for the 400-mg vial.

**Item 24D:** Enter the relevant HCPCS (J9176) and CPT codes (96413 for EMPLICITI infusion, and 96415 for each additional hour for infusions longer than 90 minutes). In addition, it is required that you enter J9176-JW on next line to record waste.

**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.

**Item 24G:** Billing units are reported here. 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.

Please see Important Safety Information for EMPLICITI on pages 17-18 and US Full Prescribing Information for EMPLICITI at the end of this document.

For reimbursement assistance, call BMS Access Support at 1-800-861-0048, 8 AM to 8 PM ET, Monday–Friday, or visit www.BMSAccessSupport.com.
Coding and Billing Units for EMPLICITI® (elotuzumab) (cont’d)

Outpatient Hospital

Form Locator (FL) 42: Enter the 4-digit revenue code that best describes the service provided, in accordance with hospital billing policy.10 For chemotherapy administration, revenue codes 0260 (intravenous [IV] therapy) or 0335 (radiology–therapeutic: chemotherapy–IV) could be used.4 The Centers for Medicare & Medicaid Services (CMS) recommends using revenue code 0636 [drugs requiring detailed coding]7

FL 43: Enter the modifier “N4” followed by the 11-digit NDC in positions 01-13.10 Report the quantity qualifier (UN) followed by the quantity administered (300 mg or 400 mg). For example, use “N400003229111UN1” for the 300-mg vial or “N400003452211UN1” for the 400-mg vial.8,10

FL 44: Enter the relevant HCPCS [J9176] and CPT codes (96413 for EMPLICITI infusion, and 96415 for each additional hour for infusions longer than 90 minutes).2,5,10 In addition, it is required that you enter J9176-JW on the next line to record waste.3

FL 46: Billing units are called service units and are placed here.10 1 mg = 1 billing unit

FLs 67A-67Q: Enter the appropriate ICD-10-CM diagnosis codes for the type of multiple myeloma being treated10

FL 80: Some payers require detailed information about the drug in FL 80.10 Typically, payers require the drug name, total dosage and strength, method of administration, 11-digit NDC, and basis of measurement

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.

Please see Important Safety Information for EMPLICITI on pages 17-18 and US Full Prescribing Information for EMPLICITI at the end of this document.

For reimbursement assistance, call BMS Access Support at 1-800-861-0048, 8 AM to 8 PM ET, Monday–Friday, or visit www.BMSAccessSupport.com.
Dosing and Administration for EMPLICITI® (elotuzumab)

EMPLICITI dosing in combination with lenalidomide and dexamethasone

- Patients must be premedicated before each dose of EMPLICITI as described below
- When administered with lenalidomide and dexamethasone, the recommended dosage of EMPLICITI is 10 mg/kg administered intravenously (IV):
  - Once a week for the first 2 cycles (28-day cycles)
  - Once every 2 weeks for cycle 3 onward (28-day cycles)
  - Continue treatment until disease progression or unacceptable toxicity

Pretreatment on days that EMPLICITI is administered

<table>
<thead>
<tr>
<th>3–24 hours prior</th>
<th>45–90 minutes prior</th>
</tr>
</thead>
<tbody>
<tr>
<td>28 mg dexamethasone orally</td>
<td>8 mg IV dexamethasone + H₁ blocker: diphenhydramine (25–50 mg orally or IV) or equivalent + H₂ blocker: ranitidine (50 mg IV or 150 mg orally) or equivalent + Acetaminophen (650–1000 mg orally)</td>
</tr>
</tbody>
</table>

Please see EMPLICITI dosing schedule on the next page.

Please refer to the EMPLICITI, lenalidomide, and dexamethasone Full Prescribing Information for additional information.

Please see Important Safety Information for EMPLICITI on pages 17-18 and US Full Prescribing Information for EMPLICITI at the end of this document.

For reimbursement assistance, call BMS Access Support at 1-800-861-0048, 8 AM to 8 PM ET, Monday–Friday, or visit www.BMSSupport.com.
EMPLICITI® dosing in combination with lenalidomide and dexamethasone®

**EMPLICITI + lenalidomide and dexamethasone dosing schedule**

<table>
<thead>
<tr>
<th>Cycles 1 and 2 (28 days each): EMPLICITI dosed once a week</th>
</tr>
</thead>
<tbody>
<tr>
<td>EMPLICITI 10 mg/kg IV</td>
</tr>
<tr>
<td>Lenalidomide 25 mg PO</td>
</tr>
<tr>
<td>Dexamethasone PO (mg)*</td>
</tr>
<tr>
<td>Dexamethasone intravenously (mg)*</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cycles 3+ (28 days each): EMPLICITI dosed once every 2 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>EMPLICITI 10 mg/kg IV</td>
</tr>
<tr>
<td>Lenalidomide 25 mg PO</td>
</tr>
<tr>
<td>Dexamethasone PO (mg)*</td>
</tr>
<tr>
<td>Dexamethasone intravenously (mg)*</td>
</tr>
</tbody>
</table>

On days that EMPLICITI is not administered, but a dose of dexamethasone is scheduled, dexamethasone 40 mg should be given orally.®

PO=orally.

*Oral dexamethasone (28 mg) taken between 3 and 24 hours before EMPLICITI infusion.

†Dexamethasone intravenously and other premedications are given 45-90 minutes prior to EMPLICITI infusion.

Please see Important Safety Information for EMPLICITI on pages 17-18 and US Full Prescribing Information for EMPLICITI at the end of this document.

For reimbursement assistance, call BMS Access Support at 1-800-861-0048, 8 AM to 8 PM ET, Monday–Friday, or visit www.BMSAccessSupport.com.
**Dosing and Administration for EMPLICITI® (elotuzumab) (cont’d)**

**EMPLICITI dosing in combination with pomalidomide and dexamethasone**

- Patients must be premedicated before each dose of EMPLICITI as described below
- When administered with pomalidomide and dexamethasone, the recommended dosage of EMPLICITI in cycles 1-2 (28-day cycle) is 10 mg/kg administered intravenously (IV) once every week
- Starting at cycle 3 (28-day cycle), 20 mg/kg EMPLICITI is administered intravenously once every 4 weeks
- EMPLICITI is administered in conjunction with the recommended dosing of pomalidomide and low-dose dexamethasone
- Continue treatment until disease progression or unacceptable toxicity

---

### Pretreatment on days that EMPLICITI is administered

<table>
<thead>
<tr>
<th>3-24 hours prior</th>
<th>45-90 minutes prior</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Oral dexamethasone:</strong></td>
<td><strong>8 mg IV dexamethasone</strong></td>
</tr>
<tr>
<td>Patients ≤75 years old: <strong>28 mg</strong></td>
<td>+</td>
</tr>
<tr>
<td>Patients &gt;75 years old: <strong>8 mg</strong></td>
<td>+ <strong>H₃ blocker: diphenhydramine (25-50 mg orally or IV) or equivalent</strong></td>
</tr>
<tr>
<td></td>
<td>+ <strong>H₂ blocker: ranitidine (50 mg IV or 150 mg orally) or equivalent</strong></td>
</tr>
<tr>
<td></td>
<td>+ <strong>Acetaminophen (650-1000 mg orally)</strong></td>
</tr>
</tbody>
</table>

Please see EMPLICITI dosing schedule on the next page.

Please refer to the EMPLICITI, pomalidomide, and dexamethasone Full Prescribing Information for additional information.

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Please see Important Safety Information for EMPLICITI on pages 17-18 and US Full Prescribing Information for EMPLICITI at the end of this document.

For reimbursement assistance, call BMS Access Support at 1-800-861-0048, 8 AM to 8 PM ET, Monday–Friday, or visit [www.BMSAccessSupport.com](http://www.BMSAccessSupport.com).
Dosing and Administration for EMPLICITI® (elotuzumab) (cont’d)

EMPLICITI dosing in combination with pomalidomide and dexamethasone

### EMPLICITI + pomalidomide and dexamethasone dosing schedule

<table>
<thead>
<tr>
<th>Cycle</th>
<th>Days</th>
<th>EMPLICITI (mg/kg)</th>
<th>Pomalidomide (mg)</th>
<th>Dexamethasone PO</th>
<th>Dexamethasone IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>10</td>
<td>4</td>
<td>40</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>2</td>
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<td>3</td>
<td></td>
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<td>4</td>
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<tr>
<td></td>
<td>28</td>
<td></td>
<td></td>
<td>20</td>
<td>-</td>
</tr>
</tbody>
</table>

Cycles 1 and 2 [28 days each]: EMPLICITI dosed once a week

Cycles 3+ [28 days each]: EMPLICITI dosed once every 4 weeks

On days that EMPLICITI is not administered, but a dose of dexamethasone is scheduled, dexamethasone 40 mg should be given orally to patients 75 years or younger and 20 mg orally to patients older than 75 years.1

PO=orally.

*Oral dexamethasone (28 mg) taken between 3 and 24 hours before EMPLICITI infusion.

†Dexamethasone intravenously and other premedications are given 45-90 minutes prior to EMPLICITI infusion.

‡Oral dexamethasone (8 mg) taken between 3 and 24 hours before EMPLICITI infusion.

**Intravenous dexamethasone 45-90 minutes before EMPLICITI infusion.

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Please see Important Safety Information for EMPLICITI on pages 17-18 and US Full Prescribing Information for EMPLICITI at the end of this document.

For reimbursement assistance, call BMS Access Support at 1-800-861-0048, 8 AM to 8 PM ET, Monday–Friday, or visit www.BMSAccessSupport.com.
Determining Your Order

Because dosing for EMPLICITI is weight-based, the dose of EMPLICITI will vary by patient, and may be provided through a combination of vial sizes.*

**Step 1:** Calculate total dose in mg needed (weight in kg x 10 = total dose in mg)

**Step 2:** Determine quantity of single-dose vials needed based on total dose (see table below)†

A person weighing **60 kg** would require a total dosage of **600 mg of EMPLICITI** (two 300-mg vials)

A person weighing **91 kg** would require a total dosage of **910 mg of EMPLICITI** (two 300-mg vials and one 400-mg vial)

A person weighing **123 kg** would require a total dosage of **1230 mg of EMPLICITI** (three 300-mg vials and one 400-mg vial)

---

*EMPLICITI is supplied in 300-mg or 400-mg single-dose vials. *
†The calculations in the examples above are all based on 10 mg/kg doses. In dosing regimen with pomalidomide and dexamethasone, dosing for EMPLICITI is 20 mg/kg starting with cycle 3.

