

Package leaflet: Information for the user

GLIADEL 7.7 mg Implant Carmustine

Read all of this leaflet carefully before you receive GLIADEL Implants 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 GLIADEL Implants are and what they are used for
2. What you need to know before you receive GLIADEL Implants
3. How GLIADEL Implants are used
4. Possible side effects
5. How to store GLIADEL Implants
6. Contents of the pack and other information

1. What GLIADEL Implants are and what they are used for

GLIADEL Implants are a way to deliver the anticancer substance carmustine directly to the site of the brain tumour after the tumour has been removed by surgery. Carmustine belongs to a group of anticancer substances that act by slowing the growth of cancer cells in brain.

GLIADEL Implants can be used in combination with radiation for the treatment of brain tumours.

GLIADEL Implants have been shown to prolong survival in patients with brain tumours.

2. What you need to know before you receive GLIADEL Implants

Do not use GLIADEL Implants if you are allergic to carmustine or Polifeprosan 20.

Warnings and precautions

Following surgery to remove the brain tumour and insert the GLIADEL Implants, your doctor or surgeon will monitor you closely for known complications. In some cases your surgeon may need to re-operate (due to complications or recurrence of the tumour). Complications include:

- Convulsions (seizures)
- Infections in the brain (infections within the skull)
- Swelling of the brain due to accumulation of fluid
- Brain fluid leak
- Wound healing problems

Your doctor will monitor you closely in case you are taking steroids due to swelling or high fluid pressure in the brain.

Prior to inserting the implants your surgeon may need to close a canal in your brain to avoid the implants passing through it which could cause an accumulation of fluids within the skull.

After insertion of Gliadel Implants, medical imaging may detect swelling of the brain due to accumulation of fluid and inflammation caused by Gliadel Implants or tumour progression.

Other medicines and GLIADEL Implants

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

Pregnancy and breast-feeding

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 receiving this medicine. GLIADEL Implants have not been studied in pregnant women. The active ingredient, carmustine, has been shown to adversely affect the development of unborn babies. GLIADEL Implants should not be used if you are pregnant or breast-feeding. Women of childbearing potential are advised to use effective contraception for 6 months after receiving GLIADEL implants. Men who have a female partner of childbearing potential should use contraception for 90 days after receiving GLIADEL implants.

Driving and using machines

Driving is not advisable after treatment. You must check with your doctor before driving or operating any tools or machines.

3. How GLIADEL Implants are used

GLIADEL Implants are for use in adults only

Your surgeon or pharmacist will ensure that the product is available for your surgery. After the surgeon removes your brain tumour, he or she inserts up to eight implants into the space the tumour once occupied. Your surgeon will decide how many implants to place into the cavity created by the removal of your brain tumour. The implants are placed in such a manner that they cover as much of the cavity as possible. After your surgery, the implants slowly dissolve over a 2 to 3 week period releasing carmustine directly to the surrounding cells.

If you have any further questions on the use of this product, ask your surgeon.

4. Possible side effects

Like all medicines, GLIADEL Implants can cause side effects, although not everybody gets them.

If you experience any of the following side effects as a **new event**, or if a side effect that you have **worsens**, tell your doctor immediately or go to the casualty department at your nearest hospital.

The most common adverse events observed during trials in either newly-diagnosed malignant glioma (brain tumour) (120 patients) or recurrent diagnosed malignant glioma (110 patients) are presented below.

The following four categories of side effects are possibly related to treatment with GLIADEL Implants.

- 1. Seizures** were very common. Most of them had a mild to moderate intensity and occurred within 5 days of the surgical treatment.
- 2. Brain swelling** was very common. The development of brain swelling could necessitate a new surgical intervention either to remove the implants or the remnants of the implants.
- 3. Mild to severe wound healing problems** were very common.
- 4. Infections in the brain** (infections within the skull) such as meningitis and abscess(es) (localised collections of pus) were common.

The following side effects were seen in the patients during the trials. They were similar to those encountered by patients who have surgery for their brain cancer without the insertion of GLIADEL Implants.

