

Package leaflet: Information for the user

Temozolomide Clonmel 5mg Hard Capsules Temozolomide Clonmel 20mg Hard Capsules Temozolomide Clonmel 100mg Hard Capsules Temozolomide Clonmel 140mg Hard Capsules Temozolomide Clonmel 180mg Hard Capsules Temozolomide Clonmel 250mg 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 Clonmel is and what it is used for
2. What you need to know before you take Temozolomide Clonmel
3. How to take Temozolomide Clonmel
4. Possible side effects
5. How to store Temozolomide Clonmel
6. Contents of the pack and other information

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

Temozolomide Clonmel contains a medicine called temozolomide. This medicine is an antitumour agent.

Temozolomide Clonmel is used for the treatment of specific forms of brain tumours:

- in adults with newly-diagnosed glioblastoma multiforme. Temozolomide Clonmel 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 Clonmel is used in these tumours if they return or get worse after standard treatment.

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

DO NOT take Temozolomide Clonmel

- 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 Clonmel

- 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 Clonmel 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 Clonmel 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 Clonmel. Your blood will be tested frequently during treatment to monitor the side effects of Temozolomide Clonmel 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 Clonmel (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 Clonmel 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 Clonmel may need to be adjusted.

Children and adolescents

Do not give temozolomide 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 Clonmel

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 Clonmel during pregnancy unless clearly indicated by your doctor.

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

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

Male fertility

Temozolomide Clonmel 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 Clonmel 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 Clonmel hard capsules contain lactose and sodium

If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

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

Temozolomide Clonmel 20 mg:

The excipient sunset yellow FCF (E110) included in the capsules shell may cause allergic reactions.

3. How to take Temozolomide Clonmel

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 Clonmel. 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 Clonmel 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 Clonmel (monotherapy phase).

During the concomitant phase, your doctor will start Temozolomide Clonmel 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 Clonmel 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 Clonmel 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 Clonmel 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 Clonmel. This adds up to a 28-day treatment cycle.

After Day 28, the next cycle will begin. You will again take Temozolomide Clonmel once daily for 5 days followed by 23 days without Temozolomide Clonmel. The Temozolomide Clonmel 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 Clonmel only

A treatment cycle with Temozolomide Clonmel lasts 28 days.

You will take Temozolomide Clonmel 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 Clonmel 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 Clonmel will be 150 mg/m² once daily for the first 5 days.

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

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

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

Take your prescribed dose of Temozolomide Clonmel 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/markings
Temozolomide Clonmel 5 mg	two stripes in green ink on the cap and “T 5 mg” in green ink on the body
Temozolomide Clonmel 20 mg	two stripes in orange ink on the cap and “T 20 mg” in orange ink on the body
Temozolomide Clonmel 100 mg	two stripes in pink ink on the cap and “T 100 mg” in pink ink on the body
Temozolomide Clonmel 140 mg	two stripes in blue ink on the cap and “T 140 mg” in blue ink on the body
Temozolomide Clonmel 180 mg	two stripes in red ink on the cap and “T 180 mg” in red ink on the body
Temozolomide Clonmel 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 Clonmel 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 Clonmel than you should

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

If you forget to take Temozolomide Clonmel

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

Temozolomide Clonmel 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 Clonmel dose will be reduced or treatment stopped.

Side effects from clinical studies:

Temozolomide Clonmel in combination treatment with radiotherapy in newly-diagnosed glioblastoma

Patients receiving Temozolomide Clonmel in combination with radiotherapy may experience different side effects than patients taking Temozolomide Clonmel 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, 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, sleepiness, difficulty 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, 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, red spots under the skin, low potassium level in the blood, weight gain, mood swings, hallucination and memory impairment, partial paralysis, 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, difficulty in urinating, vaginal bleeding, sexual impotence, absent or heavy menstrual periods, vaginal irritation, breast pain, hot flushes, shivering, discolouration of your tongue, change in your sense of smell, thirst, tooth disorder.

Temozolomide Clonmel 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 Clonmel. 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 Clonmel 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. Cases of sepsis (when bacteria and their toxins circulate in the blood and start to damage the organs) have been uncommonly reported.

