Package Leaflet: Information for the user

Temodal® 5 mg hard capsules
Temodal® 20 mg hard capsules
Temodal® 100 mg hard capsules
Temodal® 140 mg hard capsules
Temodal® 180 mg hard capsules
Temodal® 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 Temodal is and what it is used for

Temodal contains a medicine called temozolomide. This medicine is an antitumour agent.

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

2. What you need to know before you take Temodal

Do not take Temodal
- 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 Temodal,
- 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 Temodal 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 Temodal 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 Temodal. Your blood will be tested frequently during treatment to monitor the side effects of Temodal 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 Temodal (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 Temodal 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 Temodal 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 Temodal.

Other medicines and Temodal
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 Temodal during pregnancy unless clearly indicated by your doctor.

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

You should stop breast-feeding while receiving treatment with Temodal.

Male fertility
Temodal may cause permanent infertility. Male patients should use effective contraception 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
Temodal 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).

Temodal contains lactose
This medicine 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.

Temodal 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 Temodal

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 Temodal. 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 Temodal 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 Temodal (monotherapy phase).

During the concomitant phase, your doctor will start Temodal 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 Temodal 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 Temodal 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 Temodal 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 Temodal. This adds up to a 28-day treatment cycle.
After Day 28, the next cycle will begin. You will again take Temodal once daily for 5 days followed by 23 days without Temodal. The Temodal 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 Temodal only:

A treatment cycle with Temodal lasts 28 days.
You will take Temodal 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 Temodal 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 Temodal will be 150 mg/m^2 once daily for the first 5 days.
Then, you will have 23 days without Temodal. This adds up to a 28-day treatment cycle.

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

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

How to take Temodal

Take your prescribed dose of Temodal 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
Temodal **5 mg** hard capsules	green
Temodal **20 mg** hard capsules	yellow
Temodal **100 mg** hard capsules	pink
Temodal **140 mg** hard capsules	blue
Temodal **180 mg** hard capsules	orange
Temodal **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 Temodal 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 Temodal than you should
If you accidentally take more Temodal capsules than you were told to, contact your doctor, pharmacist or nurse immediately.

If you forget to take Temodal
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.

Temodal 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 Temodal 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, difficulty speaking, headache
- vomiting, nausea, diarrhoea, constipation
- rash, hair loss
- tiredness

Common side effects (may affect up to 1 in 10 people) are:
- infections, oral infections
- reduced number of blood cells (neutropenia, lymphopenia, thrombocytopenia)
- allergic reaction
- increased blood sugar
- memory impairment, depression, anxiety, confusion, inability to fall asleep or stay asleep
- impaired coordination and balance
- difficulty concentrating, change in mental status or alertness, forgetfulness
- dizziness, impaired sensations, tingling sensations, shaking, abnormal taste
- partial loss of vision, abnormal vision, double vision, painful eyes
- deafness, ringing in the ears, earache
- blood clot in lung or legs, high blood pressure
- pneumonia, shortness of breath, bronchitis, cough, inflammation of your sinuses
- stomach or abdominal pain, upset stomach/heartburn, difficulty swallowing
- dry skin, itching
- muscle damage, muscle weakness, muscle aches and pain
- painful joint, back pain
- frequent urination, difficulty withholding your urine
- fever, flu-like symptoms, pain, feeling unwell, a cold or the flu
- fluid retention, swollen legs
- liver enzyme elevations
- loss of weight, weight gain
- radiation injury

Uncommon side effects (may affect up to 1 in 100 people) are:
- brain infections (meningoencephalitis herpetic) including fatal cases
- wound infections
- new or reactivated cytomegalovirus infections
- reactivated hepatitis B virus infections
- secondary cancers including leukaemia

