אפריל 2021

Empliciti (elotuzumab) 300 mg & 400mg
Powder for concentrate for solution for infusion

רופא/ה ,רוקח/ת יקר/ה,

חברת בריסטול-מאיירס סקוויב (ישראל) מבקשת להודיע על עדכון בעלון לרופא של התכשיר אמפליסיטי (elotuzumab) בישראל.

התוויות התכשיר כפי שאושרו על ידי משרד הבריאות:

Empliciti is indicated in combination with lenalidomide and dexamethasone for the treatment of multiple myeloma in adult patients who have received at least one prior therapy.

Empliciti is indicated in combination with pomalidomide and dexamethasone for the treatment of adult patients with relapsed and refractory multiple myeloma who have received at least two prior therapies, including lenalidomide and a proteasome inhibitor, and have demonstrated disease progression on the last therapy.

בפירוט שלהלן כלולים העדכונים המהותיים בלבד (טקסט שנוסף מסומן באדום עם קו תחתי ,טקסט שהוסר מסומן ~~בכחול~~ עם קו אמצעי, טקסט ששינה מיקום מסומן בירוק עם קו תחתי/אמצעי)

למידע מלא על התרופה יש לעיין בעלון לרופא כפי שאושר על ידי משרד הבריאות.

העלון לרופא נשלח לפרסום במאגר התרופות שבאתר משרד הבריאות וניתן לקבלו מודפס על ידי פנייה לבעל הרישום בריסטול- מאיירס סקוויב (ישראל) בע"מ.

בכבוד רב,
שירן קלאורה,
רוקחת ממונה

עדכונים מהותיים בעלון לרופא:

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

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Empliciti contains sodium

This medicinal product contains 3.92 mg sodium per 300 mg vial or 5.23 mg sodium per 400 mg vial, which is equivalent to 0.2% or 0.3% respectively, of the WHO recommended maximum daily intake of 2 g sodium for an adult.

~~This medicine contains less than 1 mmol sodium (23 mg) per dose, i.e. it is essentially 'sodium free'.~~

For the full list of excipients, see section 6.1.

4. CLINICAL PARTICULARS

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4.2 Posology and method of administration

~~The a~~Administration of dexamethasone *for adults ≤ 75 years old and for > 75 years old*~~is as follows:~~

- On days that Empliciti is administered, patients ≤ 75 years old give dexamethasone 28 mg orally between 3 and 24 hours before Empliciti plus 8 mg intravenously between 45 and 90 minutes before Empliciti and for patients > 75 years old give dexamethasone 8 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, 15 and 22 of cycle 3 and all subsequent cycles), give 40 mg orally to patients ≤ 75 years old and 20 mg orally to patients > 75 years old.

Table 2: Recommended dosing schedule of Empliciti in combination with pomalidomide and dexamethasone

Cycle	**28-Day Cycles 1 and 2**				**28-Day Cycles 3+**			
Day of Cycle	1	8	15	22	1	8	15	22
Premedication	✓	✓	✓	✓	✓			
Empliciti (mg/kg bw) intravenously	10	10	10	10	20			
Pomalidomide (4 mg) orally	Days 1-21				Days 1-21			
Dexamethasone (mg) intravenously	8	8	8	8	8			
Dexamethasone (mg) orally ≤ 75 years old	28	28	28	28	28	40	40	40
Dexamethasone (mg) orally > 75 years old	8	8	8	8	8	20	20	20
Day of Cycle	1	8	15	22	1	8	15	22

Special populations

~~*Paediatric population*~~

~~There is no relevant use of Empliciti in the paediatric population for the indication of multiple myeloma.~~

Elderly

No dose adjustment is required for Empliciti in patients over 65 years of age (see section 5.2). Data on the efficacy and safety of Empliciti in patients ≥ 85 years of age are very limited. The dose for dexamethasone in combination with pomalidomide is adjusted according to age. See Administration of dexamethasone for adults ≤ 75 years old and for > 75 years old above.

Renal impairment
No dose adjustment of Empliciti is required for patients with mild (creatinine clearance (CrCl) = 60 - 89 mL/min), moderate (CrCl = 30 - 59 mL/min), severe (CrCl < 30 mL/min) renal impairment or end stage renal disease requiring dialysis (see section 5.2).

