

## A New Treatment Option for Multiple Myeloma Patients Who Have Received One to Three Prior Therapies

In November 2015, *Empliciti* was approved by the U.S. Food and Drug Administration (FDA) for the treatment of multiple myeloma as combination therapy with Revlimid® (lenalidomide) and dexamethasone (ERd) in patients who have received one to three prior therapies. In May 2014, the FDA granted *Empliciti* Breakthrough Therapy designation for this indication. The Breakthrough Therapy designation is intended to expedite the development and review of drugs for serious or life-threatening conditions and requires preliminary clinical evidence that demonstrates the drug may have substantial improvement on at least one clinically significant endpoint over available therapy.

The FDA approval of *Empliciti*, the first and only immunostimulatory antibody for multiple myeloma, was based on data from the randomized, open label, Phase 3 ELOQUENT-2 study, which evaluated *Empliciti* in combination with lenalidomide and dexamethasone (ERd). In this study, the ERd regimen:

- Resulted in a 30% reduction in the risk of disease progression or death compared to Rd alone. (HR 0.70 [95% CI: 0.57, 0.85; p = 0.0004]). With a minimum of two years follow-up,
- Delivered a benefit in PFS that was maintained over time, with PFS rates of 68% versus 57% at one year and 41% versus 27% at two years in the ERd and Rd arms, respectively.
- Demonstrated a significant improvement in overall response rate (ORR), achieving an ORR of 78.5% (95% CI: 73.6% to 82.9%) versus 65.5% in the Rd arm (95% CI: 60.1% to 70.7%).
- Resulted in fewer deaths in the ERd versus the Rd study arm (94 [29%] versus 116 [36%], respectively) at the time of the interim analysis.

Discontinuation rates due to adverse reactions were similar across the ERd and Rd control arms (6.0% versus 6.3%). Infusion reactions occurred in 10% of patients treated with ERd; these adverse events were Grade 3 or lower (Grade 3, 1%; Grade 4, 0%), and were manageable. In the trial, 1% of patients discontinued due to infusion reactions and 5% of patients required interruption of the administration of *Empliciti* for a median of 25 minutes. The most common adverse reactions in ERd and Rd, respectively (>20%) are fatigue (61.6%, 51.7%), diarrhea (46.9%, 36.0%), pyrexia (37.4%, 24.6%), constipation (35.5%, 27.1%), cough (34.3%, 18.9%), peripheral neuropathy (26.7%, 20.8%), nasopharyngitis (24.5%, 19.2%), upper respiratory tract infection (22.6%, 17.4%), decreased appetite (20.8%, 12.6%), and pneumonia (20.1%, 14.2%). Please see additional [Important Safety Information](#).

### *Empliciti* Snapshot

- Targets SLAMF7, a surface protein that is expressed on myeloma cells, Natural Killer cells, plasma cells, and at lower levels on specific immune cell subsets of differentiated cells within the hematopoietic lineage
- Approved in November 2015 by the FDA in combination with lenalidomide and dexamethasone for the treatment of patients with multiple myeloma who have received one to three prior therapies



## About *Empliciti*

Bristol-Myers Squibb and AbbVie are co-developing *Empliciti*, with Bristol-Myers Squibb solely responsible for commercial activities.

### What is *Empliciti*?

*Empliciti* (elotuzumab) is an immunostimulatory antibody that specifically targets Signaling Lymphocyte Activation Molecule Family member 7 (SLAMF7), a cell-surface glycoprotein. 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.

*Empliciti* has a dual mechanism-of-action. It directly activates the immune system through Natural Killer cells via the SLAMF7 pathway. *Empliciti* also targets SLAMF7 on myeloma cells, tagging these malignant cells for Natural Killer cell-mediated destruction via antibody-dependent cellular toxicity.

### What is Multiple Myeloma?

Multiple myeloma is a hematologic, or blood, cancer that develops in the bone marrow. It occurs when a plasma cell, a type of cell in the soft center of bone marrow, becomes cancerous and multiplies uncontrollably. Common symptoms of multiple myeloma include bone pain, fatigue, kidney impairment, and infections. Despite advances in multiple myeloma treatment over the last decade, less than half of patients survive for five or more years after diagnosis.

## EMPLICITI (elotuzumab) INDICATIONS & IMPORTANT SAFETY INFORMATION

### INDICATION

EMPLICITI™ (elotuzumab), is indicated in combination with lenalidomide and dexamethasone for the treatment of patients with multiple myeloma who have received one to three prior therapies.

### IMPORTANT SAFETY INFORMATION

#### Infusion Reaction

- In a clinical trial of patients with multiple myeloma (n=365), EMPLICITI caused infusion reactions. Common symptoms include 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. 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 infusing with EMPLICITI.

### **Infections**

- Infections were reported in 81.4% of patients in the EMPLICITI with lenalidomide/dexamethasone arm (ERd) and 74.4% in the lenalidomide/dexamethasone arm (Rd). Grade 3-4 infections were 28% (ERd) and 24.3% (Rd). Opportunistic infections were reported in 22% (ERd) and 12.9% (Rd). Fungal infections were 9.7% (ERd) and 5.4% (Rd). Herpes zoster was 13.5% (ERd) and 6.9% (Rd). Discontinuations due to infections were 3.5% (ERd) and 4.1% (Rd). Fatal infections were 2.5% (ERd) and 2.2% (Rd). Monitor patients for development of infections and treat promptly.

### **Second Primary Malignancies**

- Invasive second primary malignancies (SPM) were 9.1% (ERd) and 5.7% (Rd). The rate of hematologic malignancies were 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). Monitor patients for the development of SPMs.

### **Hepatotoxicity**

- Elevations in liver enzymes (AST/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) consistent with hepatotoxicity were 2.5% (ERd) and 0.6% (Rd). Two patients experiencing hepatotoxicity discontinued treatment; however, 6 out of 8 patients had resolution and continued 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.

### **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.

### **Pregnancy/Females and Males of Reproductive Potential**

- There are no studies with EMPLICITI with pregnant women to inform any drug associated risks
- There is a risk of fetal harm, including severe life-threatening human birth defects associated with lenalidomide and it is contraindicated for use in pregnancy. Refer to the lenalidomide 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**

- Infusion reactions were reported in approximately 10% of patients treated with EMPLICITI with lenalidomide and dexamethasone. All reports of infusion reaction were Grade 3 or lower. Grade 3 infusion reactions occurred in 1% of patients.
- Serious adverse reactions were 65.4% (ERd) and 56.5% (Rd). The most frequent serious adverse reactions in the ERd arm compared to the Rd arm were: pneumonia (15.4%, 11%), pyrexia (6.9%, 4.7%), 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%) are fatigue (61.6%, 51.7%), diarrhea (46.9%, 36.0%), pyrexia (37.4%, 24.6%), constipation (35.5%, 27.1%), cough (34.3%, 18.9%), peripheral neuropathy (26.7%, 20.8%), nasopharyngitis (24.5%, 19.2%), upper respiratory tract infection (22.6%, 17.4%), decreased appetite (20.8%, 12.6%), and pneumonia (20.1%, 14.2%).

**Please see the full Prescribing Information [here](#).**

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