PACKAGE LEAFLET

Package Leaflet: Information for the user

Temozolomide Actavis 5 mg hard capsules
Temozolomide Actavis 20 mg hard capsules
Temozolomide Actavis 100 mg hard capsules
Temozolomide Actavis 140 mg hard capsules
Temozolomide Actavis 180 mg hard capsules
Temozolomide Actavis 250 mg hard capsules

temozolomide

Read all of this leaflet carefully before you start taking 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, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What Temozolomide Actavis is and what it is used for

Temozolomide Actavis contains a medicine called temozolomide. This medicine is an antitumour agent. Temozolomide Actavis is used for the treatment of specific forms of brain tumours:
- in adults with newly-diagnosed glioblastoma multiforme. Temozolomide Actavis is first used together with radiotherapy (concomitant phase of treatment) and after that alone (monotherapy phase of treatment).
- in children 3 years and older and adult patients with malignant glioma, such as glioblastoma multiforme or anaplastic astrocytoma. Temozolomide Actavis is used in these tumours if they return or get worse after standard treatment.

2. What you need to know before you take Temozolomide Actavis

Do not take Temozolomide Actavis:
- if you are allergic to temozolomide or any of the other ingredients of this medicine (listed in section 6).
- if you have had an allergic reaction to dacarbazine (an anticancer medicine sometimes called DTIC). Signs of allergic reaction include feeling itchy, breathlessness or wheezing, swelling of the face, lips, tongue or throat and you may feel you are going to faint.
- if certain kinds of blood cells are severely reduced (myelosuppression), such as your white blood cell count and platelet count. These blood cells are important for fighting infection and for proper blood clotting. Your doctor will check your blood to make sure you have enough of these cells before you begin treatment.

Warnings and precautions
Talk to your doctor, pharmacist or nurse before taking Temozolomide Actavis,
- as you should be observed closely for the development of a serious form of chest infection called *Pneumocystis jirovecii* pneumonia (PCP). If you are a newly-diagnosed patient

(glioblastoma multiforme) you may be receiving Temozolomide Actavis for 42 days in combination with radiotherapy. In this case, your doctor will also prescribe medicine to help you prevent this type of pneumonia (PCP).
- if you have ever had or might now have a hepatitis B infection. This is because Temozolomide Actavis could cause hepatitis B to become active again, which can be fatal in some cases. Patients will be carefully checked by their doctor for signs of this infection before treatment is started.
- if you have low counts of red blood cells (anaemia), white blood cells and platelets, or blood clotting problems before starting the treatment, or if you develop them during treatment. Your doctor may decide to reduce the dose, interrupt, stop or change your treatment. You may also need other treatments. In some cases, it may be necessary to stop treatment with Temozolomide Actavis. Your blood will be tested frequently during treatment to monitor the side effects of Temozolomide Actavis on your blood cells.
- as you may have a small risk of other changes in blood cells, including leukaemia.
- if you have nausea (feeling sick in your stomach) and/or vomiting which are very common side effects of Temozolomide Actavis (see section 4), your doctor may prescribe you a medicine (an anti-emetic) to help prevent vomiting. If you vomit frequently before or during treatment, ask your doctor about the best time to take Temozolomide Actavis until the vomiting is under control. If you vomit after taking your dose, do not take a second dose on the same day.
- if you develop fever or symptoms of an infection, contact your doctor immediately.
- if you are older than 70 years of age, you might be more prone to infections, bruising or bleeding.
- if you have liver or kidney problems, your dose of Temozolomide Actavis may need to be adjusted.

Children and adolescents
Do not give this medicine to children under the age of 3 years because it has not been studied. There is limited information in patients over 3 years of age who have taken Temozolomide Actavis.

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

Pregnancy, breast-feeding and fertility
If you are pregnant, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine. This is because you must not be treated with Temozolomide Actavis during pregnancy unless clearly indicated by your doctor.

