Package leaflet: Information for the user

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Merck Serono

MERCK

Erbitux® 5 mg/mL solution for infusion

Cetuximab

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.
- 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 Erbitux is and what it is used for

What Erbitux is

Erbitux contains cetuximab, a monoclonal antibody. Monoclonal antibodies are proteins that specifically recognise and bind to other unique proteins called antigens. Cetuximab binds to the epidermal growth factor receptor (EGFR), an antigen on the surface of certain cancer cells. EGFR activates proteins called RAS. RAS proteins play an important role in the EGFR pathway - a complex signalling cascade which is involved in the development and progression of cancer. As a result of this binding, the cancer cell can no longer receive the messages it needs for growth, progression and metastasis.

What Erbitux is used for

Erbitux is used to treat two different types of cancer:

- metastatic cancer of the large intestine. In these patients, Erbitux is used alone or in combination with other anticancer medicines.
- a certain type of cancer of the head and neck (squamous cell cancer). In these patients, Erbitux is used in combination with radiation therapy or with other anticancer medicines.

2. What you need to know before you use Erbitux

Do not use Erbitux

Do not use Erbitux if you have ever had a severe hypersensitivity (allergic) reaction to cetuximab.

Before starting treatment for metastatic cancer of the large intestine your doctor will test your cancer cells if they contain the normal (wild-type) or mutant form of RAS. You must not receive Erbitux in combination with other anticancer treatment containing oxaliplatin if your cancer cells contain the mutant form of RAS.

Warnings and precautions

Talk to your doctor before using Erbitux, if any of the following information is not clear.

Erbitux may cause infusion-related side effects. Such reactions may be allergic in nature. Please read 'Infusion-related side effects' in section 4 for details, as they may have serious consequences for you, including life-threatening conditions. These side effects normally occur during the infusion, within 1 hour afterwards, or sometimes also after this period. To recognise early signs of such effects, your condition will be checked regularly while you receive each infusion of Erbitux and for at least 1 hour afterwards.

You are more likely to experience severe allergic reactions if you are allergic to red meat, or tick bites or had positive results for certain antibodies (seen in a test). Your doctor will discuss appropriate measures with you.

Erbitux may cause side effects concerning the skin. Your doctor will discuss with you whether you may need any preventive measures or early treatment. Please also read 'Side effects concerning the skin' in section 4 for details, as some skin reactions may have serious consequences for you, including life-threatening conditions.

If you have heart problems, your doctor will discuss with you whether you can receive Erbitux in combination with other anticancer medicines, especially if you are 65 years of age or older.

Erbitux may cause side effects concerning the eyes. Please tell your doctor, if you have acute or worsening eye problems such as blurred vision, eye pain, red eyes and/or severe dry eye, if you have had such problems in the past or if you use contact lenses. Your doctor will discuss with you whether you need to consult a specialist.

If you receive Erbitux in combination with anticancer medicines including platinum, it is more likely that your white blood cell count may be reduced. Your doctor will therefore monitor your blood and general condition for signs of infection (see also 'Side effects in combination with other anticancer treatments' in section 4).

If you receive Erbitux in combination with other anticancer medicines, including fluoropyrimidines, it may be more likely that you experience heart problems which may be life-threatening. Your doctor will discuss with you whether you may need any particular supervision (see also 'Side effects in combination with other anticancer treatments' in section 4).

Children and adolescents

There is no relevant use of Erbitux in children and adolescents.

Other medicines and Erbitux

Tell your doctor if you are taking, have recently taken or might take any other medicines, including medicines obtained without a prescription.

Pregnancy

Tell your doctor if you are pregnant or if you are not using reliable contraception (speak to your doctor if you are not sure). Your doctor will then discuss with you the risks and benefits of using Erbitux in these situations.

Breast-feeding

Do not breast-feed your baby during the period over which you are being treated with Erbitux and for two months after the last dose.

Driving and using machines

Do not drive or use any tools or machines if you experience treatment-related symptoms that affect your ability to concentrate and react.

3. How to use Erbitux

A doctor experienced in the use of anticancer medicines will supervise your Erbitux therapy. During each infusion and for at least 1 hour afterwards, your condition will be checked regularly for early signs of a possible infusion-related side effect.

Pre-treatment

Before the first dose, you will receive an antiallergic medicine in order to reduce the risk of an allergic reaction. Your doctor will decide whether such pre-treatment is necessary for subsequent doses.

Dosage and administration

Erbitux is usually infused into a vein (given as a drip) once a week. Your doctor will calculate the correct dose of Erbitux for you because it depends on your body surface area. The first dose (400 mg/m^2 body surface area) is infused over a period of approximately 2 hours with an infusion rate not faster than 5 mg/min. Each subsequent dose (250 mg/m^2 body surface area) is infused in approximately 1 hour with an infusion rate not faster than 10 mg/min.