Very common: may affect more than 1 in 10 people

- Psychiatric disorders

Depression

- Nervous system disorders

Weakness, especially on one side of the body; convulsion (fits); confusion; headache; swelling of the brain; somnolence (drowsiness); problems with speech

- Vascular disorders

Vein inflammation

- Gastrointestinal disorders (stomach and intestinal related disorders)

Nausea (feeling sick); vomiting; constipation

- Skin and subcutaneous (tissue under the skin) disorders

Rash; hair loss

- Renal (kidney) and urinary disorders

Infection of the urinary tract

- General disorders and administration site conditions

A worsening of your condition; infection; headache; feeling of weakness; fever or pain; abnormal (slow) healing of the surgical wound

Common: may affect up to 1 in 10 people

- Blood and lymphatic (immune) system disorders

Reduction in red blood cells which can make the skin pale and cause weakness and breathlessness; reduction in blood platelets which increases the risk of bleeding; increase in white blood cells

- Endocrine disorders (hormonal disorders)

Diabetes mellitus (abnormally high sugar level in blood)

- Metabolism & nutrition disorders

Peripheral oedema (excess fluid in the arms and legs); low blood levels of sodium which can cause tiredness and confusion, muscle twitching, fits or coma; high blood sugar levels; low blood levels of potassium which can cause muscle weakness, twitching or abnormal heart rhythm

- Psychiatric disorders

Changes in your personality; excessive anxiety; abnormal thinking; hallucinations; insomnia (little or poor sleep)

- Nervous system disorders

Amnesia (loss of memory); an increase in the blood pressure in the skull due to abnormal build up of fluid; paralysis of the face; lack of coordination; diminished sensitivity to stimulation; abnormal burning or prickling sensation; problems with walking; dizziness; epileptic seizures (fits); tremor (small shaking movements); meningitis (inflammation of the brain); abscess (localised collection of pus); loss of consciousness

- Eye disorders

Blurred or abnormal vision; swelling of the eye lining; eye pain

Vascular disorders

Bleeding; high or low blood pressure

- Respiratory disorders (Lung related disorders)

Lung infection or pneumonia which causes breathlessness, cough and raised temperature

- Gastrointestinal disorders (Stomach and intestinal related disorders)

Yeast infection of the mouth; diarrhoea; constipation; faecal incontinence (uncontrolled bowel movements); difficulty in swallowing; bleeding in the stomach or in bowels.

- Skin and subcutaneous (tissue under the skin) disorders

Rash

- Muscle, skeletal and soft tissue related disorders

General infection

- Renal (kidney) and urinary disorders

Urinary infections ; urinary incontinence

- General disorders and administration site conditions

Abdominal, back and chest pain; swelling of the face; abscess (localised collection of pus); accidental injury; allergic reaction; neck pain and infection in the blood stream.

Uncommon side effects (between 1 and 10 patients in every 1000)

Injury, poisoning and procedural complications

Pneumocephalus (air accumulation at the implant site)

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 HPRA Pharmacovigilance Website: www.hpra.ie. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store GLIADEL Implants

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

Store in a freezer at or below -20°C.

Unopened outer sachets may be kept at a temperature of not more than 22°C for a maximum of six hours.

The product may be refrozen only once if the sachets have been unopened and kept for a maximum of 6 hours at a temperature of not more than 22°C. After the refreezing, the product should be used within 30 days.

Do not use GLIADEL Implants after the expiry date which is stated on the outer carton and/or the sachet. The expiry date refers to the last day of that month. Your surgeon or hospital pharmacist will check the expiry date before implants are used.

6. Contents of the pack and other information

What GLIADEL Implants contain

- The active substance is carmustine. Each implant contains 7.7 mg of carmustine.
- The other ingredient is polifeprosan 20.

What GLIADEL Implants look like and contents of the pack

GLIADEL Implants are available in boxes containing eight implantable wafers. These wafers are off-white to pale yellow flat discoid implants. Each wafer is individually packaged in an aluminium foil laminate sachet.

Marketing Authorisation Holder and Manufacturer

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The following information is intended for medical or healthcare professionals only