Hepatic impairment
No formal studies have been conducted to evaluate the effect of hepatic impairment on the PK of necitumumab. Based on the results of the population pharmacokinetic analysis, hepatic status (as assessed by alanine aminotransferase, aspartate transaminase and total bilirubin) had no significant effect on the pharmacokinetics of necitumumab.

5.3 Preclinical safety data

Dose dependent reversible skin toxicity was observed in the 26-week monkey study. The skin effects were consistent with the known class effects of EGFR inhibitors.

Specific animal studies to test necitumumab for carcinogenic potential or potential to impair fertility have not been performed. The risk of fertility impairment is unknown. However, no adverse effects on male or female reproductive organs were observed in monkeys treated for 26 weeks with necitumumab.

Human IgG1 is known to cross the placenta; therefore, necitumumab has the potential to be transmitted from the mother to the developing foetus. No animal studies have been specifically conducted to evaluate the effect of necitumumab on reproduction and foetal development; however, based on its mechanism of action and animal models where EGFR expression is disrupted, necitumumab may cause foetal harm or developmental anomalies.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium citrate dihydrate (E331)
Citric acid anhydrous (E330)
Sodium chloride
Glycine (E640)
Mannitol (E421)
Polysorbate 80 (E433)
Water for injections

6.2 Incompatibilities

Portrazza infusions should not be administered or mixed with glucose solutions. This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.

6.3 Shelf life

Unopened vial
2 years.

After dilution
When prepared as directed, infusion solutions of Portrazza contain no antimicrobial preservatives.

It is recommended that the prepared dosing solution be used immediately in order to minimize the risk of microbial contamination. If not used immediately, the prepared necitumumab dosing solution must be stored at 2°C to 8°C for a duration not to exceed 24 hours, or may be held at 9°C to 25°C for up to 4 hours. Store protected from light. Brief exposure to ambient light is acceptable while preparation and administration is taking place.

6.4 Special precautions for storage

Store in a refrigator (2˚C - 8˚C).
Do not freeze.
Keep the vial in the outer carton in order to protect from light.

For storage conditions after dilution of the medicinal product, see section 6.3.

6.5 Nature and contents of container

50 mL solution in a vial (Type I glass) with a chlorobutyl elastomer stopper, an aluminium seal and a polypropylene cap.

Pack of 1 vial.

6.6 Special precautions for disposal and other handling

Prepare the infusion solution using aseptic technique to ensure the sterility of the prepared solution.

Each vial is intended for single use only. Inspect the contents of the vials for particulate matter and discolouration. The concentrate for solution for infusion must be clear to slightly opalescent and colourless to slightly yellow prior to dilution. If particulate matter or discolouration is identified, discard the vial.

Vials contain 800 mg as a 16 mg/mL solution of necitumumab; one 50 mL vial contains the complete dose. Only use sodium chloride 9 mg/mL (0.9 %) solution for injection as a diluent.

<u>To administer using pre-filled intravenous infusion containers</u>
Aseptically remove 50 mL of sodium chloride 9 mg/mL (0.9 %) solution for injection from the prefilled 250 mL container and transfer 50 mL of necitumumab medicinal product into the container to bring the final volume in the container back to 250 mL. Gently invert the container to mix. DO NOT FREEZE OR SHAKE the infusion solution. DO NOT dilute with other solutions or co-infuse with other electrolytes or medicines.

<u>To administer using empty intravenous infusion containers</u>
Aseptically transfer 50 mL of necitumumab medicinal product into an empty intravenous container and add 200 mL of sodium chloride 9 mg/mL (0.9 %) solution for injection to the container to bring the total volume to 250 mL. Gently invert the container to mix. DO NOT FREEZE OR SHAKE the infusion solution. DO NOT dilute with other solutions or co-infuse with other electrolytes or medicines.

Administer via an infusion pump. A separate infusion line must be used and the line must be flushed with sodium chloride 9 mg/mL (0.9 %) solution for injection at the end of the infusion.

Parenteral medicinal products should be inspected visually for particulate matter prior to administration. If particulate matter is identified, discard the infusion solution.

Discard any unused portion of necitumumab left in a vial, as the product contains no antimicrobial preservatives.