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

Duration of treatment

Erbitux is usually infused once a week. The duration of treatment may vary depending on your disease as well as from person to person and your doctor will therefore discuss with you how long you will receive Erbitux.

Combination with other anticancer treatments

If you receive Erbitux in combination with other anticancer medicines, these medicines must be administered at least 1 hour after the end of the Erbitux infusion.

If you receive Erbitux in combination with radiation therapy, treatment with Erbitux is usually started one week before radiation therapy.

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.

The main side effects of Erbitux are infusion-related side effects and side effects concerning the skin:

Infusion-related side effects

More than 10 out of 100 patients are likely to experience infusion-related side effects; in more than 1 out of 100 patients these side effects are likely to be severe. Such reactions may be allergic in nature. They normally occur during the infusion, within 1 hour afterwards, or sometimes also after this period.

Mild or moderate infusion-related side effects include:

- fever
- chills
- dizziness
- breathing difficulties

If such symptoms occur, please inform your doctor as soon as possible. Your doctor may consider reducing the infusion rate of Erbitux to manage these symptoms.

Severe infusion-related side effects include:

- severe breathing difficulties which develop rapidly
- hives
- fainting
- chest pain (a symptom of side effects on your heart)

If such symptoms occur, speak to a doctor immediately. These side effects may have serious consequences, in rare cases including life-threatening conditions, and require immediate attention. Treatment with Erbitux must then be stopped.

Side effects concerning the skin

More than 80 out of 100 patients are likely to experience side effects involving the skin. In about 15 out of 100 patients these skin reactions are likely to be severe. Most of these side effects develop within the first three weeks of treatment. They usually disappear over time after the end of Erbitux therapy.

Main side effects concerning the skin include:

- acne-like skin alterations
- itching
- dry skin
- scaling
- excessive growth of hair
- nail disorders, for example inflammation of the nail bed

In very rare cases (may affect up to 1 in 10,000 people) patients may experience blistering or peeling of the skin, which may indicate a severe skin reaction called "Stevens-Johnson syndrome". **If you experience these symptoms, please speak to a doctor immediately,** because these signs may have serious consequences including life-threatening conditions.

If you notice other extensive skin alterations, please inform your doctor as soon as possible because the Erbitux dose or the time between infusions may need to be changed. Your doctor will decide whether treatment has to be stopped if skin reactions reappear after several dose reductions.

If you notice that already affected areas of your skin get worse, speak to a doctor immediately, especially if you also experience general signs of infection such as fever and tiredness. These signs may indicate a skin infection, which may have serious consequences including life-threatening conditions.

Side effects concerning the lungs

In uncommon cases (may affect up to 1 in 100 people) patients may experience an inflammation of the lungs (called interstitial lung disease), which may have serious consequences including life-threatening conditions.

If you notice symptoms such as occurrence or worsening of breathing difficulties, speak to a doctor immediately, especially if you also experience cough or fever. Your doctor will decide whether treatment has to be stopped.

Other side effects

Very common side effects (may affect more than 1 in 10 people)

- inflammation of the lining of the intestine, mouth, and nose (in some cases severe), which may lead to nose bleeding in some patients
- decrease in blood levels of magnesium
- increase in blood levels of certain liver enzymes

Common side effects (may affect up to 1 in 10 people)

- headache
- tiredness
- irritation and redness of the eye
- diarrhoea
- drying out which may be due to diarrhoea or reduced fluid intake
- feeling sick
- vomiting
- loss of appetite, leading to weight decrease
- decrease in blood levels of calcium

Uncommon side effects (may affect up to 1 in 100 people)

- blood clots in the veins of the legs
- blood clots in the lungs
- inflammation of the eye lid or the front part of the eye

Side effects of which the frequency is not known (cannot be estimated from the available data)

- inflammation of the lining of the brain (aseptic meningitis)

Side effects in combination with other anticancer treatments

If you receive Erbitux in combination with other anticancer medicines, some of the side effects you may experience can also be related to the combination or the other medicines. Therefore, please make sure that you also read the package leaflet for the other medicines.

If you receive Erbitux in combination with anticancer medicines including platinum, it is more likely that your white blood cell count may be reduced. This may lead to infectious complications including life-threatening conditions, especially if you experience skin reactions, inflammation of the lining of the intestine and mouth or diarrhoea. **Therefore, if you experience general signs of infection such as fever and tiredness, please speak to a doctor immediately.**

If you receive Erbitux in combination with an anticancer medicine containing fluoropyrimidines, it is more likely that you experience the following side effects of this other medicine:

- chest pain
- heart attack
- heart failure
- redness and swelling of the palms of the hands or the soles of the feet which may cause the skin to peel (hand-foot syndrome)

If you receive Erbitux with radiation therapy, some of the side effects you may experience can also be related to this combination, such as:

- inflammation of the lining of the intestine and mouth
- skin reactions typical for radiation therapy
- difficulty in swallowing
- reduction in the number of white blood cells

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

United Kingdom

Yellow Card Scheme

Website: www.mhra.gov.uk/yellowcard

Ireland

HPRA Pharmacovigilance

Earlsfort Terrace

IRL - Dublin 2

Tel: +353 1 6764971

Fax: +353 1 6762517

Website: www.hpra.ie

e-mail: medsafety@hpra.ie

By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Erbitux

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

Store in a refrigerator (2°C – 8°C). Once opened, Erbitux is intended for immediate use.