Please see Important Safety Information for **EMPLICITI** on pages 17-18 and US Full Prescribing Information for **EMPLICITI** at the end of this document.

For reimbursement assistance, call BMS Access Support at 1-800-861-0048, 8 AM to 8 PM ET, Monday–Friday, or visit www.BMSAccessSupport.com.
Medicare Drug Reimbursement for EMPLICITI® (elotuzumab)

What is the Medicare reimbursement allowable for EMPLICITI?

Physicians*

- The payment limit is 106% of average sales price (ASP), not including sequestration, and represents one billing unit of EMPLICITI, which is billed for each 1 mg.†
- The amount paid to physicians for EMPLICITI HCPCS code J9176 is published at the beginning of each calendar quarter in “Payment Allowance Limits for Medicare Part B Drugs,” which can be downloaded at https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Part-B-Drugs/McrPartBDrugAvqSalesPrice/2018ASPFiles.html
- Medicare Part B will pay physicians 80% of the allowed price for EMPLICITI HCPCS code J9176; the patient is responsible for 20% co-insurance, which may be covered by secondary insurance (private supplemental coverage, Medicaid, etc).‡

Hospital outpatient facilities*

Drugs paid for 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 EMPLICITI HCPCS code J9176.

- The Payment Allowance Limits are published each quarter at https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Part-B-Drugs/McrPartBDrugAvqSalesPrice/2018ASPFiles.html

Hospital inpatient settings

- Reimbursement in the inpatient setting is bundled into the Medicare Diagnosis Related Groups called MS-DRGs.
- These prospective payment rates are updated annually.

*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%.†

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

Please see Important Safety Information for EMPLICITI on pages 17-18 and US Full Prescribing Information for EMPLICITI at the end of this document.

For reimbursement assistance, call BMS Access Support at 1-800-861-0048, 8 AM to 8 PM ET, Monday–Friday, or visit www.BMSAccessSupport.com.
Commercial Insurance Reimbursement for EMPLICITI® (elotuzumab)

Physicians
- Drug reimbursement, like service reimbursement, is usually based on a fee schedule\textsuperscript{18}
- The fee schedules are based on the ASP or AWP, as published by a credible source,\textsuperscript{19,20} or an average costing methodology as determined by the payer, such as usual, customary, and reasonable (UC&R)\textsuperscript{19-21}

Hospital outpatient facilities\textsuperscript{20}
- In this setting, reimbursement is most commonly based on percentage of charges
- Alternatively, some hospitals use the same ASP or AWP methodologies typically used by physician offices
- Other methodologies include capitated model, cost minus submitted charges, or discount off submitted charges

Hospital inpatient settings
- Inpatient rates are prospective, meaning they are predetermined per discharge\textsuperscript{14}
- There are private payers that pay on a version of the DRGs\textsuperscript{15}
- There are also payers that pay on a negotiated and fixed rate per day called a “per diem”; there are capitated rates for inpatients as well\textsuperscript{19}
- New drugs may be carved out of per diems or capitated rates, if the hospital negotiates to do so\textsuperscript{22}

Please see Important Safety Information for EMPLICITI on pages 17-18 and US Full Prescribing Information for EMPLICITI at the end of this document.

For reimbursement assistance, call BMS Access Support at 1-800-861-0048, 8 AM to 8 PM ET, Monday–Friday, or visit www.BMSAccessSupport.com.
Infusion Reactions

- Infusion reactions were reported in 10% of patients treated with EMPLICITI in the ELOQUENT-2 trial [EMPLICITI + lenalidomide + dexamethasone (ERd) vs lenalidomide + dexamethasone (Rd)] and 3.3% in the ELOQUENT-3 trial [EMPLICITI + pomalidomide + dexamethasone (EPd) vs pomalidomide + dexamethasone (Pd)].

- In the ELOQUENT-2 trial, all infusion reactions were Grade 3 or lower, with Grade 3 infusion reactions occurring in 1% of patients. The most common symptoms included fever, chills, and hypertension. Bradycardia and hypotension also developed during infusions. In the trial, 5% of patients required interruption of the administration of EMPLICITI for a median of 25 minutes due to infusion reactions, and 1% of patients discontinued due to infusion reactions. Of the patients who experienced an infusion reaction, 70% (23/33) had them during the first dose.

- In the ELOQUENT-3 trial, the only infusion reaction symptom was chest discomfort (2%), which was Grade 1. All the patients who experienced an infusion reaction had them during the first treatment cycle.

- If a Grade 2 or higher infusion reaction occurs, interrupt the EMPLICITI infusion and institute appropriate medical and supportive measures. If the infusion reaction recurs, stop the EMPLICITI infusion and do not restart it on that day. Severe infusion reactions may require permanent discontinuation of EMPLICITI therapy and emergency treatment.

- Premedicate with dexamethasone, H1 blocker, H2 blocker, and acetaminophen prior to EMPLICITI infusion.

Infections

- In the ELOQUENT-2 trial (N=635), infections were reported in 81% of patients in the ERd arm and 74% in the Rd arm. Grade 3-4 infections were 28% (ERd) and 24% (Rd). Discontinuations due to infections were 3.5% (ERd) and 4.1% (Rd). Fatal infections were 2.5% (ERd) and 2.2% (Rd). Opportunistic infections were reported in 22% (ERd) and 13% (Rd). Fungal infections were 10% (ERd) and 5% (Rd). Herpes zoster was 14% (ERd) and 7% (Rd).

- In the ELOQUENT-3 trial (N=115), infections were reported in 65% of patients in both the EPd arm and the Pd arm. Grade 3-4 infections were reported in 13% (EPd) and 22% (Pd). Discontinuations due to infections were 7% (EPd) and 5% (Pd). Fatal infections were 5% (EPd) and 3.6% (Pd). Opportunistic infections were reported in 10% (EPd) and 9% (Pd). Herpes zoster was reported in 5% (EPd) and 1.8% (Pd).

- Monitor patients for development of infections and treat promptly.

Second Primary Malignancies

- In the ELOQUENT-2 trial (N=635), invasive second primary malignancies (SPM) were 9% (ERd) and 6% (Rd). The rate of hematologic malignancies was the same between ERd and Rd treatment arms (1.6%). Solid tumors were reported in 3.5% (ERd) and 2.2% (Rd). Skin cancer was reported in 4.4% (ERd) and 2.8% (Rd).

- In the ELOQUENT-3 trial (N=115), invasive SPMs were 0% (EPd) and 1.8% (Pd).

- Monitor patients for the development of SPMs.

Hepatotoxicity

- In the ELOQUENT-2 trial (N=635), AST/ALT >3X the upper limit, total bilirubin >2X the upper limit, and alkaline phosphatase <2X the upper limit were 2.5% (ERd) vs 0.6% (Rd). Of 8 patients experiencing hepatotoxicity, 2 patients discontinued treatment while 6 patients had resolution and continued. Monitor liver enzymes periodically. Stop EMPLICITI upon ≥ Grade 3 elevation of liver enzymes. Continuation of treatment may be considered after return to baseline values.

Interference with Determination of Complete Response

- EMPLICITI is a humanized IgG kappa monoclonal antibody that can be detected on both the serum protein electrophoresis and immunofixation assays used for the clinical monitoring of endogenous M-protein. This interference can impact the determination of complete response and possibly relapse from complete response in patients with IgG kappa myeloma protein.

Please see US Full Prescribing Information for EMPLICITI® at the end of this document.

For reimbursement assistance, call BMS Access Support at 1-800-861-0048, 8 AM to 8 PM ET, Monday–Friday, or visit www.BMSAccessSupport.com.
Pregnancy/Females and Males of Reproductive Potential

- There are no available data on EMPLICITI use in pregnant women to inform a drug-associated risk of major birth defects and miscarriage.
- There is a risk of fetal harm, including severe life-threatening human birth defects, associated with lenalidomide and pomalidomide, and they are contraindicated for use in pregnancy. Refer to the respective product full prescribing information for requirements regarding contraception and the prohibitions against blood and/or sperm donation due to presence and transmission in blood and/or semen and for additional information.

Adverse Reactions

- **ELOQUENT-2 trial:**
  - Serious adverse reactions were 65% (ERd) and 57% (Rd).
  - The most frequent serious adverse reactions in the ERd arm compared to the Rd arm were: pneumonia (15%, 11%), pyrexia (7%, 5%), respiratory tract infection (3.1%, 1.3%), anemia (2.8%, 1.9%), pulmonary embolism (3.1%, 2.5%), and acute renal failure (2.5%, 1.9%).
  - The most common adverse reactions in ERd and Rd, respectively (≥20%) were fatigue (62%, 52%), diarrhea (47%, 36%), pyrexia (37%, 25%), constipation (36%, 27%), cough (34%, 19%), peripheral neuropathy (27%, 21%), nasopharyngitis (25%, 19%), upper respiratory tract infection (23%, 17%), decreased appetite (21%, 13%), and pneumonia (20%, 14%).

- **ELOQUENT-3 trial:**
  - Serious adverse reactions were 22% (EPd) and 15% (Pd).
  - The most frequent serious adverse reactions in the EPd arm compared to the Pd arm were: pneumonia (13%, 11%) and respiratory tract infection (7%, 3.6%).
  - The most common adverse reactions in EPd arm (≥20% EPd) and Pd, respectively, were constipation (22%, 11%) and hyperglycemia (20%, 15%).

Please see US Full Prescribing Information for EMPLICITI (elotuzumab) at the end of this document.

For reimbursement assistance, call BMS Access Support at 1-800-861-0048, 8 AM to 8 PM ET, Monday–Friday, or visit www.BMSAccessSupport.com.
References


Please see US Full Prescribing Information for EMPLICITI at the end of this document.

For reimbursement assistance, call BMS Access Support at 1-800-861-0048, 8 AM to 8 PM ET, Monday–Friday, or visit www.BMSAccessSupport.com.
Three Simple Ways to Get Support

Contact your Access & Reimbursement Manager for general assistance and to schedule an office visit.

Call Bristol-Myers Squibb Access Support® at 1-800-861-0048 8 AM to 8 PM ET, Monday-Friday to speak with a regionally assigned specialist.

