

Package leaflet: Information for the user

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

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

Temozolomide is an anti-cancer medicine.

Temozolomide Accord capsules are taken to treat specific forms of brain tumours:

- adults with newly diagnosed specific form of brain tumour (glioblastoma multiforme). Temozolomide is first used together with radiotherapy (concomitant phase of treatment) and after that alone (monotherapy phase of treatment).
- children 3 years and older and adult patients with specific forms of brain tumour (e.g. glioblastoma multiforme or anaplastic astrocytoma) that has returned or where the cancer has spread after standard therapy.

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

Do not take Temozolomide Accord

- 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 another anti-cancer medicine called dacarbazine. Signs of allergic reaction include feeling itchy, breathlessness or wheezing, swelling of the face, lips, tongue or throat.
- if you have a reduced number of blood cells, 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 Accord,

- 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 Accord 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.
- if you have anaemia, low blood count (such as white blood cell count and platelet count), or *blood clotting problems* before treatment, or develop them during treatment. Your doctor may need to reduce the dose of your medicine or interrupt your treatment, or you may need other treatment. Your doctor will decide whether any change in your treatment is needed. In some cases, it may be necessary to stop treatment with temozolomide. Your blood will be tested regularly to monitor your condition. If you develop fever or symptoms of an infection contact your doctor immediately.
- you may have a small risk of other changes in blood cells, including leukaemia.
- if you feel sick or vomit, which are very common side effects of Temozolomide (see section 4). If you vomit frequently before or during treatment, ask your doctor about medicines to help prevent vomiting or control the vomiting and the best time to take temozolomide until the vomiting is under control. If you vomit after 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. Older patients are more prone to infections, increased bruising or bleeding.
- if you have liver or kidney problems as 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 Accord.

Other medicines and Temozolomide Accord

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 or, 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 Accord during pregnancy unless clearly indicated by your doctor.

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

You must not breast-feed whilst you are being treated with Temozolomide Accord.

Male fertility

Temozolomide Accord may cause permanent infertility. Male patients should use effective contraception 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.

Ask your doctor for advice before taking any medicine.

Driving and using machines

When you take temozolomide you may 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 Accord contains lactose

The 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.

3. How to take Temozolomide Accord

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

How to open sachet

Open the sachet by folding and tearing along the fold line with the notch in the corner of the sachet.

Temozolomide should only be prescribed by specialists experienced in brain tumours.

Dosage and duration of treatment

Your doctor will decide the correct dose of temozolomide for you to take, based on your size (height and weight) and whether you have had chemotherapy treatment. You may be given other medicines to take before and/or after temozolomide to avoid or control vomiting.

Take your prescribed dose of Temozolomide Accord once a day. Take the dose 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. Avoid inhaling the powder. If you accidentally get some in your eyes or nose, flush the area with water.

If you are taking Temozolomide Accord in combination with radiotherapy (newly diagnosed patients):

While the radiotherapy is ongoing your doctor will start temozolomide at a dose of 75 mg/m² and the actual daily dose you take will depend on your height and weight. You will take this dose every day for 42 days (up to 49 days) in combination with radiotherapy. Based on your blood counts and how you tolerate temozolomide, the dose may be delayed or stopped.

Once the radiotherapy is completed, you will interrupt treatment for 4 weeks to give your body a chance to recover.

Then there may be up to 6 treatment cycles, and each one lasts 28 days. You will take your new dose of temozolomide capsules initially at 150 mg/m² once daily for the first five days (“dosing days”) of each cycle, followed by 23 days without temozolomide; this adds up to a 28 day treatment cycle.

After day 28, the next cycle will begin, in which you will again take this medicine once daily for five days followed by 23 days without temozolomide. Based on your blood counts and how you tolerate temozolomide during each treatment cycle, the dose may be adjusted, delayed or stopped.

If you are taking Temozolomide Accord capsules alone (without radiotherapy):

A treatment cycle with Temozolomide Accord comprises 28 days. You will take the capsules once daily for the first five days (“dosing days”) followed by 23 days without temozolomide, adding up to the 28 day treatment cycle.

After day 28, the next cycle will begin, in which you will again take this medicine once daily for five 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.

If you have not been treated before with chemotherapy, you will take your first dose of temozolomide at 200 mg/m² once daily for the first five days (“dosing days”) followed by 23 days without temozolomide. If you have been treated before with chemotherapy, you will take your first dose of temozolomide at 150 mg/m² once daily for the first five days (“dosing days”) followed by 23 days without temozolomide.

Depending on your blood test results, your doctor may adjust your dose for the next cycle. Each time you start a new treatment cycle, be sure you understand exactly how many capsules of each strength you need to take each day and how many days you will receive this dose.