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

7. MARKETING AUTHORISATION HOLDER

Eli Lilly Nederland B.V.
Papendorpseweg 83
3528 BJ Utrecht
The Netherlands

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/15/1084/001

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 15 February 2016

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu.

ANNEX II

A. MANUFACTURER(S) OF THE BIOLOGICAL ACTIVE SUBSTANCE(S) AND MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURER(S) OF THE BIOLOGICAL ACTIVE SUBSTANCE(S) AND MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer(s) of the biological active substance(s)
ImClone Systems LLC
33 ImClone Drive
Branchburg
New Jersey
NJ 08876
United States

Name and address of the manufacturer(s) responsible for batch release
Lilly, S.A.
Avda. de la Industria, 30
Alcobendas
Madrid
28108
Spain

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to restricted medical prescription (see Annex I: Summary of Product Characteristics, section 4.2).

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports**

The requirements for submission of periodic safety update reports for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.
The marketing authorisation holder shall submit the first periodic safety update report for this product within 6 months following authorisation.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk Management Plan (RMP)**

The MAH shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the Marketing Authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

- **Additional risk minimisation measures**

Prior to launch of Portrazza (necitumumab) in each Member State the MAH must agree about the content and format of the educational material, including communication media, distribution modalities, and any other aspects of the programme, with the National Competent Authority.
The MAH shall ensure that in each Member State where Portrazza (necitumumab) is marketed, all physicians (i.e. oncologists) are notified about the key conditions for the safe use of necitumumab. The materials will address the risks concerning arterial / venous thromboembolic events and cardiorespiratory disorders.

Key elements of the physician educational material:

- Importance of assessing the risks before starting treatment with necitumumab
- Description of thromboembolic events including incidence rates from clinical trials
- Advice that patients and physicians should be aware of signs and symptoms of thromboembolism. Patients should be instructed to seek medical care if they develop symptoms of thromboembolism such as shortness of breath, chest pain, arm or leg swelling.
- The need to carefully consider use of necitumumab in patients with a history of thromboembolic events or pre-existing risk factors for thromboembolic events
- Information on relative risk of VTE or ATE in patients with a history of VTE or ATE
- Advice that necitumumab should not be administered to patients with multiple risk factors for thromboembolic events unless the benefits outweigh the risks to the patient
- The need to consider thromboprophylaxis after careful assessment of a patient's risk factors
- Discontinuation of necitumumab in patients who experience a VTE or ATE should be considered after a thorough benefit risk assessment for the individual patient.
- Description of cardiorespiratory disorders including incidence rates from clinical trials
- Information that the incremental risk of cardiopulmonary arrest or sudden death in patients with a history of coronary artery disease, congestive heart failure, or arrhythmias as compared to those without these comorbid conditions is not known.
- Instruction for healthcare professionals to read the materials in conjunction with the SmPC.

The physician educational material package should also contain:

- The Summary of Product Characteristics
- Patient Information Leaflet

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON

1. NAME OF THE MEDICINAL PRODUCT

Portrazza 800 mg concentrate for solution for infusion
necitumumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One vial of 50 mL contains 800 mg necitumumab (16 mg/mL).

3. LIST OF EXCIPIENTS

Excipients: sodium citrate dihydrate, citric acid anhydrous, sodium chloride, glycine, mannitol, polysorbate 80 and water for injections. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Concentrate for solution for infusion

800 mg/ 50 mL
1 vial

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For intravenous use after dilution.
For single use only.
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Do not shake.

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.
Do not freeze.
Keep the vial in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Eli Lilly Nederland B.V.
Papendorpseweg 83
3528 BJ Utrecht
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/15/1084/001

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC:
SN:
NN:

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

VIAL LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Portrazza 800 mg sterile concentrate
necitumumab
For IV use after dilution.

2. METHOD OF ADMINISTRATION

Read the package leaflet before use.

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

800 mg/50 mL

6. OTHER

B. PACKAGE LEAFLET

Package leaflet: Information for the user

Portrazza 800 mg concentrate for solution for infusion
necitumumab

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you are given 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.
- If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Portrazza is and what it is used for

Portrazza contains the active substance necitumumab, which belongs to a group of substances called monoclonal antibodies.

Necitumumab recognises and binds specifically to a protein on the surface of some cancer cells. The protein is known as epidermal growth factor receptor (EGFR). Other body proteins (called growth factors) can attach to the EGFR and stimulate the cancer cell to grow and divide. Necitumumab hinders other proteins from binding to the EGFR and thus prevents the cancer cell from growth and division.

