B. PACKAGE LEAFLET

Package leaflet: Information for the user

Empliciti 300 mg powder for concentrate for solution for infusion
Empliciti 400 mg powder for concentrate for solution for infusion

elotuzumab

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, or pharmacist or nurse.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Empliciti is and what it is used for

Empliciti contains the active substance elotuzumab, which is a monoclonal antibody, a type of protein designed to recognise and attach to a specific target substance in the body. Elotuzumab attaches to a target protein called SLAMF7. SLAMF7 is found in large amounts on the surface of multiple myeloma cells and on certain cells of your immune system (natural killer cells). When elotuzumab binds to SLAMF7 on the multiple myeloma or natural killer cells, it stimulates your immune system to attack and destroy the multiple myeloma cells.

Empliciti is used to treat multiple myeloma (a cancer of the bone marrow) in adults. Empliciti will be given to you together with lenalidomide and dexamethasone or together with pomalidomide and dexamethasone. Multiple myeloma is a cancer of a type of white blood cell called plasma cells. These cells divide out of control and collect in the bone marrow. This results in damage to the bones and kidneys.

Empliciti is used if your cancer has not responded to, or has come back after certain treatments.

2. What you need to know before you use Empliciti

You should not be given Empliciti
- if you are allergic to elotuzumab or any of the other ingredients of this medicine (listed in section 6 “Contents of the pack and other information”). Talk to your doctor if you are not sure.

Warnings and precautions
Infusion related reaction
Tell your doctor or nurse straight away if you get any of the infusion related reactions listed at the top of section 4. These side effects mostly occur during or after the infusion of the first dose. You will be monitored for signs of such effects during and after the infusion.

Depending on the seriousness of the infusion related reactions, you may require additional treatment to prevent complications and reduce your symptoms, or your infusion of Empliciti may be interrupted. When the symptoms go away or improve, the infusion can be continued more slowly and speeded up

gradually if the symptoms do not recur. Your doctor may decide not to continue Empliciti treatment if you have a strong infusion related reaction.

Before each infusion of Empliciti, you will be given medicines to reduce infusion related reaction (see section 3 "How to use Empliciti, Medicines given before each infusion").

Before starting treatment with Empliciti, you must also read the package leaflet warnings and precautions of all medicines to be taken in combination with Empliciti for information related to these medicines. When lenalidomide is used, particular attention to pregnancy testing and prevention requirements is needed (see "Pregnancy and breast-feeding" in this section).

Children and adolescents
Empliciti is not recommended for use in children and adolescents aged under 18 years.

Other medicines and Empliciti
Tell your doctor if you are taking, have recently taken, or might take any other medicines.

Pregnancy and breast-feeding
For women taking Empliciti
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine.

You should not use Empliciti if you are pregnant, unless your doctor specifically recommends it. The effects of Empliciti in pregnant women or its possible harm to an unborn baby are unknown.
- You must use effective contraception while you are being treated with Empliciti and for 120 days after stopping treatment, if there is any chance you could become pregnant.
- If you become pregnant while using Empliciti, tell your doctor.

When Empliciti is given in combination with lenalidomide or pomalidomide, you must follow the pregnancy prevention programme for lenalidomide or pomalidomide respectively (see package leaflet for lenalidomide or pomalidomide). **Lenalidomide and pomalidomide are expected to be harmful for an unborn baby.**

It is not known, whether elotuzumab passes into breast milk or if there is any risk to the breast-fed infant. Elotuzumab will be given in combination with lenalidomide or pomalidomide and breast-feeding should be stopped because of the use of lenalidomide or pomalidomide.

For men taking Empliciti
You should use a condom while taking Empliciti and for 180 days after stopping treatment to ensure your partner does not become pregnant.

Driving and using machines
Empliciti is unlikely to affect your ability to drive or use machines. However, if you get an infusion related reaction (fever, chills, high blood pressure see section 4 "Possible side effects"), do not drive, cycle or use machines until the reaction stops.

Empliciti contains sodium
Tell your doctor if you are on a low-sodium (low-salt) diet before you are given Empliciti. This medicine contains 3.92 mg sodium (main component of cooking/table salt) per 300 mg vial or 5.23 mg sodium per 400 mg vial. This is equivalent to 0.2% or 0.3% respectively, of the recommended maximum daily dietary intake of sodium for an adult.

3. How to use Empliciti

How much Empliciti is given
The amount of Empliciti you will be given will be calculated based on your body weight.

How Empliciti is given
You will receive Empliciti under the supervision of an experienced healthcare professional. It will be given into a vein (intravenously) as a drip (infusion) over several hours.