Cases of diabetes insipidus have been uncommonly reported. Symptoms of diabetes insipidus include passing a lot of urine and feeling thirsty.

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 HPRC 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 Temozolomide Clonmel

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.

Store in the original package in order to protect from light. Keep the bottles tightly closed in order to protect from moisture. 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 Clonmel contains

- The active substance is temozolomide. Each capsule contains 5/20/100/140/180/250 mg temozolomide.
- The other ingredients are:
 - *capsule content*: lactose, colloidal anhydrous silica, sodium starch glycolate type A, tartaric acid, stearic acid.

Temozolomide Clonmel 5 mg:

- *capsule shell*: gelatin, titanium dioxide (E171), shellac, propylene glycol, indigo carmine aluminium lake (E132), yellow iron oxide (E172).

Temozolomide Clonmel 20 mg:

- *capsule shell*: gelatin, titanium dioxide (E171), shellac, propylene glycol, sunset yellow FCF aluminium lake (E110).

Temozolomide Clonmel 100 mg:

- *capsule shell*: gelatin, titanium dioxide (E171), red iron oxide (E172), shellac, propylene glycol and yellow iron oxide (E172).

Temozolomide Clonmel 140 mg:

- *capsule shell*: gelatin, titanium dioxide (E171), shellac, propylene glycol, indigo carmine aluminium lake (E132).

Temozolomide Clonmel 180 mg:

- *capsule shell*: gelatin, titanium dioxide (E171), red iron oxide (E172), shellac, propylene glycol.

Temozolomide Clonmel 250 mg:

- *capsule shell*: gelatin, titanium dioxide (E171), shellac, propylene glycol, black iron oxide (E172).

What Temozolomide Clonmel looks like and contents of the pack

Temozolomide Clonmel 5 mg hard capsules have a white opaque body and cap with two stripes in green ink on the cap and with “T 5 mg” in green ink on the body with a diameter of approximately 5.7 mm and a length of approximately 15.9 mm.

Temozolomide Clonmel 20 mg hard capsules have a white opaque body and cap with two stripes in orange ink on the cap and with “T 20 mg” in orange ink on the body with a diameter of approximately 6.2 mm and a length of approximately 18.0 mm.

Temozolomide Clonmel 100 mg hard capsules have a white opaque body and cap with two stripes in pink ink on the cap and with “T 100 mg” in pink ink on the body with a diameter of approximately 6.8 mm and a length of approximately 19.4 mm.

Temozolomide Clonmel 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 with a diameter of approximately 7.5 mm and a length of approximately 21.7 mm.

Temozolomide Clonmel 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 with a diameter of approximately 7.5 mm and a length of approximately 21.7 mm.

Temozolomide Clonmel 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 with a diameter of approximately 7.5 mm and a length of approximately 21.7 mm.

The hard capsules for oral use are dispensed in amber glass bottles containing 5 or 20 capsules.

Not all pack sizes may be marketed.

Marketing Authorisation Holder

Clonmel Healthcare Ltd, Waterford Road, Clonmel, Co. Tipperary, Ireland

Manufacturer

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

Haupt Pharma Amareg GmbH, Donaustauer Str. 378, 93055 Regensburg, Germany

STADA Arzneimittel AG, Stadastrasse 2-18, 61118 Bad Vilbel, Germany

This medicinal product is authorised in the Member States of the European Economic Area (EEA) under the following names:

Belgium:	Temozolomide EG 5, 20, 100, 140, 180, 250 mg capsules, hard
Germany:	TEMOZO-cell 5, 20, 100, 140, 180, 250 mg Hartkapseln
Denmark:	Temozolomid STADA
Ireland:	Temozolomide Clonmel 5, 20, 100, 140, 180, 250 mg capsules
Luxembourg:	Temozolomide EG 5, 20, 100, 140, 180, 250 mg gélules
Romania:	Temozolomidă HF
Sweden:	Temozolomid STADA 5, 20, 100, 140, 180, 250 mg hårda kapslar
Slovak Republic:	TEMOSTAD 5, 20, 100, 140, 180, 250 mg

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