Visit www.BMSAccessSupport.com for information and resources, including the BMS Access Support program enrollment form, to help your patients with access to Bristol-Myers Squibb oncology products.

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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.
The recommended dosage of EMPLICITI is 10 mg/kg administered intravenously every week for the first two cycles (28-day cycle) and every 2 weeks thereafter until disease progression or unacceptable toxicity.

Initial U.S. Approval: 2015

**RECENT MAJOR CHANGES**

Indications and Usage (1) 11/2018
Dosage and Administration (2.1, 2.2, 2.5) 11/2018
Warnings and Precautions (5.1, 5.2, 5.3, 5.4) 11/2018

**INDICATIONS AND USAGE**

EMPLICITI® (elotuzumab) for injection, for intravenous use

EMPLICITI is indicated in combination with pomalidomide and dexamethasone for the treatment of adult patients with multiple myeloma who have received at least two prior therapies including lenalidomide and a proteasome inhibitor. (1)

**DOSAGE AND ADMINISTRATION**

- With lenalidomide and dexamethasone: 10 mg/kg administered intravenously every week for the first two cycles and every 2 weeks thereafter until disease progression or unacceptable toxicity. (2.1)
- With pomalidomide and dexamethasone: 10 mg/kg administered intravenously every week for the first two cycles and 20 mg/kg every 4 weeks thereafter until disease progression or unacceptable toxicity. (2.2)
- Premedicate with dexamethasone, diphenhydramine, ranitidine and acetaminophen. (2.3)

**DOSE FORMS AND STRENGTHS**

For Injection: 300 mg or 400 mg lyophilized powder in a single-dose vial for reconstitution. (3)

**FULL PRESCRIBING INFORMATION: CONTENTS**

1 INDICATIONS AND USAGE
2 DOSAGE AND ADMINISTRATION
2.1 Recommended Dosing when EMPLICITI Is Used in Combination with Lenalidomide and Dexamethasone
2.2 Recommended Dosing when EMPLICITI Is Used in Combination with Pomalidomide and Dexamethasone
2.3 Premedication
2.4 Dose Modifications
2.5 Administration
2.6 Reconstitution and Preparation
3 DOSAGE FORMS AND STRENGTHS
4 CONTRAINDICATIONS
5 WARNINGS AND PRECAUTIONS
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16 HOW SUPPLIED/STORAGE AND HANDLING
17 PATIENT COUNSELING INFORMATION

*Sections or subsections omitted from the full prescribing information are not listed.

Refer to the dexamethasone and lenalidomide prescribing information for additional information.

Administer premedications before each dose of EMPLICITI [see Dosage and Administration (2.3) and Warnings and Precautions (5.1)].

Administer dexamethasone as follows:

- On days that EMPLICITI is administered, give dexamethasone 28 mg orally between 3 and 24 hours before EMPLICITI plus 8 mg intravenously between 45 and 90 minutes before EMPLICITI.
- On days that EMPLICITI is not administered but a dose of dexamethasone is scheduled (Days 8 and 22 of cycle 3 and all subsequent cycles), give 40 mg orally.

The recommended dosing is presented in Table 1.
### Table 1: Recommended Dosing Schedule of EMPLICITI in Combination with Lenalidomide and Dexamethasone

<table>
<thead>
<tr>
<th>Cycle</th>
<th>28-Day Cycles 1 and 2</th>
<th>28-Day Cycles 3+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day of Cycle</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>8</td>
</tr>
<tr>
<td>Premedication*</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>EMPLICITI (mg/kg) intravenously</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Lenalidomide (25 mg) orally</td>
<td>Days 1-21</td>
<td>Days 1-21</td>
</tr>
<tr>
<td>Dexamethasone† (mg) orally</td>
<td>28</td>
<td>28</td>
</tr>
<tr>
<td>Dexamethasone†† (mg) intravenously</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>Day of Cycle</td>
<td>1</td>
<td>8</td>
</tr>
</tbody>
</table>

* Premedicate with the following 45 to 90 minutes prior to EMPLICITI infusion: 8 mg intravenous dexamethasone, H1 blocker: diphenhydramine (25 to 50 mg orally or intravenously) or equivalent, H2 blocker: ranitidine (50 mg intravenously) or equivalent, acetaminophen (650 to 1000 mg orally).
† Oral dexamethasone (28 mg) taken between 3 and 24 hours before EMPLICITI infusion.
†† Intravenous dexamethasone 45-90 minutes before EMPLICITI infusion.

### 2.2 Recommended Dosing when EMPLICITI Is Used in Combination with Pomalidomide and Dexamethasone

The recommended dosage of EMPLICITI is 10 mg/kg administered intravenously every week for the first two cycles (28-day cycle). Starting at cycle 3 (28-day cycle), administer EMPLICITI 20 mg/kg intravenously every 4 weeks. Administer EMPLICITI in conjunction with pomalidomide and low-dose dexamethasone as described below (Table 2). Continue treatment until disease progression or unacceptable toxicity.

Refer to the dexamethasone and pomalidomide prescribing information for additional information.

Administer premedications before each dose of EMPLICITI [see Dosage and Administration (2.3) and Warnings and Precautions (5.1)].

Administer dexamethasone as follows:

- On days that EMPLICITI is administered, for patients 75 years or younger give dexamethasone 28 mg orally between 3 and 24 hours before EMPLICITI and for patients older than 75 years give dexamethasone 8 mg orally between 3 and 24 hours before EMPLICITI plus 8 mg intravenously between 45 and 90 minutes before EMPLICITI for patients older than 75 years.
- On days that EMPLICITI is not administered but a dose of dexamethasone is scheduled (Days 8, 15 and 22 of cycle 3 and all subsequent cycles), give 40 mg orally to patients 75 years or younger and 20 mg orally to patients older than 75 years.

The recommended dosing is presented in Table 2.

### Table 2: Recommended Dosing Schedule of EMPLICITI in Combination with Pomalidomide and Dexamethasone

<table>
<thead>
<tr>
<th>Cycle</th>
<th>28-Day Cycles 1 and 2</th>
<th>28-Day Cycles 3+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day of Cycle</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>8</td>
</tr>
<tr>
<td>Premedication*</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>EMPLICITI (mg/kg) intravenously</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Pomalidomide (4 mg) orally</td>
<td>Days 1-21</td>
<td>Days 1-21</td>
</tr>
<tr>
<td>Dexamethasone† (mg) orally &lt;75 years old</td>
<td>28</td>
<td>28</td>
</tr>
<tr>
<td>Dexamethasone† (mg) orally &gt;75 years old</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>Dexamethasone†† (mg) intravenously</td>
<td>8</td>
<td>8</td>
</tr>
</tbody>
</table>

* Premedicate with the following 45 to 90 minutes prior to EMPLICITI infusion: 8 mg intravenous dexamethasone, H1 blocker: diphenhydramine (25 to 50 mg orally or intravenously) or equivalent, H2 blocker: ranitidine (50 mg intravenously) or equivalent, acetaminophen (650 to 1000 mg orally).
† Oral dexamethasone taken between 3 and 24 hours before EMPLICITI infusion.
†† Intravenous dexamethasone 45-90 minutes before EMPLICITI infusion.

### 2.3 Premedication

**Dexamethasone**

When EMPLICITI is used in combination with lenalidomide or pomalidomide and dexamethasone, divide dexamethasone into an oral and intravenous dose and administer as shown in Table 1 and Table 2 [see Dosage and Administration (2.1, 2.2)].

### Other Medications

In addition to dexamethasone, complete administration of the following medications 45 to 90 minutes prior to EMPLICITI infusion:

- H1 blocker: diphenhydramine (25 to 50 mg orally or intravenously) or equivalent H1 blocker.
- H2 blocker: ranitidine (50 mg intravenously or 150 mg orally) or equivalent H2 blocker.
- Acetaminophen (650 to 1000 mg orally).

### 2.4 Dose Modifications

If the dose of one drug in the regimen is delayed, interrupted, or discontinued, the treatment with the other drugs may continue as scheduled. However, if dexamethasone is delayed or discontinued, base the decision whether to administer EMPLICITI on clinical judgment (i.e., risk of hypersensitivity).

If a Grade 2 or higher infusion reaction occurs during EMPLICITI administration, interrupt the infusion and institute appropriate medical and supportive measures. Upon resolution to Grade 1 or lower, restart EMPLICITI at 0.5 mL per minute and gradually increase at a rate of 0.5 mL per minute every 30 minutes as tolerated to the rate at which the infusion reaction occurred. Resume the escalation regimen if there is no recurrence of the infusion reaction (see Table 3 and Table 4).

In patients who experience an infusion reaction, monitor vital signs every 30 minutes for 2 hours after the end of the EMPLICITI infusion. If the infusion reaction recurs, stop the EMPLICITI infusion and do not restart on that day [see Warnings and Precautions (5.1)].

Severe infusion reactions may require permanent discontinuation of EMPLICITI therapy and emergency treatment.

Dose delays and modifications for dexamethasone, pomalidomide and lenalidomide should be performed as recommended in their Prescribing Information.

### 2.5 Administration

Administer the entire EMPLICITI infusion with an infusion set and a sterile, nonpyrogenic, low-protein-binding filter (with a pore size of 0.2 to 1.2 micrometer) using an automated infusion pump.

Initiate EMPLICITI infusion at a rate of 0.5 mL per minute for 10 mg/kg dose. The infusion rate may be increased in a stepwise fashion as described in Table 3 if no infusion reactions develop. The maximum infusion rate should not exceed 5 mL per minute.

**Table 3: Infusion Rate for EMPLICITI 10 mg/kg**

<table>
<thead>
<tr>
<th>Cycle 1, Dose 1</th>
<th>Cycle 1, Dose 2</th>
<th>Cycle 1, Dose 3 and 4 and All Subsequent Cycles</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time Interval</td>
<td>Rate</td>
<td>Time Interval</td>
</tr>
<tr>
<td>0-30 min</td>
<td>0.5 mL/min</td>
<td>0-30 min</td>
</tr>
<tr>
<td>60 min or more</td>
<td>2 mL/min</td>
<td>-</td>
</tr>
</tbody>
</table>

Initiate EMPLICITI infusion rate at 3 mL per minute for 20 mg/kg dose. The infusion rate may be increased in a stepwise fashion as described in Table 4 if no infusion reactions develop. The maximum infusion rate should not exceed 5 mL per minute.