Empliciti is taken in treatment cycles that are 28 days (4 weeks) long in combination with other medicines used to treat multiple myeloma.
When given in combination with lenalidomide and dexamethasone, Empliciti is given as follows:
- In cycles 1 and 2, once weekly on days 1, 8, 15, and 22.
- In cycles 3 and beyond, once every 2 weeks on days 1 and 15.

When given in combination with pomalidomide and dexamethasone, Empliciti is given as follows:
- In cycles 1 and 2, once weekly on days 1, 8, 15, and 22.
- In cycles 3 and beyond, once every 4 weeks on day 1.

Your doctor will continue to treat you with Empliciti for as long as the disease improves or remains stable and side effects are tolerable.

Medicines given before each infusion
You must receive the following medicines before each infusion of Empliciti to help reduce possible infusion related reactions:
- medicine to reduce an allergic reaction (an anti-histamine)
- medicine to reduce inflammation (dexamethasone)
- medicine to reduce pain and fever (paracetamol)

If you miss a dose of Empliciti
Empliciti is used in combination with other medicines for multiple myeloma. If any medicine in the treatment is delayed, interrupted, or discontinued, your doctor will decide how your treatment should be continued.

If you are given too much Empliciti
As Empliciti will be given to you by a healthcare professional, it is unlikely you will be given too much. In the unlikely case of an overdose, your doctor will monitor you for side effects.

If you stop using Empliciti
Stopping your treatment with Empliciti may stop the effect of the medicine. Do not stop treatment unless you have discussed this with your doctor.

If you have any further questions on the use of this medicine, ask your doctor.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. Your doctor will discuss these with you and will explain the risks and benefits of your treatment.

The following side effects have been reported in clinical trials with elotuzumab:

Infusion related reactions
Empliciti has been associated with infusion related reactions (see section 2 “Warnings and precautions”). **Tell your doctor or nurse straight away if you feel unwell during infusion.** Below is a list of typical symptoms associated with infusion related reactions:
- Fever
- Chills
- High blood pressure

Other symptoms may occur as well. Your doctor may consider slowing the Empliciti infusion or interrupting it to manage these symptoms.

Other side effects

Very common (may affect more than 1 in 10 people)
- Fever
- Sore throat
- Pneumonia
- Weight decrease
- Low white blood cell count
- Cough
- Common cold
- Headache
- Diarrhoea
- Feeling tired or weak

Common (may affect up to 1 in 10 people)
- Chest pain
- Blood clots in the veins (thrombosis)
- Painful skin rash with blisters (shingles, zona)
- Night sweats
- Mood changes
- Decreased sensitivity, especially in the skin
- Allergic reactions (hypersensitivity)
- Pain in the mouth/throat region/sore throat

Uncommon (may affect up to 1 in 100 people)
- Sudden life-threatening allergic reaction (anaphylactic reaction)

Tell your doctor immediately if you get any of the side effects listed above. Do not try to treat your symptoms with other medicines.

Reporting of side effects
If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Empliciti

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the vial label and carton after EXP. The expiry date refers to the last day of that month.

Store in a refrigerator (2°C - 8°C).
Do not freeze.
Store in the original package in order to protect from light.

After reconstitution, the reconstituted solution should be transferred from the vial to the infusion bag immediately.

After dilution, the infusion must be completed within 24 hours of preparation. The product should be used immediately. If not used immediately, the solution for infusion may be stored in the refrigerator (2 °C - 8 °C) for up to 24 hours.

Any unused medicine or waste material should be disposed of in accordance with local requirements.

6. Contents of the pack and other information

What Empliciti contains

- The active substance is elotuzumab.
  Each vial of powder contains either 300 mg or 400 mg of elotuzumab.
  After reconstitution, each mL of concentrate contains 25 mg of elotuzumab.

- The other ingredients (excipients) are sucrose, sodium citrate (see section 2 "Empliciti contains sodium"), citric acid monohydrate, and polysorbate 80 (E433).

What Empliciti looks like and contents of the pack

Empliciti powder for concentrate for solution for infusion (powder for concentrate) is a white to off white whole or fragmented cake provided in a glass vial.

Empliciti is available in packs containing 1 vial.

Marketing Authorisation Holder
Bristol-Myers Squibb Pharma EEIG
Plaza 254
Blanchardstown Corporate Park 2
Dublin 15, D15 T867
Ireland

Manufacturer
CATALENT ANAGNI S.R.L.
Loc. Fontana del Ceraso snc
Strada Provinciale Casilina, 41
03012 ANAGNI (FR)
Italy

Swords Laboratories Unlimited Company t/a Bristol-Myers Squibb Cruiserath Biologics
Cruiserath Road, Mulhuddart
Dublin 15, D15 H6EF
Ireland

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The following information is intended for healthcare professionals only:

<u>Preparation and administration of Empliciti</u>

Calculating the dose
Calculate the dose (mg) and determine the number of vials needed for the dose (10 mg/kg or 20 mg/kg) based on body weight (bw). More than one vial of Empliciti may be needed to give the total dose for the patient.