Effective contraceptive precautions must be taken by **both male and female patients** who are taking Temozolomide Actavis (see also "Male fertility" below).

You should stop breast-feeding while receiving treatment with Temozolomide Actavis.

Male fertility
Temozolomide Actavis may cause permanent infertility. Male patients should use effective contraceptions and not father a child for up to 6 months after stopping treatment. It is recommended to seek advice on conservation of sperm prior to treatment.

Driving and using machines
Temozolomide Actavis may make you feel tired or sleepy. In this case, do not drive or use any tools or machines or cycle until you see how this medicine affects you (see section 4).

Temozolomide Actavis contains lactose
Temozolomide Actavis contains lactose (a kind of sugar). If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.

3. How to take Temozolomide Actavis

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

Dosage and duration of treatment

Your doctor will work out your dose of Temozolomide Actavis. This is based on your size (height and weight) and if you have a recurrent tumour and have had chemotherapy treatment in the past. You may be given other medicines (anti-emetics) to take before and/or after taking Temozolomide Actavis to prevent or control nausea and vomiting.

Patients with newly-diagnosed glioblastoma multiforme:
If you are a newly-diagnosed patient, treatment will occur in two phases:
- treatment together with radiotherapy (concomitant phase) first
- followed by treatment with only Temozolomide Actavis (monotherapy phase).

During the concomitant phase, your doctor will start Temozolomide Actavis at a dose of 75 mg/m^2 (usual dose). You will take this dose every day for 42 days (up to 49 days) in combination with radiotherapy. The Temozolomide Actavis dose may be delayed or stopped, depending on your blood counts and how you tolerate your medicine during the concomitant phase. Once the radiotherapy is completed, you will interrupt treatment for 4 weeks. This will give your body a chance to recover. Then, you will start the monotherapy phase.

During the monotherapy phase, the dose and way you take Temozolomide Actavis will be different. Your doctor will work out your exact dose. There may be up to 6 treatment periods (cycles). Each one lasts 28 days. You will take your new dose of Temozolomide Actavis alone once daily for the first 5 days ("dosing days") of each cycle. The first dose will be 150 mg/m^2. Then you will have 23 days without Temozolomide Actavis . This adds up to a 28-day treatment cycle. After Day 28, the next cycle will begin. You will again take Temozolomide Actavis once daily for 5 days followed by 23 days without Temozolomide Actavis . The Temozolomide Actavis dose may be adjusted, delayed or stopped depending on your blood counts and how you tolerate your medicine during each treatment cycle.

Patients with tumours that have returned or worsened (malignant glioma, such as glioblastoma multiforme or anaplastic astrocytoma) taking Temozolomide Actavis only:

A treatment cycle with Temozolomide Actavis lasts 28 days. You will take Temozolomide Actavis alone once daily for the first 5 days. This daily dose depends on whether or not you have received chemotherapy before.

If you have not been previously treated with chemotherapy, your first dose of Temozolomide Actavis will be 200 mg/m^2 once daily for the first 5 days. If you have been previously treated with chemotherapy, your first dose of Temozolomide Actavis will be 150 mg/m^2 once daily for the first 5 days. Then, you will have 23 days without Temozolomide Actavis . This adds up to a 28-day treatment cycle.

After Day 28, the next cycle will begin. You will again receive Temozolomide Actavis once daily for 5 days, followed by 23 days without Temozolomide Actavis .

Before each new treatment cycle, your blood will be tested to see if the Temozolomide Actavis dose needs to be adjusted. Depending on your blood test results, your doctor may adjust your dose for the next cycle.

How to take Temozolomide Actavis

For oral use.

Take your prescribed dose of Temozolomide Actavis once a day, preferably at the same time each day.
Take the capsules on an empty stomach; for example, at least one hour before you plan to eat breakfast. Swallow the capsule(s) whole with a glass of water. Do not open, crush or chew the capsules. If a capsule is damaged, avoid contact of the powder with your skin, eyes or nose. If you accidentally get some in your eyes or nose, flush the area with water. Depending on the prescribed dose, you may have to take more than one capsule together, eventually with different strengths (content of active substance, in mg). The colour of the capsule cap is different for each strength (see in the table below).

