Package leaflet: Information for the patient
Temozolomide 140 mg capsules
Temozolomide 180 mg capsules
Temozolomide 250 mg 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 is and what it is used for

This medicine is an antitumour agent.

Temozolomide is used for the treatment of specific forms of brain tumours:
- in adults with newly-diagnosed glioblastoma multiforme. Temozolomide 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 is used in these tumours if they return or get worse after standard treatment.

2. What you need to know before you take Temozolomide

Do not take Temozolomide
- 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.
- 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
- 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 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 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. Your blood will be tested frequently during treatment to monitor the side effects of temozolomide 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 (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 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 infection, bruising or bleeding.
- if you have liver or kidney problems, your dose of temozolomide 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.

Other medicines and Temozolomide
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines, especially if you have taken:
- valproic acid (a medicine used to treat seizures)
- medicines which would supress the immune system (such as ciclosporin, azathioprine)

Pregnancy, breast-feeding and fertility
Pregnancy
If you are pregnant or breast-feeding, 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 during pregnancy unless clearly indicated by your doctor.

Breast-feeding
You should stop breast-feeding while receiving treatment with temozolomide.

Fertility
Effective contraceptive precautions must be taken by female patients who are able to become pregnant during treatment with temozolomide and for at least 6 months following completion of treatment.

Male fertility
Temozolomide may cause permanent infertility. Male patients should use effective contraceptions and not father a child for at least 3 months after stopping treatment. It is recommended to seek advice on conservation of sperm prior to treatment.

Driving and using machines
Temozolomide 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 **contains lactose**
Temozolomide capsules contain 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.

Temozolomide contains sodium

This medicine contains less than 1 mmol sodium (23 mg) per capsule, that is to say essentially 'sodium-free'.

3. How to take Temozolomide

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. 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 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 (monotherapy phase).

During the concomitant phase, your doctor will start temozolomide at a dose of 75 mg/m² (usual dose). You will take this dose every day for 42 days (up to 49 days) in combination with radiotherapy. The temozolomide dose may be delayed or stopped, depending on you 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 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 alone once daily for the first 5 days ("dosing days") of each cycle. The first dose will be 150 mg/m². Then you will have 23 days without temozolomide. This adds up to a 28-day treatment cycle.
After Day 28, the next cycle will begin. You will again take temozolomide once daily for 5 days followed by 23 days without temozolomide. The second dose will be 200 mg/m^2. The temozolomide 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 *only*

A treatment cycle with temozolomide lasts 28 days.

You will take temozolomide 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 will be 200 mg/m² once daily for the first 5 days. If you have been previously treated with chemotherapy, your first dose of temozolomide will be 150 mg/m² once daily for the first 5 days.

Then, you will have 23 days without temozolomide. This adds up to a 28-day treatment cycle.

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

Before each new treatment cycle, your blood will be tested to see if the temozolomide 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

Take your prescribed dose of temozolomide 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 and marking of the capsule is different for each strength (see table below).

Strength	Colour/marking
Temozolomide 140 mg	Two stripes in blue ink on the cap and "T 140 mg" in blue ink on the body
Temozolomide 180 mg	Two stripes in red ink on the cap and "T 180 mg" in red ink on the body
Temozolomide 250 mg	Two stripes in black ink on the cap and "T 250 mg" in black ink on the body

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

If you forget to take Temozolomide
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:

- sudden, severe allergic reaction with breathing difficulty, swelling, lightheadedness, fast heartbeat, sweating and loss of consciousness (anaphylaxis)
- uncontrolled bleeding(haemorrhage)
- episodes of spasms and reduced consciousness (convulsions)

- an epileptic seizure, or series of seizures, lasting longer than 5 minutes (status epilepticus)
- severe headache that does not go away (cerebral haemorrhage)
- life-threatening reaction with flu-like effects and blistering in the skin or painful rash, mouth eyes and genitals (toxic epidermal necrolysis, Stevens-Johnson syndrome, erythema multiforme)
- rapid swelling under the skin in areas such as the face, throat, arms and legs which can be life threatening if throat swelling blocks the airway (angioedema)
- flu-like symptoms with a rash, fever, swollen glands, and abnormal blood test results (including increased white blood cells (eosinophilia) and liver enzymes) (Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)).

Temozolomide 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 dose will be reduced or treatment stopped.