Patients who have escalated to 5 mL/min at 10 mg/kg dose must decrease the rate to 3 mL/min at the first infusion at 20 mg/kg.

**Table 4: Infusion Rate for EMPLICITI 20 mg/kg**

<table>
<thead>
<tr>
<th>Dose 1</th>
<th>Dose 2 and all subsequent doses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time Interval</td>
<td>Rate</td>
</tr>
<tr>
<td>0-30 min</td>
<td>3 mL/min</td>
</tr>
<tr>
<td>30 min or more</td>
<td>4 mL/min</td>
</tr>
</tbody>
</table>

Adjust the infusion rate following a Grade 2 or higher infusion reaction [see Dosage and Administration (2.4)].

Do not mix EMPLICITI with, or administer as an infusion with, other medicinal products. No physical or biochemical compatibility studies have been conducted to evaluate the coadministration of EMPLICITI with other agents.
In the ELOQUEST-3 trial, the only infusion reaction symptom was chest discomfort (2%), which was Grade 1. All patients in the ELOQUEST-3 trial who experienced an infusion reaction had them during the first treatment cycle.

Administer premedication consisting of dexamethasone, antihistamines (H1 and H2 blockers) and acetylsalicylic acid prior to EMPLICITI infusion [see Dosage and Administration (2.3)].

Interrupt EMPLICITI infusion for Grade 2 or higher infusion reactions and institute appropriate medical management [see Dosage and Administration (2.4)].

### 5.2 Infections

In the ELOQUEST-2 trial (N=635), infections were reported in 81% of patients in EMPLICITI combined with lenalidomide and dexamethasone (E-Ld) arm and 74% in lenalidomide and dexamethasone (Ld). In the ELOQUEST-3 trial (N=115), infections were reported in 65% of patients in both EMPLICITI combined with pomalidomide and dexamethasone (E-Pd) arm and in pomalidomide and dexamethasone (Pd) arm. In the ELOQUEST-2 trial, Grade 3 to 4 infections were noted in 23% and 24% of E-Ld- and Ld-treated patients and in the ELOQUEST-3 trial, 13% and 22% of E-Pd- and Pd-treated patients, respectively. Discontinuations due to infections occurred in 3.5% of E-Ld-treated and 4.1% of Ld-treated patients in the ELOQUEST-2 trial and 7% of E-Pd-treated and 5% of Pd-treated patients in the ELOQUEST-3 trial. Fatal infections were reported in 2.5% and 2.2% of E-Ld- and Ld-treated patients in the ELOQUEST-2 trial and 5% and 3.6% of E-Pd- and Pd-treated patients in the ELOQUEST-3 trial.

Opportunistic infections were reported in 22% of patients in the E-Ld arm and 13% of patients in the Ld arm in the ELOQUEST-2 trial and 10% of patients in the E-Pd arm and 9% of patients in the Pd arm in the ELOQUEST-3 trial. In the ELOQUEST-2 trial, fungal infections occurred in 10% of patients in the E-Ld arm and 5% of patients in the Ld arm. Herpes zoster was reported in 14% of patients treated with E-Ld and 7% of patients treated with Ld in the ELOQUEST-2 trial and 5% of patients treated with E-Pd and 1.8% of patients treated with Pd in the ELOQUEST-3 trial. Monitor patients for development of infections and treat promptly.

### 5.3 Second Primary Malignancies

In the ELOQUEST-2 trial (N=635), invasive second primary malignancies (SPM) have been observed in 9% of patients treated with E-Ld and 6% of patients treated with Ld and in the ELOQUEST-3 trial (N=115) in 1.8% of patients treated with Pd and in none of the patients treated with E-Pd. In the ELOQUEST-2 trial, the rate of hematologic malignancies was the same between E-Ld and Ld treatment arms (1.6%). Solid tumors were reported in 3.5% and 2.2% of E-Ld- and Ld-treated patients, respectively. Skin cancer was reported in 4.4% and 2.8% of patients treated with E-Ld and Ld, respectively. Monitor patients for the development of second primary malignancies.

### 5.4 Hepatotoxicity

In the ELOQUEST-2 trial (N=635), elevations in liver enzymes [aspartate transaminase (AST)/alanine transaminase (ALT)] greater than 3 times the upper limit, total bilirubin greater than 2 times the upper limit, and alkaline phosphatase less than 2 times the upper limit] were consistent with hepatotoxicity were reported in 2.5% and 0.6% of E-Ld- and Ld-treated patients. Two patients experiencing hepatotoxicity were not able to continue treatment; however, 6 out of 8 patients had resolution and were able to continue treatment. Monitor liver enzymes periodically. Stop EMPLICITI upon Grade 3 or higher elevation of liver enzymes. After return to baseline values, continuation of treatment may be considered.

### 5.5 Interference with Determination of Complete Response

EMPLICITI is a humanized IgG kappa monoclonal antibody that can be detected on both the serum protein electrophoresis (SPEP) and immunofixation (IFE) assays used for the clinical monitoring of endogenous M-protein [see Drug Interactions (7.2)]. This interference can impact the determination of complete response and possibly relapse from complete response in patients with IgG kappa myeloma protein.

### 6 ADVERSE REACTIONS

The following clinically significant adverse reactions are described in detail in other sections of the label:

- Infusion reaction [see Warnings and Precautions (5.1)].
- Infections [see Warnings and Precautions (5.2)].
- Second Primary Malignancies [see Warnings and Precautions (5.3)].
- Hepatotoxicity [see Warnings and Precautions (5.4)].
- Interference with determination of complete response [see Warnings and Precautions (5.5)].

### 6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

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**Table 5: Reconstitution Instructions for EMPLICITI**

<table>
<thead>
<tr>
<th>Strength</th>
<th>Amount of Sterile Water for Injection, USP Required for Reconstitution</th>
<th>Deliverable Volume of Reconstituted EMPLICITI in the Vial</th>
<th>Postreconstitution Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>300 mg vial</td>
<td>13 mL</td>
<td>12 mL*</td>
<td>25 mg/mL</td>
</tr>
<tr>
<td>400 mg vial</td>
<td>17 mL</td>
<td>16 mL*</td>
<td>25 mg/mL</td>
</tr>
</tbody>
</table>

* After reconstitution, each vial contains overfill to allow for withdrawal of 12 mL (300 mg) and 16 mL (400 mg), respectively.

Reconstitution:

- Aseptically reconstitute each EMPLICITI vial with a syringe of adequate size and a less than or equal to 18-gauge needle (e.g., 17-gauge). A slight back pressure may be experienced during administration of the Sterile Water for Injection, USP, which is considered normal.
- Hold the vial upright and swirl the solution by rotating the vial to dissolve the lyophilized cake. Invert the vial a few times in order to dissolve any powder that may be present on top of the vial or the stopper. Avoid vigorous agitation. DO NOT SHAKE. The lyophilized powder should dissolve in less than 10 minutes.
- After the remaining solids are completely dissolved, allow the reconstituted solution to stand for 5 to 10 minutes. The reconstituted preparation results in a colorless to slightly yellow, clear to slightly opalescent solution. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Discard the solution if any particulate matter or discoloration is observed.

Dilution:

- Once the reconstitution is completed, withdraw the necessary volume for the calculated dose from each vial, up to a maximum of 16 mL from 400 mg vial and 12 mL from 300 mg vial.
- Further dilute with either 0.9% Sodium Chloride Injection, USP or 5% Dextrose Injection, USP into an infusion bag made of polyvinyl chloride or polyolefin. The final infusion concentration should range between 1 mg/mL and 6 mg/mL.
- The volume of 0.9% Sodium Chloride Injection, USP or 5% Dextrose Injection, USP should be adjusted so as not to exceed 5 mL/kg of patient weight at any given dose of EMPLICITI.

Complete the EMPLICITI infusion within 24 hours of reconstitution of the EMPLICITI lyophilized powder. If not used immediately, the infusion solution may be stored under refrigeration conditions: 2°C to 8°C (36°F-46°F) and protected from light for up to 24 hours (a maximum of 8 hours of the total 24 hours can be at room temperature, 20°C to 25°C [68°F-77°F], and room light).

**3 DOSAGE FORMS AND STRENGTHS**

For injection: 300 mg or 400 mg of elotuzumab as a white to off-white lyophilized powder in a single-dose vial for reconstitution.

**4 CONTRAINDICATIONS**

None.

**5 WARNINGS AND PRECAUTIONS**

### 5.1 Infusion Reactions

EMPLICITI can cause infusion reactions. Infusion reactions were reported in 10% of patients treated with EMPLICITI in the ELOQUEST-2 trial and 3.3% in the ELOQUEST-3 trial. In the ELOQUEST-2 trial, all reports of infusion reaction were Grade 3 or lower. In the ELOQUEST-2 trial, Grade 3 infusion reactions occurred in 1% of patients. The most common symptoms of an infusion reaction included fever, chills, and hypertension. Bradycardia and hypotension also developed during infusions.

In the ELOQUEST-2 trial, 5% of patients required interruption of the administration of EMPLICITI for a median of 25 minutes due to infusion reactions, and 1% of patients discontinued due to infusion reactions. Of the patients who experienced an infusion reaction, 70% (23/33) had them during the first dose.
**EMPLICITI** (elotuzumab)

**EMPLICITI in Combination with Lenalidomide and Dexamethasone [ELOQUENT-2]**

The safety data described in this section are based on the ELOQUENT-2 study, a randomized, open-label clinical trial in patients with previously treated multiple myeloma. In ELOQUENT-2, EMPLICITI 10 mg/kg was administered with lenalidomide and dexamethasone [see Clinical Studies (14)]. For adverse reaction evaluation, EMPLICITI combined with lenalidomide and dexamethasone was compared with lenalidomide and dexamethasone alone.

The mean age of the population was 66 years and 57% of patients were 65 years of age or older. Sixty percent (60%) of the population were male, 84% were white, 10% were Asian, and 4% were black. The Eastern Cooperative Oncology Group (ECOG) performance status was 0 in 47%, 1 in 44%, and 2 in 9% of patients. These data reflect exposure of 318 patients to EMPLICITI and 317 to control with a median number of cycles of 19 for EMPLICITI and 14 for control.

