IMPORTANT: PLEASE READ

PART III: CONSUMER INFORMATION

PrERBITUX®
(cetuximab)
Pronounced: ER bih tucks

www.lilly.ca

This leaflet is part III of a three-part "Product Monograph" published when ERBITUX was approved for sale in Canada and is designed specifically for Consumers. Keep this leaflet. You may need to read it again.

This leaflet is a summary and will not tell you everything about ERBITUX. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:

Cetuximab, the active substance in ERBITUX, belongs to a group of medicines called monoclonal antibodies. 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 tumour cells. As a result of this binding, the tumour cell can no longer receive the messages it needs for growth, progression and metastasis.

ERBITUX is not taken by mouth, but given with fluids through an intravenous (I.V.) line, a thin plastic tube placed in a vein in your hand or arm. When ERBITUX is given intravenously with other fluids, it is called an infusion.

If you receive ERBITUX in combination with 5-fluorouracil or irinotecan, please make sure that you also read the package leaflet for 5-fluorouracil or irinotecan.

ERBITUX is used in combination with radiation therapy to treat patients with cancer of the head and neck region.

Metastatic colorectal cancer is cancer of the colon (large intestine) or rectum that has spread to other organs in the body. ERBITUX is used to treat wild-type *K-Ras* (non-mutated) EGFR-expressing metastatic cancer of colon or rectum:

- In combination with FOLFIRI (irinotecan, 5-fluorouracil, leucovorin) in patients who have not received prior therapy for metastatic colorectal cancer.
- In combination with irinotecan in patients who cannot tolerate other irinotecan-based chemotherapy.
- In patients who cannot tolerate irinotecan.
- In patients who have failed on both irinotecan- and oxaliplatin-based chemotherapy and who have received a fluoropyrimidine.

If you have colorectal cancer and *Ras* mutation, your physician may not prescribe ERBITUX.

When it should not be used:
Do not use ERBITUX if you are allergic to cetuximab or any other ingredient in ERBITUX.

What the medicinal ingredient is:
The medicinal ingredient in ERBITUX is cetuximab.

What the nonmedicinal ingredients are:
Disodium phosphate, sodium chloride, sodium dihydrogen phosphate and water for injection.

What dosage forms it comes in:
ERBITUX 2 mg/mL solution for infusion is supplied as liquid concentrate in single 50 mL and 100 mL vials for intravenous use.

What should you tell your doctor before you start taking ERBITUX

This information will help you and your doctor decide whether you should use ERBITUX and what extra care may need to be taken while you are on it.

BEFORE beginning treatment with ERBITUX, make sure your doctor or pharmacist know if:

- You ever had a bad reaction/allergy to ERBITUX or any of the non-medicinal ingredients;
- You are taking or have taken recently any medication including prescription or non-prescription drugs;
- You have a history of breathing problems or lung disease, especially interstitial pneumonitis (swelling of the lungs causing coughing and trouble breathing) or pulmonary fibrosis (scarring and thickening in the lungs with trouble breathing);
- You have a history of heart disease such as heart attack, angina, coronary artery disease (blocked or hardening of the arteries), high or low blood pressure, heart arrhythmia (irregular heartbeat, palpitations), or heart failure;
- You drive and use machines. It is recommended you not drive or operate any tools or machines if you have side effects that affect your concentration or reaction time;
- You have an allergy to red meat, have had a history of a tick bite or have certain antibodies. You may be more likely to experience severe allergic reactions

under these circumstances.
- You are pregnant or you or your partner could become pregnant. ERBITUX causes foetal loss (miscarriage) in animal studies. Your doctor will then discuss with you the risks and benefits of using ERBITUX during pregnancy. Reliable birth control should be used by both males and females and for 6 months after the last dose of ERBITUX;
- You breast-feed. It is not known whether ERBITUX is present in breast milk. It is not recommended to breast-feed your baby while you are being treated with ERBITUX and for two months after the last dose.

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions

Infusion Reactions: Severe, potentially fatal, allergic/hypersensitivity reactions including sudden breathing problems (wheezing, trouble breathing, hoarse voice), low blood pressure/feeling faint, shock, loss of consciousness, heart attack, and/or cardiac arrest have occurred with ERBITUX especially during or shortly after infusions.

Most (90%) reactions happened with the first infusion of ERBITUX.

A physician will supervise your infusions, and treatment for severe allergic reactions will be immediately available.

Severe reactions require immediately stopping of the ERBITUX infusion and permanently stopping any further treatment with ERBITUX. Patients who have any reactions should be observed until after all signs and symptoms have stopped.

Cardiopulmonary Arrest (Heart and breathing stop): Sudden death occurred in 2% of head and neck patients who received radiation therapy with ERBITUX in a clinical trial.

ERBITUX may cause allergic side effects. To recognise early signs of such effects, your condition will be checked regularly while you receive each infusion and for at least 1 hour afterwards. Allergic side effects may sometimes also occur after this period. Please contact your doctor if you experience symptoms such as fever, chills, rash, or breathing difficulties. Speak to a doctor at once if you have asthma-like symptoms (e.g. wheezing, trouble breathing, hoarse voice, trouble speaking, swelling of your face and lips, tongue or throat), chest pain, heart palpitations/irregular heart beat, a rash with hives or if you feel faint. Such side effects may be serious and require immediate attention. Treatment with ERBITUX must then be stopped permanently for any severe reaction. Severe allergic reactions have occurred in patients who have not received treatment with ERBITUX before.

ERBITUX can change the normal levels of salts (electrolytes) in your blood such as magnesium, potassium, and calcium. Your doctor will test your blood as appropriate before and regularly during and for two months after treatment with ERBITUX.