Portrazza is used in combination with other anti-cancer medicines for the treatment of adults with certain type of lung cancer at an advanced stage (squamous non-small cell lung cancer), whose cancer cells have the EGFR protein on their surface. The anti-cancer medicines it is combined with are gemcitabine and cisplatin.

2. What you need to know before you are given Portrazza

You must not be given Portrazza
- if you have ever had a severe allergic reaction to necitumumab or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions
Talk to your doctor or nurse **immediately** if any of the following applies to you (or you are not sure) **during or after treatment** with Portrazza:

– **Blood clots in the arteries or the veins**
Portrazza can cause blood clots in your arteries or your veins. Symptoms may include swelling, pain and tenderness of the limb, difficulty breathing, chest pain, or an abnormal heartbeat and

discomfort. Your doctor will discuss with you whether you need any preventive measures. See also section 4 for the symptoms of blood clots.

- **Cardiorespiratory disorders**
  Cases of cardiorespiratory disorders and unexplained death were observed in patients treated with Portrazza in combination with gemcitabine and cisplatin and in patients treated with gemcitabine and cisplatin alone. The causes of these deaths and their relationship to treatment were not always known. Portrazza may increase this risk. Your doctor will discuss this with you.

- **Infusion-related reaction**
  Infusion-related reactions may occur during treatment with Portrazza. Such reactions may be allergic. Your doctor will discuss with you whether you need any preventive measures or early treatment. Your doctor or nurse will check for side effects during your infusion. If you have a severe infusion-related reaction, your doctor may recommend adjusting the dose of Portrazza, or stop your treatment with Portrazza. See section 4 for more details about infusion-related reactions which may occur during or after the infusion.

- **Skin reactions**
  Portrazza may cause side effects involving the skin. Your doctor will discuss with you whether you need any preventive measures or early treatment. If you have a severe skin reaction, your doctor may recommend adjusting the dose of Portrazza, or stop your treatment with Portrazza. See section 4 for more details about skin reactions.

- **Blood levels of magnesium, calcium, potassium and phosphate**
  During treatment, your doctor will check your blood periodically for levels of several substances such as magnesium, calcium, potassium and phosphate. If these levels are too low, your doctor may prescribe appropriate supplements.

- **Infections**
  If you have signs of infection before start of treatment please tell your doctor.

Children and adolescents
Portrazza should not be given to patients under the age of 18 years because there is no information about how it works in this age group.

Other medicines and Portrazza
Tell your doctor if you are taking, have recently taken or might take any other medicines. This includes medicines obtained without a prescription and herbal medicines.

Pregnancy and breast-feeding
Before starting treatment you must tell your doctor if you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby.

Avoid getting pregnant while receiving this medicine and for at least 3 months after the last dose of Portrazza as this medicine may potentially cause harm to your unborn child. Talk to your doctor about the best contraception for you.

Do not breast-feed your baby during treatment with Portrazza and for at least 4 months after you receive the last dose, as this medicine may harm the growth and development of your baby.

Driving and using machines
If you experience any symptoms affecting your ability to concentrate and react, do not drive or use machines until the effect goes away.

Portrazza contains sodium
This medicine contains 76 mg sodium per dose. This should be taken into consideration by patients on a controlled sodium diet.

3. How you are given Portrazza

A doctor experienced in the use of anti-cancer medicines will supervise your Portrazza therapy.

Premedication
You may be given medicines to reduce the risk of an infusion-related reaction or a skin reaction before you receive Portrazza.

Dose and administration
The recommended dose of Portrazza is 800 mg on days 1 and 8 of each 3-week cycle. Portrazza is given in combination with the medicines gemcitabine and cisplatin for up to 6 cycles and then it is given on its own. The number of infusions that you receive will depend on how and for how long you respond to treatment with Portrazza. Your doctor will discuss this with you.

This medicine is given as an intravenous (into a vein) infusion via a drip. The drip lasts about 60 minutes.

Detailed instructions for your doctor or your nurse on how to prepare Portrazza infusion are included at the end of this package leaflet (see 'Handling instructions').