Serious adverse reactions were reported in 65% of patients treated on the EMPLICITI arm and 57% for patients treated on the control arm. The most frequent serious adverse reactions in the EMPLICITI arm compared to the control arm were: pneumonia (15% vs. 11%), pyrexia (7% vs. 5%), respiratory tract infection (3.1% vs. 1.3%), anemia (2.9% vs. 1.9%), pulmonary embolism (3.1% vs. 2.5%), and acute renal failure (2.5% vs. 1.9%).

The proportion of patients who discontinued any component of the treatment regimen due to adverse reactions as listed below was similar for both treatment arms: 6.0% for patients treated on the EMPLICITI arm and 6.3% for patients treated on the control.

Adverse reactions occurring at a frequency of 10% or higher in the EMPLICITI arm and 5% or higher than the lenalidomide and dexamethasone arm for the randomized trial in multiple myeloma are presented in Table 6.

### Table 6: ELOQUENT-2: Adverse Reactions with a 10% or Higher Incidence for EMPLICITI-Treated Patients and a 5% or Higher Incidence than Lenalidomide and Dexamethasone-Treated Patients [All Grades]

<table>
<thead>
<tr>
<th>Primary Term</th>
<th>EMPLICITI + Lenalidomide and Dexamethasone N=318</th>
<th>Lenalidomide and Dexamethasone N=317</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All Grades</td>
<td>Grade 3/4</td>
</tr>
<tr>
<td>Fatigue*</td>
<td>62</td>
<td>13</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>47</td>
<td>5.0</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>37</td>
<td>2.5</td>
</tr>
<tr>
<td>Constipation</td>
<td>36</td>
<td>1.3</td>
</tr>
<tr>
<td>Cough†</td>
<td>34</td>
<td>0.3</td>
</tr>
<tr>
<td>Peripheral Neuropathy‡</td>
<td>27</td>
<td>3.8</td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>25</td>
<td>0</td>
</tr>
<tr>
<td>Upper Respiratory Tract Infection</td>
<td>23</td>
<td>0.6</td>
</tr>
<tr>
<td>Decreased Appetite</td>
<td>21</td>
<td>1.6</td>
</tr>
<tr>
<td>Pneumonia§</td>
<td>20</td>
<td>14</td>
</tr>
<tr>
<td>Pain in Extremities</td>
<td>16</td>
<td>0.9</td>
</tr>
<tr>
<td>Headache</td>
<td>15</td>
<td>0.3</td>
</tr>
<tr>
<td>Vomiting</td>
<td>14</td>
<td>0.3</td>
</tr>
<tr>
<td>Weight Decreased</td>
<td>14</td>
<td>1.3</td>
</tr>
<tr>
<td>Lymphopenia</td>
<td>13</td>
<td>9</td>
</tr>
<tr>
<td>Cataracts</td>
<td>12</td>
<td>6</td>
</tr>
<tr>
<td>Oropharyngeal Pain</td>
<td>10</td>
<td>0.0</td>
</tr>
</tbody>
</table>

* The term fatigue is a grouping of the following terms: fatigue and asthenia.
† The term cough is a grouping of the following terms: cough, productive cough, and upper airway cough.
‡ The term peripheral neuropathy is a grouping of the following terms: peripheral neuropathy, axonal neuropathy, peripheral motor neuropathy, peripheral sensory neuropathy, and polyneuropathy.
§ The term pneumonia is a grouping of the following terms: pneumonia, atypical pneumonia, bronchopneumonia, lobar pneumonia, bacterial pneumonia, fungal pneumonia, pneumonia influenza, and pneumococcal pneumonia.

Laboratory abnormalities worsening from baseline and occurring at a frequency of 10% or higher in the EMPLICITI group and 5% or higher than the lenalidomide and dexamethasone group (criteria met for all Grades or Grade 3/4) for ELOQUENT-2 are presented in Table 7.

### Table 7: ELOQUENT-2: Laboratory Abnormalities Worsening from Baseline and with a 10% or Higher Incidence for EMPLICITI-Treated Patients and a 5% Higher Incidence than Lenalidomide and Dexamethasone-Treated Patients [Criteria met for All Grades or Grade 3/4]

<table>
<thead>
<tr>
<th>Laboratory Parameter</th>
<th>EMPLICITI + Lenalidomide and Dexamethasone N=318</th>
<th>Lenalidomide and Dexamethasone N=317</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hgb</td>
<td>99</td>
<td>77</td>
</tr>
<tr>
<td>Lymphocytosis</td>
<td>91</td>
<td>32</td>
</tr>
<tr>
<td>Platelet</td>
<td>84</td>
<td>19</td>
</tr>
<tr>
<td>NEUTROPHILS</td>
<td>200</td>
<td>14</td>
</tr>
<tr>
<td>ESR</td>
<td>73</td>
<td>3.9</td>
</tr>
<tr>
<td>Platelet</td>
<td>91</td>
<td>32</td>
</tr>
<tr>
<td>Osmolality</td>
<td>39</td>
<td>1.3</td>
</tr>
</tbody>
</table>

Chemistry

<table>
<thead>
<tr>
<th></th>
<th>EMPLICITI + Lenalidomide and Dexamethasone N=318</th>
<th>Lenalidomide and Dexamethasone N=317</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypoglycemia</td>
<td>89</td>
<td>17</td>
</tr>
<tr>
<td>Hypocalcemia</td>
<td>78</td>
<td>11</td>
</tr>
<tr>
<td>Low Bicarbonite</td>
<td>63</td>
<td>0.4</td>
</tr>
<tr>
<td>Hyperkalemia</td>
<td>32</td>
<td>7</td>
</tr>
</tbody>
</table>

Vital sign abnormalities were assessed by treatment arm for the randomized trial in multiple myeloma and are presented in Table 8. Percentages are based on patients who had at least one vital sign abnormality any time during the course of study.

### Table 8: ELOQUENT-2 Vital Sign Abnormalities

<table>
<thead>
<tr>
<th>Vital Sign Parameter</th>
<th>EMPLICITI + Lenalidomide and Dexamethasone N=318</th>
<th>Lenalidomide and Dexamethasone N=317</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic Blood Pressure ≥160 mmHg</td>
<td>33</td>
<td>21</td>
</tr>
<tr>
<td>Diastolic Blood Pressure ≥100 mmHg</td>
<td>17</td>
<td>12</td>
</tr>
<tr>
<td>Systolic Blood Pressure &lt;90 mmHg</td>
<td>29</td>
<td>8</td>
</tr>
<tr>
<td>Heart Rate ≥100 bpm</td>
<td>48</td>
<td>30</td>
</tr>
<tr>
<td>Heart Rate &lt;60 bpm</td>
<td>66</td>
<td>31</td>
</tr>
</tbody>
</table>

**EMPLICITI in Combination with Pomalidomide and Dexamethasone [ELOQUENT-3]**

The safety data described in this section are based on ELOQUENT-3, a randomized, open-label clinical trial in patients with previously treated multiple myeloma. In ELOQUENT-3, EMPLICITI 10 mg/kg and 20 mg/kg was administered with pomalidomide and dexamethasone [see Clinical Studies (14)]. For adverse reaction evaluation, EMPLICITI combined with pomalidomide and dexamethasone was compared with pomalidomide and dexamethasone alone.

The mean age of the population was 66 years and 63% of patients were 65 years of age or older. Fifty-seven percent of the population were male, 78% were white, 20% were Asian, and none were black. The ECOG performance status was 0 in 43%, 1 in 46%, and 2 in 10% of patients. These data reflect exposure of 60 patients to EMPLICITI and 55 to control with a median number of cycles of 9 for EMPLICITI and 5 for control.

Serious adverse reactions were reported in 22% of patients treated on the EMPLICITI arm and 15% for patients treated on the control arm. The most frequent serious adverse reactions in the EMPLICITI arm compared to the control arm were: pneumonia (13% vs. 11%) and respiratory tract infection (7% vs. 3.6%). The proportion of patients who discontinued any component of the treatment regimen due to adverse reactions were 5.0% of the patients in the EMPLICITI arm and 1.8% of the patients in the control arm.

Adverse reactions occurring at a frequency of 10% or higher in the EMPLICITI arm and 5% or higher than the pomalidomide and dexamethasone arm for the randomized trial in multiple myeloma are presented in Table 9.
Table 9: ELOQUENT-3: Laboratory Abnormalities Worsening from Baseline and with a 10% or Higher Incidence for EMPLICITI-Treated Patients [All Grades]

<table>
<thead>
<tr>
<th>Laboratory Parameter</th>
<th>EMPLICITI + Pomalidomide and Dexamethasone N=60</th>
<th>Pomalidomide and Dexamethasone N=55</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All Grades Grade 3/4</td>
<td>All Grades Grade 3/4</td>
</tr>
<tr>
<td>Constipation</td>
<td>22 1.7</td>
<td>11 0</td>
</tr>
<tr>
<td>Hypertension</td>
<td>20 8</td>
<td>15 7</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>18 10</td>
<td>13 11</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>18 0</td>
<td>9 0</td>
</tr>
<tr>
<td>Respiratory Tract Infection</td>
<td>17 0</td>
<td>9 1.8</td>
</tr>
<tr>
<td>Bone Pain</td>
<td>15 3.3</td>
<td>9 0</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>15 3.3</td>
<td>7 1.8</td>
</tr>
<tr>
<td>Muscle Spasms</td>
<td>13 0</td>
<td>5 0</td>
</tr>
<tr>
<td>Edema Peripheral</td>
<td>13 0</td>
<td>7 0</td>
</tr>
<tr>
<td>Lymphopenia</td>
<td>10 8</td>
<td>1.8 1.8</td>
</tr>
</tbody>
</table>

* The term pneumonia is grouping of the following terms: pneumonia, atypical pneumonia, lower respiratory tract infection, pneumococcal sepsis, pneumonia bacterial, pneumonia influenza.