To date, ERBITUX has not been investigated in children. Similarly, ERBITUX has not been studied in patients with liver or kidney disease.

INTERACTIONS WITH THIS MEDICATION

There are no other known interactions with ERBITUX plus any other medication, including irinotecan.
- Advise your doctor or pharmacist if you are taking or plan on taking any other medication.

Do not start using a new medication without telling your doctor or pharmacist.

PROPER USE OF THIS MEDICATION

Usual dose:
Initial dose of 400 mg/m^2 as a 120-minute infusion. Subsequent weekly doses of 250 mg/m^2 are infused over 60 minutes.

If you receive radiation therapy with ERBITUX, you will finish the ERBITUX dose one hour before you receive your radiation therapy.

If you receive 5-fluorouracil or irinotecan with ERBITUX in the same week, irinotecan will be given after the end of the ERBITUX infusion.

Missed Dose:
It is very important that you receive ERBITUX on schedule. If you miss a dose of ERBITUX, contact your doctor immediately. Your doctor will decide when you should receive your next dose.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Like all medicines, ERBITUX can have side effects. The most common are skin reactions (including rash, itching and nail changes), headache, diarrhea and infections.

Allergic side effects
About 3% patients are likely to experience severe allergic side effects.

Fever, chills, rash, and breathing difficulties are typical for mild or moderate allergic side effects. Please tell your doctor, if such symptoms occur. Your doctor may consider reducing the infusion rate of ERBITUX to

manage these symptoms.

If asthma-like symptoms (e.g. wheezing, trouble breathing, hoarseness, trouble speaking) or a rash with hives develop rapidly or if you feel faint, these may be signs of a severe allergic side effect. Speak to a doctor at once because such side effects may have serious consequences and require immediate attention. In such cases, treatment with ERBITUX must be stopped.

Intravenous medications may be given to help prevent these allergic reactions, especially before the first dose of Erbitux. The risk for having an allergic reaction can occur despite receiving medication to prevent these reactions.

Skin reactions
More than 80% patients had side effects involving the skin. The main symptoms are acne-like rash which can be itchy, dry, scaly or cracking skin and inflammation, infection or swelling at the base of the nails or loss of the nails. Most of these side effects develop within two weeks of treatment. They usually disappear over time after the end of ERBITUX therapy, but the ERBITUX dose or the interval between infusions may need to be changed.

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.

Therefore, please inform your doctor if you notice extensive rash. Your doctor will decide whether treatment has to be stopped if skin reactions reappear after several dose reductions.

ERBITUX can make your skin more sensitive to sunlight, and severe sunburn or worsening rash may result. Limit sun and tanning bed exposure during treatment with ERBITUX and for 2 months following the last dose of ERBITUX.

Eye reactions
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, pink eye, inflammation of the cornea 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.

Other
If you receive ERBITUX in combination with 5-fluorouracil or irinotecan, please make sure that you also read the package leaflet for 5-fluorouracil or irinotecan.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / effect		Talk with your doctor or pharmacist		Stop taking drug and call your doctor or pharmacist
		Only if severe	In all cases	
Very Common ≥ 10%	Skin reactions		Y	
Common ≥ 1%, < 10%	Infusion reactions Asthma-like symptoms (e.g. wheezing, severe breathing difficulties, hoarseness, difficulty speaking) or rash with wheals or if you faint		Y	
	Cardiopulmonary arrest (heart attack) and/or heart failure in patients with squamous cell carcinoma of the head & neck treated with radiation therapy and ERBITUX or in patients with advanced colorectal cancer treated with 5-FU and irinotecan and ERBITUX		Y	
	Hand-foot syndrome (e.g. redness, swelling and pain on the palms of the hands and/or feet) when used with 5-FU and irinotecan and ERBITUX in advanced colorectal cancer		Y	
Uncommon ≥ 0.1%, < 1%	Acute or worsening eye problems (blurred vision, eye pain, pink eye, inflammation of the cornea and/or severe dry eye		Y	

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM				
Symptom / effect		**Talk with your doctor or pharmacist**		**Stop taking drug and call your doctor or pharmacist**
Reported from post-marketing with unknown frequency	Blistering or peeling of the skin, which may indicate a severe skin reaction called "Stevens-Johnson syndrome"		**Y**	

This is not a complete list of side effects. If you have any unexpected effects while taking ERBITUX, contact your doctor or pharmacist.

HOW TO STORE IT

ERBITUX is administered in out-patient clinics or in hospital settings.

ERBITUX should be stored in the refrigerator at 2˚-8˚ C (36˚-46˚F). Do not freeze.

REPORTING SUSPECTED SIDE EFFECTS

To monitor drug safety, Health Canada through the Canada Vigilance Program collects information on serious and unexpected side effects of drugs. If you suspect you have had a serious or unexpected reaction to this drug, you may notify Canada Vigilance:

By toll-free telephone: 1-866-234-2345
By toll free fax: 1-866-678-6789
Online: www.healthcanada.gc.ca/medeffect
By email: Canada Vigilance@hc-sc.gc.ca

By regular mail:
Canada Vigilance National Office
Marketed Health Products Safety and
Effectiveness Information Bureau
Marketed Health Products Directorate
Health Products and Food Branch
Health Canada
Tunney's Pasture, AL0701C
Ottawa, ON K1A 0K9

NOTE: Should you require information related to the management of the side effect, please contact your health care provider before notifying Canada Vigilance. The Canada Vigilance Program does not provide medical advice.

More Information

This leaflet was prepared by Eli Lilly Canada Inc.and ImClone LLC.

This document plus the full product monograph, prepared for health professionals, can be obtained by contacting Eli Lilly Canada Inc. at 1-888-545-5972 or visit the website at www.lilly.ca.

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