- The total elotuzumab dose in mg equals the patient's bw in kg multiplied by the elotuzumab dose (10 or 20 mg/kg).

Reconstitution of vials
Aseptically reconstitute each Empliciti vial with a syringe of adequate size and an 18 gauge or smaller needle as shown in Table 1. A slight back pressure may be experienced during administration of the water for injections, which is considered normal.

Table 1: Reconstitution instructions

Strength	Amount of water for injections, required for reconstitution	Final volume of reconstituted Empliciti in the vial	Post-reconstitution concentration
300 mg vial	13.0 mL	13.6 mL	25 mg/mL
400 mg vial	17.0 mL	17.6 mL	25 mg/mL

Hold the vial upright and swirl the solution by rotating the vial to dissolve the lyophilised cake. Then 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 lyophilised 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 solution is colourless to slightly yellow and clear to very opalescent. Empliciti should be inspected visually for particulate matter and discolouration prior to administration. Discard the solution if any particulate matter or discolouration is observed.

Preparation of the solution for infusion
The reconstituted solution should be diluted with sodium chloride 9 mg/mL (0.9%) solution for injection or 5% glucose injection to obtain a final infusion concentration range between 1 mg/mL and 6 mg/mL. The volume of sodium chloride 9 mg/mL (0.9%) solution for injection or 5% glucose injection should be adjusted so as to not exceed 5 mL/kg of bw at any given dose of Empliciti.

Calculate the volume (mL) of diluent (either sodium chloride 9 mg/mL (0.9%) solution for injection or 5% glucose injection) needed to make up the solution for infusion for the patient.

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. Each vial contains a slight overfill to ensure sufficient extractable volume.

Transfer the withdrawn volumes of all vials needed according to the calculated dose for this patient into one single infusion bag made of polyvinyl chloride or polyolefin containing the calculated volume of diluent. Gently mix the infusion by manual rotation. Do not shake.

Empliciti is for single use only. Discard any unused portion left in the vial.

Administration
The entire Empliciti infusion should be administered with an infusion set and a sterile, non-pyrogenic, low-protein-binding filter (with a pore size of 0.2-1.2 µm) using an automated infusion pump.

Empliciti infusion is compatible with:
- PVC and polyolefin containers
- PVC infusion sets
- polyethersulfone and nylon in-line filters with pore sizes of 0.2 µm to 1.2 µm.

Infusion rate for Empliciti 10 mg/kg bw
Empliciti at 10 mg/kg bw dose should be initiated at an infusion rate of 0.5 mL/min. If well tolerated, the infusion rate may be increased stepwise as described in Table 2. The maximum infusion rate should not exceed 5 mL/min.

Table 2: Infusion rate for Empliciti 10 mg/kg bw

Cycle 1, Dose 1		Cycle 1, Dose 2		Cycle 1, Dose 3 and 4 and all subsequent Cycles
Time interval	**Rate**	**Time interval**	**Rate**	**Rate**
0 - 30 min	0.5 mL/min	0 - 30 min	3 mL/min	5 mL/min*
30 - 60 min	1 mL/min	≥ 30 min	4 mL/min*	
≥ 60 min	2 mL/min*	-	-	

* Continue this rate until infusion is completed.

Infusion rate for Empliciti 20 mg/kg bw
Empliciti at 20 mg/kg bw dose should be initiated at an infusion rate of 3 mL/min. If well tolerated, the infusion rate maybe increased in a stepwise fashion as described in Table 3. The maximum infusion rate should not exceed 5 mL/min.
Patients who have escalated to 5 mL/min at 10 mg/kg bw dose must decrease the rate to 3 mL/min at the first infusion at 20 mg/kg bw.

Table 3: Infusion rate for Empliciti 20 mg/kg bw

Dose 1		Dose 2 and all subsequent doses
Time interval	**Rate**	**Rate**
0-30 min	3 mL/min	5 mL/min*
≥ 30 min	4 mL/min*	

* Continue this rate until infusion is completed.

The Empliciti infusion should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2°C − 8°C protected from light. Do not freeze the reconstituted or diluted solution. The solution for infusion may be stored for a maximum of 8 hours of the total 24 hours at 20°C − 25°C and room light. This 8-hour period should be inclusive of the product administration period.

Disposal
Do not store any unused portion of the infusion solution for reuse. Any unused medicine or waste material should be disposed of in accordance with local requirements.