6. Contents of the pack and other information

What Erbitux contains

– The active substance is cetuximab.

Each mL of the solution for infusion contains 5 mg cetuximab.

Each vial of 20 mL contains 100 mg cetuximab.

Each vial of 100 mL contains 500 mg cetuximab.

– The other ingredients are sodium chloride, glycine, polysorbate 80, citric acid monohydrate, sodium hydroxide and water for injections.

What Erbitux looks like and contents of the pack

Erbitux 5 mg/mL solution for infusion is supplied in vials containing 20 mL or 100 mL.

Each pack contains 1 vial.

Not all vial sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Merck KGaA

64271 Darmstadt

Germany

This leaflet was last revised in 11/2014.

Other sources of information

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

The following information is intended for medical or healthcare professionals only:

Handling instructions

Erbitux may be administered via a gravity drip, an infusion pump or a syringe pump. Since Erbitux is only compatible with sterile sodium chloride 9 mg/mL (0.9%) solution for injection, it must not be mixed with other intravenously applied medicinal products. A separate infusion line must be used for the infusion, and the line must be flushed with sterile sodium chloride 9 mg/mL (0.9%) solution for injection at the end of infusion.

Erbitux 5 mg/mL is compatible

- with polyethylene (PE), ethyl vinyl acetate (EVA) or polyvinyl chloride (PVC) bags,
- with polyethylene (PE), polyurethane (PUR), ethyl vinyl acetate (EVA), polyolefine thermoplastic (TP) or polyvinyl chloride (PVC) infusion sets,
- with polypropylene (PP) syringes for syringe pump.

Erbitux 5 mg/mL is chemically and physically stable for up to 48 hours at 25°C, if the solution is prepared as described hereafter. However, since it does not contain any antimicrobial preservative or bacteriostatic agent, it is intended for immediate use. Care must be taken to ensure aseptic handling when preparing the infusion. Erbitux 5 mg/mL must be prepared as follows:

- For administration with infusion pump or gravity drip (diluted with sterile sodium chloride 9 mg/mL (0.9%) solution): Take an infusion bag of adequate size of sterile sodium chloride 9 mg/mL (0.9%) solution. Calculate the required volume of Erbitux. Remove an adequate volume of the sodium chloride solution from the infusion bag, using an appropriate sterile syringe with a suitable needle. Take an appropriate sterile syringe and attach a suitable needle. Draw up the required volume of Erbitux from a vial. Transfer the Erbitux into the prepared infusion bag. Repeat this procedure until the calculated volume has been reached. Connect the infusion line and prime it with the diluted Erbitux before starting the infusion. Use a gravity drip or an infusion pump for administration. The first dose (400 mg/m^2 body surface area) is infused over a period of approximately 2 hours with an infusion rate not faster than 5 mg/min. Each subsequent dose (250 mg/m^2 body surface area) is infused in approximately 1 hour with an infusion rate not faster than 10 mg/min.
- For administration with infusion pump or gravity drip (undiluted): Calculate the required volume of Erbitux. Take an appropriate sterile syringe (minimum 50 mL) and attach a suitable needle. Draw up the required volume of Erbitux from a vial. Transfer the Erbitux into a sterile evacuated container or bag. Repeat this procedure until the calculated volume has been reached. Connect the infusion line and prime it with Erbitux before starting the infusion. The first dose (400 mg/m^2 body surface area) is infused over a period of approximately 2 hours with an infusion rate not faster than 5 mg/min. Each subsequent dose (250 mg/m^2 body surface area) is infused in approximately 1 hour with an infusion rate not faster than 10 mg/min.
- For administration with a syringe pump: Calculate the required volume of Erbitux. Take an appropriate sterile syringe and attach a suitable needle. Draw up the required volume of Erbitux from a vial. Remove the needle and put the syringe into the syringe pump. Connect the infusion line to the syringe and start the infusion after priming the line with Erbitux or sterile sodium chloride 9 mg/mL (0.9%) solution. Repeat this procedure until the calculated volume has been infused. The first dose (400 mg/m^2 body surface area) is infused over a period of approximately 2 hours with an infusion rate not faster than 5 mg/min. Each subsequent dose is (250 mg/m^2 body surface area) is infused in approximately 1 hour with an infusion rate not faster than 10 mg/min.