Strength	Colour of the cap
Temozolomide Actavis **5 mg** hard capsules	green
Temozolomide Actavis **20 mg** hard capsules	orange
Temozolomide Actavis **100 mg** hard capsules	purple
Temozolomide Actavis **140 mg** hard capsules	blue
Temozolomide Actavis **180 mg** hard capsules	chocolate brown
Temozolomide Actavis **250 mg** hard capsules	white

You should make sure you fully understand and remember the following:
- how many capsules you need to take every dosing day. Ask your doctor or pharmacist to write it down (including the colour).
- which days are your dosing days.

Review the dose with your doctor each time you start a new cycle, since it may be different from the last cycle.

Always take Temozolomide Actavis exactly as your doctor has told you. It is very important to check with your doctor or pharmacist if you are not sure. Errors in how you take this medicine may have serious health consequences.

If you take more Temozolomide Actavis than you should
If you accidentally take more Temozolomide Actavis capsules than you were told to, contact your doctor, pharmacist or nurse immediately.

If you forget to take Temozolomide Actavis
Take the missed dose as soon as possible during the same day. If a full day has gone by, check with your doctor. Do not take a double dose to make up for a forgotten dose, unless your doctor tells you to do so.

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

4. Possible side effects

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

Contact your doctor **immediately** if you have any of the following:
- a severe allergic (hypersensitive) reaction (hives, wheezing or other breathing difficulty, swelling of the face, lips, tongue or throat, feeling faint),
- uncontrolled bleeding,

- seizures (convulsions),
- fever,
- severe headache that does not go away.

Temozolomide Actavis treatment can cause a reduction in certain kinds of blood cells. This may cause you to have increased bruising or bleeding, anaemia (a shortage of red blood cells), fever, and reduced resistance to infections. The reduction in blood cell counts is usually short-lived. In some cases, it may be prolonged and may lead to a very severe form of anaemia (aplastic anaemia). Your doctor will monitor your blood regularly for any changes, and will decide if any specific treatment is needed. In some cases, your Temozolomide Actavis dose will be reduced or treatment stopped.

Side effects from clinical studies:

Temozolomide Actavis in combination treatment with radiotherapy in newly-diagnosed glioblastoma
Patients receiving Temozolomide Actavis in combination with radiotherapy may experience different side effects than patients taking Temozolomide Actavis alone. The following side effects may occur, and may require medical attention.

Very common (may affect more than 1 in 10 people): loss of appetite, headache, constipation (difficulty passing stools), nausea (feeling sick in your stomach), vomiting, rash, hair loss, tiredness.

Common (may affect up to 1 in 10 people): oral infections, cold sores (herpes simplex virus infection), sore throat, wound infection, reduced number of blood cells (neutropenia, thrombocytopenia, lymphopenia, leukopenia), increased sugar in the blood, loss of weight, change in mental status or alertness, anxiety/depression, mood swings, sleepiness, difficulty with speech and speaking, impaired balance, dizziness, confusion, forgetfulness, difficulty concentrating, inability to fall asleep or stay asleep, tingling sensation, bruising, shaking, abnormal or blurry vision, double vision, hearing impairment, shortness of breath, cough, blood clot in the legs, fluid retention, swollen legs, inflammation of the mouth and lips, diarrhoea, stomach or abdominal pain, heartburn, upset stomach, difficulty swallowing, dry mouth, skin irritation or redness, dry skin, itching, muscle weakness, painful joints, muscle aches and pains, frequent urination, difficulty with holding your urine, allergic reaction, fever, radiation injury, face swelling, pain, abnormal taste, abnormal liver function tests.