Other clinically important adverse reactions reported in patients treated with EMPLICITI that did not meet the criteria for inclusion in Table 6 and 9 but occurred at a frequency of 5% or greater in the EMPLICITI group and at a frequency at least twice the control rate for the randomized trial in multiple myeloma are listed below:

- General disorders and administration site conditions: chest pain, night sweats
- Nervous system disorders: hypoesthesia
- Psychiatric disorders: mood altered
- Laboratory abnormalities worsening from baseline and occurring at a frequency of 10% or higher in ELOQUENT-3 in the EMPLICITI group and 5% or higher than the pomalidomide and dexamethasone group (criteria met for all Grades or Grade 3/4) for the randomized trial in multiple myeloma are presented in Table 10.

Table 10: ELOQUENT-3: Laboratory Abnormalities Worsening from Baseline and with a 10% or Higher Incidence for EMPLICITI-Treated Patients and a 5% Higher Incidence than Pomalidomide and Dexamethasone-Treated Patients [Criteria met for All Grades or Grade 3/4]

<table>
<thead>
<tr>
<th>Laboratory Parameter</th>
<th>EMPLICITI + Pomalidomide and Dexamethasone N=60</th>
<th>Pomalidomide and Dexamethasone N=55</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All Grades Grade 3/4</td>
<td>All Grades Grade 3/4</td>
</tr>
<tr>
<td>Hematology</td>
<td>98 70</td>
<td>91 35</td>
</tr>
<tr>
<td>Leukopenia</td>
<td>80 52</td>
<td>87 35</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>78 17</td>
<td>73 20</td>
</tr>
<tr>
<td>Liver and Renal Function Tests</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypoalbuminemia</td>
<td>65 1.7</td>
<td>56 1.8</td>
</tr>
<tr>
<td>Chemistry</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypocalcemia</td>
<td>58 3.3</td>
<td>40 1.8</td>
</tr>
<tr>
<td>Hyperglycemia</td>
<td>40 3.3</td>
<td>25 1.8</td>
</tr>
<tr>
<td>Hypotenremia</td>
<td>40 5</td>
<td>18 0</td>
</tr>
<tr>
<td>Hypokalemia</td>
<td>23 5</td>
<td>16 3.6</td>
</tr>
</tbody>
</table>

Vital sign abnormalities were assessed by treatment arm for the randomized trial in multiple myeloma and are presented in Table 11. Percentages are based on all treated patients.

Table 11: ELOQUENT-3: Vital Sign Abnormalities

<table>
<thead>
<tr>
<th>Vital Sign Parameter</th>
<th>EMPLICITI + Pomalidomide and Dexamethasone N=60</th>
<th>Pomalidomide and Dexamethasone N=55</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All Grades Grade 3/4</td>
<td>All Grades Grade 3/4</td>
</tr>
<tr>
<td>Systolic Blood Pressure ≥160 mmHg</td>
<td>18 13</td>
<td>8 4.0</td>
</tr>
<tr>
<td>Diastolic Blood Pressure ≥100 mmHg</td>
<td></td>
<td>7 7</td>
</tr>
<tr>
<td>Heart Rate ≥100 bpm</td>
<td>23 24</td>
<td>23 24</td>
</tr>
<tr>
<td>Heart Rate &lt;60 bpm</td>
<td>43 22</td>
<td>22 22</td>
</tr>
</tbody>
</table>

6.2 Immunogenicity

As with all therapeutic proteins, there is a potential for immunogenicity to EMPLICITI. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of incidence of antibodies to EMPLICITI in the studies described below with the incidences of antibodies in other studies or to other products may be misleading.

Of 390 patients across four clinical studies including ELOQUENT-2 and in 53 patients in the ELOQUENT-3 trial, who were treated with EMPLICITI and evaluable for the presence of anti-product antibodies, 72 patients (18.5%) in the four clinical trials and 19 patients (36%) in the ELOQUENT-3 trial tested positive for treatment-emergent anti-product antibodies by an electrochemiluminescent (ECL) assay. In 63 (88%) of the 72 patients in the four clinical trials, anti-product antibodies occurred within the first 2 months of the initiation of EMPLICITI treatment and resolved by 2 to 4 months in 49 (78%) patients. In the ELOQUENT-3 trial, in all 19 patients, anti-product antibodies occurred within the first 2 months of the initiation of EMPLICITI treatment and were resolved by 2 to 3 months in 18 (95%) patients.

Neutralizing antibodies post-treatment were detected in 19 of 299 patients in the four clinical trials and 2 of 53 patients in the ELOQUENT-3 trial who were evaluable for the presence of neutralizing antibodies.

7 DRUG INTERACTIONS

7.1 Drug Interactions

For important drug interactions involving lenalidomide, pomalidomide and dexamethasone, refer to their respective prescribing information.

7.2 Laboratory Test Interference

EMPLICITI may be detected in the SPEP and serum immunofixation assays of myeloma patients and could interfere with correct response classification. A small peak in the early gamma region on SPEP that is IgG can cause interference in SPEP and serum immunofixation may potentially be attributed to EMPLICITI, particularly in patients whose endogenous myeloma protein is IgA, IgM, IgD, or lambda light chain restricted. This interference can impact the determination of complete response and possibly relapse from complete response in patients with IgG kappa myeloma protein [see Warnings and Precautions (5.5)].

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no available data on EMPLICITI use in pregnant women to inform a drug associated risk of major birth defects and miscarriage. Animal reproduction studies have not been conducted with elotuzumab.

EMPLICITI is administered in combination with lenalidomide and dexamethasone. Lenalidomide and pomalidomide can cause embryo-fetal harm and are contraindicated for use in pregnancy. Refer to the lenalidomide, pomalidomide and dexamethasone prescribing information for additional information.

The background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.
EMPLICITI® (elotuzumab)

8.2 Lactation

Risk Summary

There are no data on the presence of EMPLICITI in human milk, the effects on the breastfeeding child, or the effects on milk production. Because of the potential for serious adverse reactions in the breastfeeding child from elotuzumab administered in combination with lenalidomide and dexamethasone or pomalidomide and dexamethasone, advise lactating women not to breastfeed during treatment with EMPLICITI. Refer to the lenalidomide, pomalidomide and dexamethasone prescribing information for additional information.

8.3 Females and Males of Reproductive Potential

Pregnancy Testing

Refer to the lenalidomide and pomalidomide labeling for pregnancy testing requirements prior to initiating treatment in females of reproductive potential.

When EMPLICITI is used with lenalidomide or pomalidomide, there is a risk of fetal harm, including severe life-threatening human birth defects associated with lenalidomide and pomalidomide, and the need to follow requirements regarding pregnancy avoidance, including testing.

Contraception

Females

Refer to the lenalidomide and pomalidomide labeling for contraception requirements prior to initiating treatment in females of reproductive potential.

Males

Lenalidomide and pomalidomide are present in the blood and semen of patients receiving the drug. Refer to the lenalidomide and pomalidomide full prescribing information for requirements regarding contraception and the prohibitions against blood and/or sperm donation due to presence and transmission in blood and/or semen and for additional information.

8.4 Pediatric Use

Safety and effectiveness have not been established in pediatric patients.

8.5 Geriatric Use

Of the 646 patients across treatment groups in the ELOQUENT-2 randomized trial designed to evaluate the use of EMPLICITI in combination with lenalidomide and low-dose dexamethasone in multiple myeloma, 52% were 65 years of age or older; the number of patients 65 years or older was similar between treatment groups. No overall differences in efficacy or safety were observed between patients 65 years or older and younger patients (less than 65 years of age).

Of the 117 patients across treatment groups in the ELOQUENT-3 randomized trial designed to evaluate the use of EMPLICITI in combination with pomalidomide and low-dose dexamethasone in multiple myeloma, 62% were 65 years of age or older; the number of patients 65 years or older was similar between treatment groups. This study did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects.

10 OVERDOSAGE

The dose of EMPLICITI at which severe toxicity occurs is not known. EMPLICITI does not appear to be removed by dialysis as determined in a study of patients with renal impairment.

In case of overdosage, monitor patients closely for signs or symptoms of adverse reactions and institute appropriate symptomatic treatment.

11 DESCRIPTION

Elotuzumab is a humanized recombinant monoclonal antibody directed to SLAMF7, a cell surface glycoprotein. Elotuzumab consists of the complementary determining regions (CDR) of the mouse antibody, MuLuc63, grafted onto human IgG1 heavy and kappa light chain frameworks. Elotuzumab is produced in NS0 cells by recombinant DNA technology. Elotuzumab has a theoretical mass of 148.1 kDa for the intact antibody.

EMPLICITI® (elotuzumab) is a sterile, nonpyrogenic, preservative-free lyophilized powder for reconstitution. Elotuzumab has a theoretical mass of 148.1 kDa for the intact antibody.

Elotuzumab is a humanized IgG1 monoclonal antibody that specifically targets the SLAMF7 (Signaling Lymphocytic Activation Molecule Family member 7) protein. SLAMF7 is expressed on myeloma cells independent of cytogenetic abnormalities. SLAMF7 is also expressed on Natural Killer cells, plasma cells, and at lower levels on specific immune cell subsets of differentiated cells within the hematopoietic lineage.

Elotuzumab directly activates Natural Killer cells through both the SLAMF7 pathway and Fc receptors. Elotuzumab also targets SLAMF7 on myeloma cells and facilitates the interaction with Natural Killer cells to mediate the killing of myeloma cells through antibody-dependent cellular cytotoxicity (ADCC). In preclinical models, the combination of elotuzumab and lenalidomide resulted in enhanced activation of Natural Killer cells that was greater than the effects of either agent alone and increased anti-tumor activity in vitro and in vivo.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Elotuzumab is a humanized IgG1 monoclonal antibody that specifically targets the SLAMF7 (Signaling Lymphocytic Activation Molecule Family member 7) protein. SLAMF7 is expressed on myeloma cells independent of cytogenetic abnormalities. SLAMF7 is also expressed on Natural Killer cells, plasma cells, and at lower levels on specific immune cell subsets of differentiated cells within the hematopoietic lineage.

Elotuzumab directly activates Natural Killer cells through both the SLAMF7 pathway and Fc receptors. Elotuzumab also targets SLAMF7 on myeloma cells and facilitates the interaction with Natural Killer cells to mediate the killing of myeloma cells through antibody-dependent cellular cytotoxicity (ADCC). In preclinical models, the combination of elotuzumab and lenalidomide resulted in enhanced activation of Natural Killer cells that was greater than the effects of either agent alone and increased anti-tumor activity in vitro and in vivo.