Other side effects that have been reported are listed below:

Very Common side effects (may affect more than 1 in 10 people) are:
- loss of appetite (anorexia)
- weakness or the inability to move on one side of the body (hemiparesis)
- difficulty speaking (aphasia/dysphasia)
- headache
- diarrhoea
- constipation
- nausea
- vomiting
- rash
- hair loss (alopecia)
- tiredness (fatigue)

Common side effects (may affect up to 1 in 10 people) are:
- infections, such as herpes zoster (a painful, blistering rash in one part of the body), and oral infections such as candidiasis oral (thrush, a fungal infection caused by *Candida*).
- sore throat (pharyngitis)
- low levels of white blood cells with fever due to infection (febrile neutropenia).
- reduced number of blood cells (neutropenia, thrombocytopenia, lymphopenia, leukopenia, anaemia).
- allergic reaction
  a disorder with signs such as weight gain, fat build-up on the face and bruising, caused by too much of a type of steroid hormone (cushingoid).
  increased blood sugar (hyperglycaemia)
- agitation
- memory impairment (amnesia)
- depression,
- anxiety
- confusion,
- inability to fall asleep or stay asleep (insomnia).
- impaired coordination (ataxia)
- impaired balance
- difficulty processing information (impaired cognition).
- difficulty concentrating
- change in mental status or alertness (decreased consciousness).
- dizziness
- impaired sensations (hypoesthesia).
- forgetfulness (impaired memory)
- disorders of the brain or nerves (neurologic disorder).

- nerve damage (neuropathy)
- tingling sensations (paraesthesia)
- sleepiness (somnolence)
- speech disorder
- abnormal taste (taste perversion)
- shaking (tremor)
- partial loss of vision (hemianopia).
- blurred vision
- abnormal vision (vision disorder, visual field defect)
- double vision (diplopia)
- painful eyes (eye pain)
- deafness
- a spinning sensation (vertigo)
- ringing in the ears (tinnitus)
- earache
- blood clot in lung or legs (embolism pulmonary, deep vein thrombosis)
- high blood pressure (hypertension)
- infection of the lungs (pneumonia, upper respiratory infection)
- shortness of breath (dyspnoea)
- inflammation of your sinuses (sinusitis)
- inflammation of the airways in the lungs (bronchitis)
- cough
- inflammation of the lining of the mouth (stomatitis)
- stomach or abdominal pain
- heartburn (dyspepsia)
- difficulty swallowing (dysphagia)
- reddening of the skin (erythema)
- dry skin
- itching (pruritus)
- muscle damage (myopathy)
- muscle weakness
- painful joint (arthralgia, musculoskeletal pain)
- back pain
- muscle pain (myalgia, musculoskeletal pain)
- frequent urination (micturition frequency)
- difficulty withholding your urine (urinary incontinence)
- fever
- flu-like symptoms
- weakness (asthenia)
- feeling generally unwell (malaise)
- pain
- fluid retention (oedema), especially of the ankles and feet (peripheral oedema)
- increase in liver enzymes
- weight loss
- weight gain
- radiation injury

Uncommon side effects (may affect up to 1 in 100 people) are:
- opportunistic infections including infections of the lungs (*Pneumocystis jirovecii* pneumonia)
- bacteria and their toxins circulating in the blood leading to organ damage (sepsis)
- brain infections (meningoencephalitis herpetic) including fatal cases
- new or reactivated cytomegalovirus infections
- reactivated hepatitis B virus infections
- viral infection of the mouth, such as cold sores, or the genitals (herpes simplex)
- reactivation of infections
- wound infections
- infections causing diarrhoea and vomiting (gastroenteritis)