Uncommon (may affect up to 1 in 100 people): flu-like symptoms, shingles (herpes zoster virus infection), red spots under the skin, low potassium level in the blood, weight gain, restlessness, lack of interest or emotions (apathy), changes in behaviour, hallucination and memory impairment, partial paralysis, lack of muscle control, impaired coordination, impaired sensations, partial loss of vision, dry or painful eyes, deafness, infection of the middle ear, ringing in the ears, earache, palpitations (when you can feel your heart beat), blood clot in the lung, high blood pressure, pneumonia, inflammation of your sinuses, bronchitis, a cold or the flu, swollen stomach, difficulty controlling your bowel movements, haemorrhoids, peeling skin, increased skin sensitivity to sunlight, change in skin colour, increased sweating, muscle damage, back pain, painful or difficult urination, vaginal bleeding, sexual impotence, absent or heavy menstrual periods, vaginal irritation, breast pain, weakness, hot flushes, shivering, discolouration of your tongue, change in your sense of smell, thirst, tooth disorder.

Temozolomide Actavis monotherapy in recurrent or progressive glioma
The following side effects may occur, and may require medical attention.

Very common (may affect more than 1 in 10 people): reduced number of blood cells (neutropenia or lymphopenia, thrombocytopenia), loss of appetite, headache, vomiting, nausea (feeling sick in your stomach), constipation (difficulty passing stools), tiredness.

Common (may affect up to 1 in 10 people): loss of weight, sleepiness,dizziness, tingling sensation, shortness of breath, diarrhoea, abdominal pain, upset stomach, rash, itching, hair loss, fever, weakness, shivering, feeling unwell, pain, change in taste.

Uncommon (may affect up to 1 in 100 people): reduced blood cell counts (pancytopenia, anaemia, leukopenia).

Rare (may affect up to 1 in 1,000 people): cough, infections including pneumonia.

Very rare (may affect up to 1 in 10,000 people): skin redness, urticaria (hives), skin eruption, allergic reactions.

Other side effects:

Cases of elevations of liver enzymes have been commonly reported. Cases of increased bilirubin, problems with bile flow (cholestasis), hepatitis and injury to the liver, including fatal liver failure, have been uncommonly reported.
Very rare cases of severe rash with skin swelling, including on the palms of the hands and soles of the feet, or painful reddening of the skin and/or blisters on the body or in the mouth have been observed. Tell your doctor **immediately** if this occurs.

Very rare cases of lung side effects have been observed with Temozolomide Actavis . Patients usually present with shortness of breath and cough. Tell your doctor if you notice any of these symptoms.

In very rare cases, patients taking Temozolomide Actavis and medicines like it may have a small risk of developing secondary cancers, including leukaemia.

New or reactivated (recurring) cytomegalovirus infections and reactivated hepatitis B virus infections have been uncommonly reported. Cases of brain infections caused by herpes virus (meningoencephalitis herpetic), including fatal cases, have been uncommonly reported.

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6767836. 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 Temozolomide Actavis

Keep this medicine out of the sight and reach of children, preferably in a locked cupboard. Accidental ingestion can be lethal for children.

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

Bottle presentation
Do not store above 30 °C.
Store in the original bottle and keep the bottle tightly closed.

Sachet presentation
5 mg and 20 mg: Do not store above 25 °C.
100 mg, 140 mg, 180 mg and 250 mg: Do not store above 30 °C.

Tell your pharmacist if you notice any change in the appearance of the capsules.

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 Temozolomide Actavis contains
The active substance is temozolomide.

Temozolomide Actavis 5 mg hard capsules: Each capsule contains 5 mg temozolomide.
Temozolomide Actavis 20 mg hard capsules: Each capsule contains 20 mg temozolomide.
Temozolomide Actavis 100 mg hard capsules: Each capsule contains 100 mg temozolomide.
Temozolomide Actavis 140 mg hard capsules: Each capsule contains 140 mg temozolomide.
Temozolomide Actavis 180 mg hard capsules: Each capsule contains 180 mg temozolomide.
Temozolomide Actavis 250 mg hard capsules: Each capsule contains 250 mg temozolomide.