12.2 Pharmacodynamics

Cardiac Electrophysiology

EMPLICITI does not prolong the QT interval to any clinically relevant extent when administered with lenalidomide and dexamethasone at the recommended dose or as monotherapy (at a dose 2 times the recommended dose).

12.3 Pharmacokinetics

Elotuzumab exhibits nonlinear pharmacokinetics (PK) resulting in greater than proportional increases in area under the concentration-time curve (AUC) indicative of target-mediated clearance. The administration of the recommended 10 mg/kg EMPLICITI regimen with lenalidomide and dexamethasone is predicted to result in geometric mean (CV%) steady-state trough concentrations of 194 μg/mL (52%). The administration of the recommended EMPLICITI regimen with pomalidomide and dexamethasone is predicted to result in geometric mean (CV%) steady-state trough concentrations of 124 μg/mL (59%).

Elimination

The clearance of elotuzumab in combination with lenalidomide and dexamethasone decreased from a geometric mean (CV%) of 17.5 (21.2%) to 5.8 (31%) mL/day/kg with an increase in dose from 0.5 (i.e., 0.05 times the recommended dosage) to 20 mg/kg (i.e., 2 times the recommended dosage). When elotuzumab is administered with lenalidomide and dexamethasone, approximately 97% of the maximum steady-state concentration is predicted to be eliminated with a geometric mean (CV%) of 82.4 (48%) days. When elotuzumab is administered with pomalidomide and dexamethasone, approximately 97% of the maximum steady-state concentration is predicted to be eliminated with a geometric mean (CV%) of 78 (42%) days.

Specific Populations

Clinically significant differences were not observed in the PK of elotuzumab based on age (37 to 88 years), sex, race, baseline lactate dehydrogenase, albumin, renal impairment (creatinine clearance (CLcr) 15 to 89 mL/min), end-stage renal disease (CLcr <15 mL/min) with or without hemodialysis, mild hepatic impairment (total bilirubin ≤ upper limit of normal (ULN) and aspartate transaminase (AST) < ULN) or total bilirubin 1 to 1.5 times the ULN and AST any value), and coadministration with lenalidomide/dexamethasone or pomalidomide/dexamethasone. The PK of elotuzumab in patients with moderate (total bilirubin > 1.5 to 3 times the ULN and AST any value) to severe (total bilirubin > 3 times the ULN and AST any value) hepatic impairment is unknown.

The clearance of elotuzumab increased with increasing body weight supporting a weight-based dose.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

No carcinogenicity or mutagenicity data are available for elotuzumab in animals or humans. Fertility studies have not been performed for elotuzumab.

14 CLINICAL STUDIES

ELOQUENT-2 (NCT01239797)

The efficacy and safety of EMPLICITI in combination with lenalidomide and dexamethasone were evaluated in ELQUENT-2, a randomized, open-label trial in patients with multiple myeloma who had received one to three prior therapies and had documented progression following their most recent therapy.

Eligible patients were randomized in a 1:1 ratio to receive either EMPLICITI in combination with lenalidomide and low-dose dexamethasone or lenalidomide and low-dose dexamethasone. Treatment was administered in 4-week cycles until disease progression or unacceptable toxicity. EMPLICITI 10 mg/kg was administered intravenously each week for the first 2 cycles and every 2 weeks thereafter. Prior to EMPLICITI infusion, dexamethasone was administered as a divided dose: an oral dose of 28 mg and an
In the control group and on weeks without EMPLICITI, dexamethasone 40 mg was administered as a single oral dose weekly. Lenalidomide 25 mg was taken orally once daily for the first 3 weeks of each cycle. Assessment of tumor response was conducted every 4 weeks.

A total of 646 patients were randomized to receive treatment: 321 to EMPLICITI in combination with lenalidomide and low-dose dexamethasone and 325 to lenalidomide and low-dose dexamethasone.

Demographics and baseline disease characteristics were balanced between treatment arms. The median age was 66 years (range, 37-91); 57% of patients were 65 years or older; 60% of patients were male; whites comprised 84% of the study population, Asians 10%, and blacks 4%. The ECOG performance status was 0 in 47%, 1 in 44%, and 2 in 9% of patients, and ISS Stage was I in 43%, II in 32%, and III in 21% of patients, respectively. The median number of prior therapies was 2. Thirty-five percent (35%) of patients were refractory (progression during or within 60 days of last therapy) and 65% were relapsed (progression after 60 days of last therapy). Prior therapies included stem cell transplant (55%), bortezomib (65%), thalidomide (48%), and lenalidomide (6%).

The efficacy of EMPLICITI was evaluated by progression-free survival (PFS) as assessed by hazard ratio, and overall response rate (ORR) as determined by a blinded Independent Review Committee using the European Group for Blood and Marrow Transplantation (EBMT) response criteria. Efficacy results are shown in Table 12 and Figure 1. The median number of treatment cycles was 19 for the EMPLICITI group and 14 for the comparator arm with a minimum follow-up of two years. A pre-planned final overall survival (OS) analysis was performed after at least 427 deaths occurred. The minimum follow-up was 70-6 months. The OS results at final analysis reached statistical significance. A significantly longer OS was observed in patients in the E-Ld arm compared to patients in Ld arm, representing an 18% reduction in the risk of death. Efficacy results are presented in Table 12 and Figure 2.

### Table 12: ELOQUENT-2 Efficacy Results

<table>
<thead>
<tr>
<th></th>
<th>EMPLICITI + Lenalidomide/Dexamethasone</th>
<th>Lenalidomide/Dexamethasone</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PFS</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hazard Ratio [95% CI]</td>
<td>0.70 [0.57, 0.85]</td>
<td></td>
</tr>
<tr>
<td>Stratified log-rank test p-value*</td>
<td>0.0004</td>
<td></td>
</tr>
<tr>
<td>Median PFS in months [95% CI]</td>
<td>19.4 [16.6, 22.2]</td>
<td>14.9 [12.1, 17.2]</td>
</tr>
<tr>
<td><strong>Response</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall Response (ORR)† n (%)</td>
<td>252 (78.5) [95% CI]</td>
<td>213 (65.5) [60.1, 70.7]</td>
</tr>
<tr>
<td>p-value‡</td>
<td>0.0002</td>
<td></td>
</tr>
<tr>
<td>Complete Response (CR + sCR)§ n (%)</td>
<td>14 (4.4) [73.6, 82.9]</td>
<td>24 (7.4) [67.2, 80.0]</td>
</tr>
<tr>
<td>Very Good Partial Response (VGPR)† n (%)</td>
<td>91 (28.3) [23.1, 33.7]</td>
<td>67 (20.6) [57.4, 77.0]</td>
</tr>
<tr>
<td>Partial Response (PR)§ n (%)</td>
<td>147 (45.8) [40.5, 51.0]</td>
<td>122 (37.5) [31.6, 43.1]</td>
</tr>
<tr>
<td><strong>Overall Survival</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hazard Ratio [95.4% CI]</td>
<td>0.82 [0.68, 1.00]</td>
<td></td>
</tr>
<tr>
<td>Stratified log-rank test p-value*</td>
<td>0.0040</td>
<td></td>
</tr>
<tr>
<td>Median OS in months [95% CI]</td>
<td>48.3 [40.3, 51.9]</td>
<td>39.6 [33.3, 45.3]</td>
</tr>
</tbody>
</table>

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* p-value based on the log-rank test stratified by 82 microglobulins (<3.5 mg/L vs ≥3.5 mg/L), number of prior lines of therapy (1 vs 2 or 3), and prior immunomodulatory therapy (no vs prior thalidomide only vs other).

† European Group for Blood and Marrow Transplantation (EBMT) response criteria.

‡ p-value based on the Cochran-Mantel-Haenszel chi-square test stratified by 62 microglobulins (<3.5 mg/L vs ≥3.5 mg/L), number of prior lines of therapy (1 vs 2 or 3), and prior immunomodulatory therapy (no vs prior thalidomide only vs other).

§ Complete response (CR) + stringent complete response (sCR).

EMPLICITI’s interference with the assessment of myeloma protein with immunofixation and serum protein electrophoresis assay may interfere with correct response classification [see Drug Interactions (7)].

The efficacy and safety of EMPLICITI in combination with pomalidomide and dexamethasone were evaluated in ELOQUENT-3, a randomized, open-label trial in patients with relapsed or refractory multiple myeloma.

Eligible patients were randomized in a 1:1 ratio to receive either EMPLICITI in combination with pomalidomide and low-dose dexamethasone or pomalidomide and low-dose dexamethasone. Treatment was administered in 4-week cycles until disease progression or unacceptable toxicity. EMPLICITI 10 mg/kg was administered intravenously each week for the first 2 cycles and 20 mg/kg every 4 weeks thereafter.

Prior to EMPLICITI infusion, dexamethasone was administered. Dexamethasone was administered on day 1, 8, 15, and 22 of each cycle. On weeks with EMPLICITI infusion, dexamethasone was administered as a divided dose: subjects 75 years or younger, an oral dose of 29 mg and an intravenous dose of 8 mg, and in subjects older than 75 years an oral dose of 8 mg and an intravenous dose of 8 mg. On weeks without an EMPLICITI infusion and in the control group, dexamethasone was administered in subjects 75 years or younger as an oral dose of 40 mg and in subjects older than 75 years as an oral dose of 20 mg dexamethasone was administered orally. Assessment of tumor response was conducted every 4 weeks.

A total of 117 patients were randomized to receive treatment: 60 to EMPLICITI in combination with pomalidomide and low-dose dexamethasone and 57 to pomalidomide and low-dose dexamethasone.
Demographics and baseline disease characteristics were balanced between treatment arms. The median age was 67 years (range, 36-81); 62% of patients were 65 years or older; 57% of patients were male; whites comprised 77% of the study population, Asians 21%, and blacks 1%. The ECOG performance status was 0 in 44%, 1 in 46%, and 2 in 10% of patients, and ISS Stage was 1 in 50%, II in 39%, and III in 12% of patients. The chromosomal lab abnormalities as determined by FISH of del 17p and t(4;14) were present in 5% and 11% of patients, respectively. The median number of prior therapies was 3. Eighty-seven percent (87%) of patients were refractory to lenalidomide, 80% refractory to a proteasome inhibitor, 70% were refractory to both lenalidomide and a proteasome inhibitor. Prior therapies included stem cell transplant (55%), bortezomib (100%), lenalidomide (99%), cyclophosphamide (66%), melphalan (63%), carfilzomib (21%), and daratumumab (3%).