Dose adjustments
During each infusion, your doctor or nurse will check for side effects. If you have an infusion-related reaction during treatment, your drip will be slowed down and future doses will also be given more slowly. The infusion duration should not exceed 2 hours. See also section 2 under "Warnings and precautions".

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

The important side effects of Portrazza are skin reactions and blood clots in the veins.

Seek medical help immediately if you experience any of the following:

Blood clots in the veins
Venous blood clots are likely to occur in approximately 8 out of 100 patients. In approximately 4 out of 100 patients these side effects are likely to be severe. They can lead to a blockage of a blood vessel in the leg. Symptoms may include swelling, pain and tenderness of the limb. Blood clots can also lead to a blockage in the blood vessels of the lung. Symptoms may include difficulty breathing, chest pain, or an abnormal heartbeat and discomfort.

Skin reactions
Skin reactions may occur in approximately 80 out of 100 patients who take Portrazza and are usually mild to moderate. In approximately 5 out of 100 patients these skin reactions are likely to be severe. Symptoms of severe skin reactions may include acne-like skin conditions and skin rash. The skin rash commonly resembles acne and often involves the face, upper chest and back, but can affect any area of the body. Most of these side effects usually disappear over time after the end of Portrazza therapy.

Other side effects include:

Very common (may affect more than 1 in 10 people):
- itching; dry skin; scaling; nail disorders (skin reactions)
- vomiting
- fever or high temperature (pyrexia)
- decreased weight
- mouth ulcers and cold sores (stomatitis)

Common (may affect up to 1 in 10 people)
- headache
- coughing up blood (haemoptysis)
- nosebleed (epistaxis)
- strange tastes; metallic taste (dysgeusia)
- eye inflammation (conjunctivitis)
- blood clots in the arteries
- urinary tract infection (bladder and/or kidneys)
- pain when passing urine (dysuria)
- difficulty in swallowing (dysphagia)
- muscle spasms
- inflammation of veins in the legs (phlebitis)
- allergic reactions
- pain in your mouth and throat (oropharyngeal pain)

Portrazza may also cause changes in the results of blood tests. These include low blood levels of magnesium, calcium, potassium or phosphate.

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 national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Portrazza

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 outer carton and vial label after EXP. The expiry date refers to the last day of that month.

Store in a refrigerator (2 °C – 8 °C).
Do not freeze.
Keep the vial in the outer carton in order to protect from light.

Infusion solution: After dilution and preparation, the medicine must 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 to 8 ºC, or up to 4 hours at 9 ºC to 25 ºC. Do not freeze or shake the infusion solution. Do not administer the solution if you notice any particulate matter or discoloration.

This medicine is for single use only.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Portrazza contains
- The active substance is necitumumab. Each millilitre of the concentrate for solution for infusion contains 16 mg of necitumumab.
  Each 50 mL vial contains 800 mg of necitumumab.
- The other ingredients are sodium citrate dihydrate (E331), citric acid anhydrous (E330), sodium chloride *(see section 2 "Portrazza contains sodium")*, glycine (E640), mannitol (E421), polysorbate 80 (E433) and water for injections.

What Portrazza looks like and contents of the pack
Portrazza 800 mg concentrate for solution for infusion (sterile concentrate) is a clear to slightly opalescent and colourless to slightly yellow liquid in a glass vial with a rubber stopper.

It is available in packs of:
- 1 vial of 50 mL

Marketing Authorisation Holder
Eli Lilly Nederland B.V., Papendorpseweg 83, 3528 BJ Utrecht, The Netherlands

Manufacturer
Lilly S.A., Avda de la Industria, 30, Alcobendas, Madrid, 28108, Spain