- reduced blood cell counts (pancytopenia, anaemia, leukopenia)
- red spots under the skin
- diabetes insipidus (symptoms include increased urination and feeling thirsty), low potassium level in the blood
- mood swings, hallucination
- partial paralysis, change in your sense of smell
- hearing impairment, infection of the middle ear
- palpitations (when you can feel your heart beat), hot flushes
- swollen stomach, difficulty controlling your bowel movements, haemorrhoids, dry mouth
- hepatitis and injury to the liver (including fatal liver failure), cholestasis, increased bilirubin
- blisters on body or in mouth, skin peeling, skin eruption, painful reddening of the skin, severe rash with skin swelling (including palms and soles)
- increased sensitivity to sunlight, urticaria (hives), increased sweating, change in skin colour
- difficulty in urinating
- vaginal bleeding, vaginal irritation, absent or heavy menstrual periods, breast pain, sexual impotence
- shivering, face swelling, discolouration of the tongue, thirst, tooth disorder
- dry eyes

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 Temodal

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 in order to protect from moisture.
Keep the bottle tightly closed.

Sachet presentation
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 Temodal contains
The active substance is temozolomide.
Temodal 5 mg hard capsules: Each capsule contains 5 mg temozolomide.
Temodal 20 mg hard capsules: Each capsule contains 20 mg temozolomide.
Temodal 100 mg hard capsules: Each capsule contains 100 mg temozolomide.

Temodal 140 mg hard capsules: Each capsule contains 140 mg temozolomide.
Temodal 180 mg hard capsules: Each capsule contains 180 mg temozolomide.
Temodal 250 mg hard capsules: Each capsule contains 250 mg temozolomide.

The other ingredients are:
capsule content:
anhydrous lactose, colloidal anhydrous silica, sodium starch glycolate type A, tartaric acid, stearic acid (see section 2 "Temodal contains lactose").
capsule shell:
Temodal 5 mg hard capsules: gelatin, titanium dioxide (E 171), sodium laurilsulfate, yellow iron oxide (E 172), indigo carmine (E 132).
Temodal 20 mg hard capsules: gelatin, titanium dioxide (E 171), sodium laurilsulfate, yellow iron oxide (E 172).
Temodal 100 mg hard capsules: gelatin, titanium dioxide (E 171), sodium laurilsulfate, red iron oxide (E 172).
Temodal 140 mg hard capsules: gelatin, titanium dioxide (E 171), sodium laurilsulfate, indigo carmine (E 132).
Temodal 180 mg hard capsules: gelatin, titanium dioxide (E 171), sodium laurilsulfate, yellow iron oxide (E 172), and red iron oxide (E 172).
Temodal 250 mg hard capsules: gelatin, titanium dioxide (E 171), sodium laurilsulfate.
printing ink:
shellac, propylene glycol (E 1520), purified water, ammonium hydroxide, potassium hydroxide, and black iron oxide (E 172).

What Temodal looks like and contents of the pack

Temodal 5 mg hard capsules have an opaque white body, an opaque green cap, and are imprinted with black ink.
Temodal 20 mg hard capsules have an opaque white body, an opaque yellow cap, and are imprinted with black ink.
Temodal 100 mg hard capsules have an opaque white body, an opaque pink cap, and are imprinted with black ink.
Temodal 140 mg hard capsules have an opaque white body, a blue cap, and are imprinted with black ink.
Temodal 180 mg hard capsules have an opaque white body, an opaque orange cap, and are imprinted with black ink.
Temodal 250 mg hard capsules have an opaque white body and cap, and are imprinted with black ink.

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

Sachet presentation
The hard capsules (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

Marketing Authorisation Holder in Great Britain: Merck Sharp & Dohme (UK) Limited, 120 Moorgate, London, EC2M 6UR United Kingdom

Marketing Authorisation Holder in UK (Northern Ireland): Merck Sharp & Dohme B.V., Waarderweg 39, 2031 BN Haarlem, The Netherlands

Manufacturer: SP Labo N.V., Industriepark 30, B-2220 Heist-op-den-Berg, Belgium

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Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu.

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