Hepatic impairment
No dose adjustment for Empliciti is required for patients with mild hepatic impairment (total bilirubin ~~[~~(TB~~]~~) ≤ to the upper limit of normal ~~[~~(ULN~~]~~) and aspartate aminotransferase (AST) > ULN or TB < 1 to 1.5 × ULN and any AST). Empliciti has not been studied in patients with moderate (TB > 1.5 to 3 × ULN and any AST) or severe (TB > 3 × ULN and any AST) hepatic impairment (see section 5.2).

Paediatric population
There is no relevant use of Empliciti in the paediatric population for the indication of multiple myeloma.
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4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

The prescribing information leaflets~~Summary of Product Characteristics~~ for lenalidomide, pomalidomide and dexamethasone~~all medicinal products~~ used in combination with Empliciti must be consulted before starting therapy.

4.4 Special warnings and precautions for use
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Excipients
This medicinal product contains 3.92 mg sodium per 300 mg vial or 5.23 mg sodium per 400 mg vial, which is equivalent to 0.2% or 0.3% respectively, of the WHO recommended maximum daily intake of 2 g sodium for an adult.

4.5 Interaction with other medicinal products and other forms of interaction
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The Summary of Product Characteristics for lenalidomide, pomalidomide and dexamethasone~~all medicinal products~~ used in combination with Empliciti must be consulted before starting therapy.

4.6 Fertility, pregnancy and lactation

Woman of childbearing potential/Contraception in the males and females
Empliciti should not be used in women of childbearing potential, unless the clinical condition of the woman requires treatment with elotuzumab. Women of childbearing potential should use effective contraception during and for 120 days following treatment.

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4.8 Undesirable effects

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Tabulated list of adverse reactions
Adverse reactions reported in 682 patients with multiple myeloma who were treated with elotuzumab in 8 clinical trials are presented in Table 5.

These reactions are presented by system organ class and by frequency. Frequencies are defined as: very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1,000 to < 1/100); rare (≥ 1/10,000 to < 1/1,000); very rare (< 1/10,000); and not known (cannot be estimated from available data). Within each frequency grouping, adverse reactions are presented in the order of decreasing seriousness.

Table 5: Adverse reactions in patients with multiple myeloma treated with Empliciti

System Organ Class	Adverse reactions	Frequency overall	Grade 3/4 frequency
Infections and infestations	Pneumonia[a]	Very common	Common
	Herpes ~~zoster~~[a] zoster[b]	Common	Uncommon
	Upper respiratory tract infection	Very common	Common
	Nasopharyngitis	Very common	Not known~~None reported~~
	~~Pneumonia[b]~~	~~Very common~~	~~Common~~
	~~Upper respiratory tract infection~~	~~Very common~~	~~Common~~
Blood and lymphatic system disorders	Lymphopenia[c]	Very common	Common
	Leukopenia	Common	Common
Immune system disorders	Anaphylactic reaction	Uncommon	Uncommon
	Hypersensitivity	Common	Uncommon
Psychiatric disorders	Mood altered	Common	Not known~~None reported~~
Nervous system disorders	Headache	Very common	Uncommon
	Hypoaesthesia	Common	Uncommon
Vascular disorders	Deep vein thrombosis	Common	Common
Respiratory, thoracic and mediastinal disorders	Cough[d]	Very common	Uncommon
	Oropharyngeal pain	Common	Not known~~None reported~~
Gastrointestinal disorders	Diarrhoea	Very common	Common
Skin and subcutaneous tissue disorders	Night sweats	Common	Not known~~None reported~~
General disorders and administration site conditions	Chest pain	Common	Common
	Fatigue	Very common	Common
	Pyrexia	Very common	Common
Investigations	Weight decreased	Very common	Uncommon
Injury, poisoning and procedural complications	Infusion related reaction	Common	Uncommon

[a] 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.

[b] The term herpes zoster is a grouping of the following terms: herpes zoster, oral herpes, and herpes virus infection.

~~[b] 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.~~

[c] The term lymphopenia includes the following terms: lymphopenia and lymphocyte count decreased.

[d] The term cough includes the following terms: cough, productive cough, and upper airway cough syndrome.

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