The other ingredients (excipients) are: capsule content: anhydrous lactose, colloidal anhydrous silica, sodium starch glycolate (type A), tartaric acid, stearic acid (see section 2 "Temozolomide Actavis contains lactose"). capsule shell:
Temozolomide Actavis 5 mg hard capsules: gelatin, titanium dioxide (E 171), yellow iron oxide (E 172), indigotine – FD&C Blue2 (E132). *Temozolomide Actavis 20 mg hard capsules*: gelatin, titanium dioxide (E 171), red iron oxide (E172), yellow iron oxide (E 172). *Temozolomide Actavis 100 mg hard capsules*: gelatin, titanium dioxide (E 171), red iron oxide (E 172), indigotine – FD&C Blue2 (E132). *Temozolomide Actavis 140 mg hard capsules*: gelatin, titanium dioxide (E 171), indigotine – FD&C Blue2 (E132). *Temozolomide Actavis 180 mg hard capsules*: gelatin, titanium dioxide (E 171), black iron oxide (E172), yellow iron oxide (E 172), and red iron oxide (E 172). *Temozolomide Actavis 250 mg hard capsules*: gelatin, titanium dioxide (E 171). Printing ink: shellac, macrogol, concentrated ammonia solution, potassium hydroxide, and black iron oxide (E 172).

What Temozolomide Actavis looks like and contents of the pack
The 5 mg hard capsule are size 0 (21.7 mm in length), have an opaque white body, an opaque green cap. The body is imprinted with "5" in black ink.
The 20 mg hard capsule are size 0 (21.7 mm in length), have an opaque white body, an opaque orange cap. The body is imprinted with "20" in balck ink.
The 100 mg hard capsule are size 0 (21.7 mm in length), have an opaque white body, an opaque purple cap. The body is imprinted with "100" in black ink.
The 140 mg hard capsule are size 0 (21.7 mm in length), have an opaque white body, an opaque blue cap. The body is imprinted with "140" in black ink.
The 180 mg hard capsule are size 0 (21.7 mm in length), have an opaque white body, an opaque chocolate brown cap. The body is imprinted with "180" in black ink.
The 250 mg hard capsule are size 0 (21.7 mm in length), have an opaque white body, an opaque white cap. The body is imprinted with "250" in black ink.

Bottle presentation
The hard capsules for oral use are dispensed in High Density Polyethylene (HDPE) bottles containing 5 capsules. The carton contains 1 bottle.

Sachet presentation
The hard capsules for oral use are individually sealed in sachets and dispensed in cartons containing 5 or 20 hard capsules.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Actavis Group PTC ehf.
Reykjavikurvegi 76-78
220 Hafnarfjordur
Iceland

This medicinal product is authorised in the Member States of the EEA under the following names:

NL	Temozolomide Actavis 5 mg, capsules, hard Temozolomide Actavis 20 mg, capsules, hard Temozolomide Actavis 100 mg, capsules, hard Temozolomide Actavis 140 mg, capsules, hard Temozolomide Actavis 180 mg, capsules, hard Temozolomide Actavis 250 mg, capsules, hard
BG	Temozolomide Actavis
HU	Temozolomide Actavis 5 mg kemény kapszula Temozolomide Actavis 20 mg kemény kapszula Temozolomide Actavis 100 mg kemény kapszula Temozolomide Actavis 140 mg kemény kapszula Temozolomide Actavis 180 mg kemény kapszula Temozolomide Actavis 250 mg kemény kapszula
IE	Temozolomide Actavis 5 mg Hard Capsules Temozolomide Actavis 20 mg Hard Capsules Temozolomide Actavis 100 mg Hard Capsules Temozolomide Actavis 140 mg Hard Capsules Temozolomide Actavis 180 mg Hard Capsules Temozolomide Actavis 250 mg Hard Capsules
PL	Temozolomide Actavis
UK	Temozolomide Actavis

This leaflet was last revised in June 2017