The efficacy of EMPLICITI was evaluated by progression-free survival (PFS) and overall response rate (ORR) as determined by the investigator. Efficacy results are shown in Table 13 and Figure 3. The median number of treatment cycles was 9 for the EMPLICITI group and 5 for the comparator arm with a minimum follow-up of 9.1 months.

**Table 13: ELOQUENT-3 Efficacy Results**

<table>
<thead>
<tr>
<th>EMPLICITI + Dexamethasone</th>
<th>Pomalidomide/Dexamethasone</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=60</td>
<td>N=57</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>PFS</th>
<th>Hazard Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stratified log-rank test p-value*</td>
<td>0.54 (0.34, 0.86)</td>
</tr>
</tbody>
</table>

Median PFS in months (95% CI) 10.25 [5.59, NE] 4.67 [2.83, 7.16]

Response

Overall Response (ORR)† n (%) 32 (53.3) 15 (26.3) 40.0, 66.3 [15.5, 39.7]
p-value‡ 0.0029

Complete Response (CR + sCR)† n (%) 5 (8.3)¶ 1 (1.8)

Very Good Partial Response (VGPR) n (%) 7 (11.7) 4 (7.0)

Partial Response (PR) n (%) 20 (33.3) 10 (17.5)

* p-value based on the log-rank test stratified by stage of disease at study entry (International Staging System I-II vs III) and number of prior lines of therapy (2-3 vs >=4) at randomization.

‡ p-value based on the Cochrane-Mantel-Haenszel chi-square test stratified by stage of disease at study entry (International Staging System I-II vs III) and number of prior lines of therapy (2-3 vs >=4) at randomization.

¶ Complete response (CR) + stringent complete response (sCR).

EMPLICITI’s interference with the assessment of myeloma protein with immunofixation and serum protein electrophoresis assay may interfere with correct response classification [see Drug Interactions (7)].

**Figure 3: ELOQUENT-3 Progression-Free Survival**

EMPLICITI (elotuzumab) is white to off-white lyophilized powder available as follows:

<table>
<thead>
<tr>
<th>Carton Content</th>
<th>NDC</th>
</tr>
</thead>
<tbody>
<tr>
<td>One 300 mg single-dose vial</td>
<td>0003-2291-11</td>
</tr>
<tr>
<td>One 400 mg single-dose vial</td>
<td>0003-4522-11</td>
</tr>
</tbody>
</table>

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

**17 PATIENT COUNSELING INFORMATION**

Advise the patient to read the FDA-approved patient labeling (Patient Information).

**Infusion Reactions**

- EMPLICITI may cause infusion reactions. Advise patients to contact their healthcare provider if they experience signs and symptoms of infusion reactions, including fever, chills, rash, or breathing problems within 24 hours of infusion [see Warnings and Precautions (5.1)].
- Advise patients that they will be required to take the following oral medications prior to EMPLICITI dosing to reduce the risk of infusion reaction [see Dosage and Administration (2.3)].
  - Dexamethasone orally as prescribed
  - H1 blocker: diphenhydramine or equivalent (if oral)
  - H2 blocker: ranitidine or equivalent (if oral)
  - Acetaminophen (650 to 1000 mg orally)

**Pregnancy**

- Advise patients that lenalidomide and pomalidomide have the potential to cause fetal harm and have specific requirements regarding contraception, pregnancy testing, blood and sperm donation, and transmission in sperm. Lenalidomide and pomalidomide are only available through a REMS program [see Use in Specific Populations (8.1)].

**Infections**

- Inform patients of the risk of developing infections during treatment with EMPLICITI, and to report any symptoms of infection [see Warnings and Precautions (5.2)].

**Second Primary Malignancies**

- Inform patients of the risk of developing SPM during treatment with EMPLICITI [see Warnings and Precautions (5.3)].

**Hepatotoxicity**

- Inform patients of the risk of hepatotoxicity during treatment with EMPLICITI and to report any signs and symptoms associated with this event to their healthcare provider for evaluation [see Warnings and Precautions (5.4)].
EMPLICITI is used with other prescription medicines called REVLIMID® (lenalidomide) and dexamethasone or POMALYST® (pomalidomide) and dexamethasone. Read the Medication Guide that comes with REVLIMID if used with REVLIMID and POMALYST if used with POMALYST. You can ask your healthcare provider or pharmacist for information about dexamethasone.

What is EMPLICITI?
EMPLICITI is a prescription medicine used to treat:

- multiple myeloma in combination with the medicines REVLIMID (lenalidomide) and dexamethasone in adults who have received one to three prior treatments for their multiple myeloma.
- multiple myeloma in combination with the medicines POMALYST (pomalidomide) and dexamethasone in adults who have received at least two prior treatments including REVLIMID (lenalidomide) and a proteasome inhibitor.

It is not known if EMPLICITI is safe and effective in children.

Before you receive EMPLICITI, tell your healthcare provider about all of your medical conditions, including if you:

- have an infection
- are pregnant or plan to become pregnant. It is not known if EMPLICITI may harm your unborn baby. However, REVLIMID and POMALYST may cause birth defects or death of an unborn baby.
  - Before receiving EMPLICITI with REVLIMID and dexamethasone, or EMPLICITI with POMALYST and dexamethasone, females and males must agree to the instructions in the REVLIMID REMS® program for the use of EMPLICITI in combination with REVLIMID and dexamethasone and the POMALYST REMS® program for the use of EMPLICITI in combination with POMALYST and dexamethasone.
  - The REVLIMID REMS and POMALYST REMS programs have specific requirements about birth control (contraception), pregnancy testing, blood donation, and sperm donation that you need to know. Talk to your healthcare provider to learn more about REVLIMID or POMALYST.
- are breastfeeding or plan to breastfeed. It is not known if EMPLICITI passes into breast milk. You should not breastfeed during treatment with EMPLICITI and REVLIMID and dexamethasone or EMPLICITI and POMALYST and dexamethasone.
- Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

How will I receive EMPLICITI?

- EMPLICITI will be given to you by intravenous (IV) infusion into your vein.
- Your EMPLICITI treatment schedule is divided into cycles that are 28 days (4 weeks) long. A cycle includes the number of days you are on treatment and also the time you spend resting in between treatments.
- EMPLICITI with REVLIMID and dexamethasone is usually given as follows:
  - Cycles 1 and 2 (28 days per cycle), you will receive EMPLICITI one time every week.
  - Cycles 3 and up (28 days per cycle), you will receive EMPLICITI one time every 2 weeks.
**EMPLICITI**® (elotuzumab)

- **EMPLICITI with POMALYST and dexamethasone** is usually given as follows:
  - Cycle 1 and 2 (28 days per cycle), you will receive EMPLICITI one time every week.
  - Cycle 3 and up (28 days per cycle), you will receive EMPLICITI one time every 4 weeks.
- Your healthcare provider will decide how many treatments you will receive.
- Before every EMPLICITI infusion, you will receive medicines to help reduce the risk of infusion reactions.
- If you miss any appointments call your healthcare provider as soon as possible.

### What are the possible side effects of EMPLICITI?

**EMPLICITI may cause serious side effects, including:**

- **Infusion reactions.** Infusion reactions can happen during your infusion or within 24 hours after your infusion of EMPLICITI. Your healthcare provider will give you medicines before each infusion of EMPLICITI to help reduce the risk of an infusion reaction.
  
  If you have an infusion reaction while receiving EMPLICITI, your healthcare provider will slow or stop your infusion and treat your reaction. If you have a severe infusion reaction, your healthcare provider may stop your treatment completely. Tell your healthcare provider or get medical help right away if you have any of these symptoms after your infusion with EMPLICITI:

  - fever
  - chills
  - rash
  - chest pain
  - trouble breathing
  - dizziness
  - light-headedness

- **Infections.** People with multiple myeloma who receive EMPLICITI with REVLIMID and dexamethasone or EMPLICITI with POMALYST and dexamethasone may develop infections that can be serious. Tell your healthcare provider right away if you have any signs and symptoms of an infection, including:

  - fever
  - flu-like symptoms
  - cough
  - shortness of breath
  - burning with urination
  - a painful skin rash

- **Risk of new cancers (malignancies).** People with multiple myeloma who receive EMPLICITI with REVLIMID and dexamethasone or EMPLICITI with POMALYST and dexamethasone have a risk of developing new cancers. Talk with your healthcare provider about your risk of developing new cancers if you receive EMPLICITI. Your healthcare provider will check you for new cancers during your treatment with EMPLICITI.

- **Liver problems.** EMPLICITI may cause liver problems. Your healthcare provider will do blood tests to check your liver during treatment with EMPLICITI. Tell your healthcare provider if you have signs and symptoms of liver problems, including: tiredness, weakness, loss of appetite, yellowing of your skin or eyes, color changes in your stools, confusion, or swelling of the stomach area.

The most common side effects of EMPLICITI when used with **REVLIMID** and dexamethasone include:

- fatigue
- diarrhea
- fever
- constipation
- cough
- numbness, weakness, tingling, or burning pain in your arms or legs
- sore throat or runny nose
- upper respiratory tract infection
- decreased appetite
- pneumonia

The most common side effects of EMPLICITI when used with **POMALYST** and dexamethasone include:

- constipation
- high blood sugar

These are not all of the possible side effects of EMPLICITI.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088. You may also report side effects to Bristol-Myers Squibb at 1-800-721-5072.
General information about the safe and effective use of EMPLICITI

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. You can ask your pharmacist or healthcare provider for information about EMPLICITI that is written for health professionals.

What are the ingredients of EMPLICITI?

**Active ingredient:** elotuzumab

**Inactive ingredients:** citric acid monohydrate, polysorbate 80, sodium citrate, sucrose

For more information, call 1-844-EMPLICITI (844-367-5424) or visit EMPLICITI.com.

EMPLICITI® is a trademark of Bristol-Myers Squibb Company. All other trademarks are the property of their respective owners.

Manufactured by: Bristol-Myers Squibb Company, Princeton, NJ 08543 USA

U.S. License No. 1713

This Patient Information has been approved by the U.S. Food and Drug Administration.

Revised: 11/2018