- bone marrow not making enough healthy blood cells or platelets (myelodysplastic syndromes)
- secondary cancers including leukaemia
- reduced blood cell counts (pancytopenia, aplastic anaemia)
- red spots under the skin (petechiae)
- diabetes insipidus (symptoms include increased urination and feeling thirsty)
- low potassium level in the blood (hypokalaemia)
- increase in liver enzymes (alkaline phosphatase and gamma-glutamyltransferase increased)
- behaviour disorder
- mood swings (emotional lability)
- hallucination
- lack of interest or energy (apathy)
- partial paralysis (hemiplegia)
- effects on a part of the brain that regulates movement, which may result in tremor, muscle spasms or movement disorders (extrapyramidal disorder)
- change in your sense of smell (parosmia)
- Unusual walking pattern (gait abnormality)
- increased sensation to touch, pain and temperature (hyperaesthesia)
- sensory disturbance
- abnormal coordination
- reduced sharpeness of vision (reduced visual acuity)
- dry eyes
- hearing impairment,
- noise sensitivity (hyperacusis)
- infection of the middle ear (otitis media)
- palpitations (when you can feel your heart beat)
- reddening of the skin (flushing)
- hot flushes
- inability of the lungs to work properly (respiratory failure)
- inflammation in the lungs causing shortness of breath and cough (interstitial pneumonitis/pneumonitis)
- lung damage with tissue scarring and thickening (pulmonary fibrosis)
- a blocked nose (nasal congestion)
- swollen stomach (abdominal distension)
- lack of control over passing stools (faecal incontinence)
- stomach and gut disorders (gastrointestinal disorder)
- haemorrhoids
- dry mouth
- fatal liver failure (hepatic failure)
- injury to the liver (hepatic injury)
- inflammation of the liver (hepatitis)
- reduced flow of bile from the liver because of a blockage (cholestasis)
- high blood levels of bilirubin, which can cause yellowing of the skin and eyes, indicating liver problems (hyperbilirubinaemia)
- redness and shedding of skin over a larger area of the body, which may be itchy or painful (erythroderma, skin exfoliation)
- increased sensitivity to sunlight (photosensitivity reaction)
- itchy rash (urticaria, exanthema)
- inflammation of the skin (dermatitis)
- increased sweating
- change in skin colour (abnormal pigmentation)
- painful urination (dysuria)
- vaginal bleeding (vaginal haemorrhage)
- heavy menstrual periods (menorrhagia)
- absence of menstrual periods (amenorrhoea)
- vaginal inflammation and irritation (vaginitis)
- breast pain
- sexual impotence
- condition aggravated

- shivering (rigors)
- face swelling (face oedema)
- discolouration of the tongue
- thirst
- tooth disorder

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 the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

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

5. How to store Temozolomide

Keep this medicine out of the sight and the 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 after EXP. The expiry date refers to the last day of that month.

Bottle packs
Do not store above 30°C. Store in the original package in order to protect from light. Keep the bottles tightly closed in order to protect from moisture.

After first opening, the medicinal product should be used within 21 days.

Sachets 140 mg – 250 mg only
Do not store above 30°C. Store in the original package in order to protect from light.

Do not use this medicine 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 contains

The active substance is temozolomide. Each capsule contains 140 mg/180 mg/250 mg temozolomide.
The other ingredients are:
- *capsule content:* anhydrous lactose, colloidal anhydrous silica, sodium starch glycolate type A, tartaric acid, stearic acid.
- *capsule shell :*gelatin, titanium dioxide (E 171)

Temozolomide 140 mg:
- *Printing ink:* shellac, propylene glycol, indigo carmine (E132) aluminium lake

Temozolomide 180 mg:
- *Printing ink:* red iron oxide (E 172), shellac, propylene glycol

Temozolomide 250 mg:
- *Printing ink:* shellac, propylene glycol, black iron oxide (E 172).

What Temozolomide looks like and contents of the pack

Temozolomide 140 mg hard capsules have a white opaque body and cap with two stripes in blue ink on the cap and with “T 140 mg” in blue ink on the body.

Temozolomide 180 mg hard capsules have a white opaque body and cap with two stripes in red ink on the cap and with “T 180 mg” in red ink on the body.

Temozolomide 250 mg hard capsules have a white opaque body and cap with two stripes in black ink on the cap and with “T 250 mg” in black ink on the body.

Bottle packs
The hard capsules for oral use are dispensed in amber glass bottles containing 5 or 20 capsules. The carton contains 1 bottle.

Sachets
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 Authorization Holder

Mylan, Potters Bar, Hertfordshire, EN6 1TL, United Kingdom.

Manufacturer

Nerpharma S.r.l. Pharmaceutical Sciences, Viale Pasteur, 10, 20014 Nerviano (MI), Italy

Haupt Pharma Amareg GmbH, Donaustaufer Straße 378, 93055 Regensburg, Germany

Delorbis Pharmaceuticals Ltd, 17 Athinon Street, Ergates Industrial Area, 2643 Ergates, P.O.BOX 28629, 2081 Lefkosia, Cyprus

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