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

Belgique/België/Belgien
Eli Lilly Benelux S.A./N.V.
Tél/Tel: + 32-(0)2 548 84 84

България
ТП "Ели Лили Недерланд" Б.В. - България
тел. + 359 2 491 41 40

Česká republika
ELI LILLY ČR, s.r.o.
Tel: + 420 234 664 111

Danmark
Eli Lilly Danmark A/S
Tlf: +45 45 26 60 00

Deutschland
Lilly Deutschland GmbH
Tel. + 49-(0) 6172 273 2222

Eesti
Eli Lilly Holdings Limited Eesti filiaal
Tel: +372 6 817 280

Ελλάδα
ΦΑΡΜΑΣΕΡΒ-ΛΙΛΛΥ Α.Ε.Β.Ε.
Τηλ: +30 210 629 4600

España
Lilly S.A.
Tel: + 34-91 663 50 00

Lietuva
Eli Lilly Holdings Limited atstovybė
Tel. +370 (5) 2649600

Luxembourg/Luxemburg
Eli Lilly Benelux S.A./N.V.
Tél/Tel: + 32-(0)2 548 84 84

Magyarország
Lilly Hungária Kft.
Tel: + 36 1 328 5100

Malta
Charles de Giorgio Ltd.
Tel: + 356 25600 500

Nederland
Eli Lilly Nederland B.V.
Tel: + 31-(0) 30 60 25 800

Norge
Eli Lilly Norge A.S.
Tlf: + 47 22 88 18 00

Österreich
Eli Lilly Ges.m.b.H.
Tel: + 43-(0) 1 711 780

Polska
Eli Lilly Polska Sp. z o.o.
Tel: +48 22 440 33 00

France
Lilly France SAS
Tél: +33-(0) 1 55 49 34 34

Hrvatska
Eli Lilly Hrvatska d.o.o.
Tel: +385 1 2350 999

Ireland
Eli Lilly and Company (Ireland) Limited
Tel: + 353-(0) 1 661 4377

Ísland
Icepharma hf.
Sími + 354 540 8000

Italia
Eli Lilly Italia S.p.A.
Tel: + 39- 055 42571

Κύπρος
Phadisco Ltd
Τηλ: +357 22 715000

Latvija
Eli Lilly Holdings Limited pārstāvniecība Latvijā
Tel: +371 67364000

Portugal
Lilly Portugal Produtos Farmacêuticos, Lda
Tel: + 351-21-4126600

România
Eli Lilly România S.R.L.
Tel: + 40 21 4023000

Slovenija
Eli Lilly farmacevtska družba, d.o.o.
Tel: +386 (0)1 580 00 10

Slovenská republika
Eli Lilly Slovakia, s.r.o.
Tel: + 421 220 663 111

Suomi/Finland
Oy Eli Lilly Finland Ab
Puh/Tel: + 358-(0) 9 85 45 250

Sverige
Eli Lilly Sweden AB
Tel: + 46-(0) 8 7378800

United Kingdom
Eli Lilly and Company Limited
Tel: + 44-(0) 1256 315000

This leaflet was last revised in <{**month YYYY**}>.

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu.

Handling instructions
Portrazza 800 mg
concentrate for solution for infusion
necitumumab

The following information is intended for healthcare professionals only:

Prepare the infusion solution using the aseptic technique to ensure the sterility of the prepared solution.

Each vial is intended for single use only. Inspect the contents of the vials for particulate matter and discolouration. The concentrate for solution for infusion must be clear to slightly opalescent and colourless to slightly yellow prior to dilution. If particulate matter or discolouration is identified, discard the vial.

Vials contain 800 mg as a 16 mg/mL solution of necitumumab; one 50 mL vial contains the complete dose. Only use sodium chloride 9 mg/mL (0.9%) solution for injection as a diluent.

To administer using pre-filled intravenous infusion containers
Aseptically remove 50 mL of sodium chloride 9 mg/mL (0.9%) solution for injection from the prefilled 250 mL container and transfer 50 mL of necitumumab medicine into the container to bring the final volume in the container back to 250 mL. Gently invert the container to mix. DO NOT FREEZE OR SHAKE the infusion solution. DO NOT dilute with other solutions or co-infuse with other electrolytes or medicines.

To administer using empty intravenous infusion containers
Aseptically transfer 50 mL of necitumumab medicine into an empty intravenous container and add 200 mL of sterile sodium chloride 9 mg/mL (0.9%) solution for injection to the container to bring the total volume to 250 mL. Gently invert the container to mix. DO NOT FREEZE OR SHAKE the infusion solution. DO NOT dilute with other solutions or co-infuse with other electrolytes or medicines.

Administer via an infusion pump. A separate infusion line must be used and the line must be flushed with sodium chloride 9 mg/mL (0.9%) solution for injection at the end of the infusion.

Parenteral medicines should be inspected visually for particulate matter prior to administration. If particulate matter is identified, discard the infusion solution.

Discard any unused portion of necitumumab left in a vial, as the product contains no antimicrobial preservatives.

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