All patients

Temozolomide comes in different strength capsules (shown on the outer label in mg). Each strength has a different colour cap. Depending on the dose of temozolomide that your doctor prescribes, you may have to take several capsules on each dosing day of the treatment cycle.

- Be sure you understand exactly how many capsules you need to take of each strength. Ask your doctor or pharmacist to write down the number of each strength (including colour) that you need to take each dosing day.
- Be sure you know exactly which days are your dosing days.
- Be sure you review the dose with your health care provider each time you start a new cycle. Sometimes the dose or the mix of capsules you need to take will be different from the last cycle.
- Once you take the medicine home, if you are confused or unsure about how to take your dose, call for re-instruction before beginning the treatment cycle. Errors in how you take this medicine may have serious health consequences.

If you take more Temozolomide Accord than you should

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

If you forget to take Temozolomide Accord

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 double the next 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.

Patients taking temozolomide in combination with radiation therapy may experience different side effects than patients taking temozolomide alone.

Contact your doctor immediately if you have any of the following:

- a severe allergic reaction (hypersensitive) (hives, wheezing or other breathing difficulty),
- uncontrolled bleeding,
- Seizures (convulsions),
- fever,
- chills,
- severe headache that does not go away.

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/or a reduced resistance to infections. The reduction of blood cells is usually temporary, but in some cases may be for longer 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 discontinued.

Other side effects that have been reported are listed below:

Very common side effects (may affect more than 1 in 10 people):

- 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):

- infections, oral infections, wound 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, dry or 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):

- brain infections (meningoencephalitis herpetic) including fatal cases
- 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

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 national reporting system listed in Appendix V](#). By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Temozolomide Accord

Keep this medicine out of the sight and reach of children, preferably in a locked cupboard. Accidentally 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

Do not store above 25°C.

Store in the original bottle.

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

Sachet

Do not store above 25 °C.

Store in the original package in order to protect from moisture.

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 Accord contains

- The active substance is temozolomide.
Temozolomide Accord 5 mg hard capsules: Each capsule contains 5 mg temozolomide.
Temozolomide Accord 20 mg hard capsules: Each capsule contains 20 mg temozolomide.
Temozolomide Accord 100 mg hard capsules: Each capsule contains 100 mg temozolomide.

- Temozolomide Accord 140 mg hard capsules:* Each capsule contains 140 mg temozolomide.
- Temozolomide Accord 180 mg hard capsules:* Each capsule contains 180 mg temozolomide.
- Temozolomide Accord 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.
 - capsule shell:
 - Temozolomide Accord 5 mg hard capsules:* gelatine, titanium dioxide (E 171), yellow iron oxide (E 172), indigo carmine (E 132), water.
 - Temozolomide Accord 20 mg hard capsules:* gelatine, titanium dioxide (E 171), yellow iron oxide (E 172), water.
 - Temozolomide Accord 100 mg hard capsules:* gelatine, titanium dioxide (E 171), red iron oxide (E 172), water.
 - Temozolomide Accord 140 mg hard capsules:* gelatine, titanium dioxide (E 171), indigo carmine (E 132), water.
 - Temozolomide Accord 180 mg hard capsules:* gelatine, titanium dioxide (E 171), yellow iron oxide (E 172), red iron oxide (E 172), water.
 - Temozolomide Accord 250 mg hard capsules:* gelatine, titanium dioxide (E 171), water.
 - printing ink:
shellac, propylene glycol, black iron oxide (E172) and potassium hydroxide.

What Temozolomide Accord looks like and contents of the pack

Temozolomide Accord 5 mg hard capsules have a white body, a green cap, and are imprinted ‘TMZ’ on cap and ‘5’ on body with black ink.

Temozolomide Accord 20 mg hard capsules have a white body, a yellow cap, and are imprinted ‘TMZ’ on cap and ‘20’ on body with black ink.

Temozolomide Accord 100 mg hard capsules have a white body, a pink cap, and are imprinted ‘TMZ’ on cap and ‘100’ on body with black ink.

Temozolomide Accord 140 mg hard capsules have a white body, a blue cap, and are imprinted ‘TMZ’ on cap and ‘140’ on body with black ink.

Temozolomide Accord 180 mg hard capsules have a white body, a maroon cap, and are imprinted ‘TMZ’ on cap and ‘180’ on body with black ink.

Temozolomide Accord 250 mg hard capsules have a white body, a white cap, and are imprinted ‘TMZ’ on cap and ‘250’ on body with black ink.

The hard capsules are dispensed in amber glass bottles containing 5 or 20 capsules. Each carton contains 1 bottle.

The hard capsules are dispensed in sachet containing 1 capsule. Each carton contains 5 or 20 sachets.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder

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This leaflet was last revised in

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency website:
<http://www.ema.europa.eu>.