PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) - 1986

This medicine is dispensed with a doctor's prescription only.

TEMO 5 mg, TEMO 20 mg, TEMO 100 mg, TEMO 140 mg, TEMO 250 mg
Capsules

Each capsule contains:
Temozolomide 5mg, 20mg, 100mg, 140mg, 250mg

For a list of inactive ingredients, see section 6.1 "What Temo contains". See also section 2.7 "Important information regarding some of the ingredients of Temo".

Read this entire leaflet carefully before using this medicine.
- This leaflet contains concise information about **Temo**. If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for your treatment. Do not pass it on to others. It might harm them, even if you think that their medical condition is similar to yours.
- This medicine is not intended for children under 3 years of age, since there is no information regarding use in patients under the age of 3. The information concerning children over 3 years of age is limited.

1. WHAT IS TEMO AND WHAT IS IT USED FOR?

1.1 What is Temo?
Temo contains the active ingredient temozolomide. This medicine is intended for the treatment of cancerous tumors or different types of brain tumors. **Temo** belongs to the group of cytotoxic medicines or chemotherapy medicines.
Therapeutic group: Antineoplastic preparation.

1.2 What is Temo used for?
Temo capsules are intended for the treatment of:
- Adult patients suffering from newly diagnosed glioblastoma multiforme (a unique form of brain tumor) combined with radiation treatment and subsequently as monotherapy treatment.
- Children over 3 years of age, adolescents and adults suffering from malignant glioma such as glioblastoma multiforme or anaplastic astrocytoma (unique forms of brain tumors), that recur or continue to develop after standard treatment.
- **Temo** capsules are also intended as a first line of treatment for adult patients suffering from advanced metastatic malignant melanoma.

2. BEFORE TAKING TEMO

☒ 2.1 Do not take Temo:
- If you are allergic to the active ingredient temozolomide or to any of the other ingredients of this medicine, listed in section 6.1.
- If you have had an allergic reaction to dacarbazine (an anticancer medicine sometimes called DTIC) in the past. Signs of an allergic reaction include feeling itchy, breathlessness or wheezing, swelling of the face, lips, tongue or throat.
- If there is a severe decrease of certain blood cells (myelosuppression), such as your white blood cell count and platelet count. These blood cells are important for fighting infections and for proper blood clotting. Your doctor will perform blood tests to make sure you have enough of these blood cells before starting treatment.
- If you are pregnant or breastfeeding.

2.2 Special warnings regarding the use of Temo
Before treatment with **Temo**, talk to your doctor, pharmacist or nurse in the following cases:
- Since you must be observed closely for the development of a serious case of a chest infection called pneumocystis jirovecii pneumonia (PCP). If you are a newly diagnosed patient (glioblastoma multiforme), you may receive **Temo** for 42 days in combination with radiation. In this case, your doctor will also prescribe you a medicine that will help prevent this type of pneumonia (PCP).
- If you have suffered in the past or might be suffering from hepatitis B. This is because **Temo** may cause the reactivation of a virus that causes hepatitis B which could even be life-threatening in certain cases. The patients will be meticulously tested by their doctor for signs of this infection before starting treatment.
- If you have a low count of red blood cells (anemia), white blood cells and platelets, or blood clotting problems before starting treatment or if you developed them during treatment. Your doctor might reduce the dosage, intervene, stop or change your treatment. You might also need other treatments. In certain cases, it may be necessary to stop treatment with **Temo**. Blood tests will be performed frequently during the course of treatment in order to monitor the side effects of **Temo** on your blood cells. as you may have a small risk of additional changes in your blood cells, including leukemia.
- If you have nausea and/or vomiting, which are very common side effects of **Temo** (see section 4), your doctor may prescribe you an anti-emetic medicine to help prevent vomiting. If you vomit frequently before or during treatment, ask your doctor about the best time to take **Temo** until the vomiting is under control. If you vomit after taking the dose, do not take a second dose on the same day.
- If you develop a fever or symptoms of an infection, refer to your doctor immediately.
- If you are older than 70 years of age, since you might be more prone to infections, bruising or bleeding.
- If you have liver or kidney problems, there may be a need to adjust the dosage of **Temo**.
- When using the medicine, there is a risk of liver damage, including liver failure that may be life-threatening. Therefore, it is necessary to perform liver function tests before and during treatment with **Temo.**

☒ 2.3 Taking other medicines and Temo
If you are taking or have recently taken other medicines, including non-prescription medicines and nutritional supplements, tell the attending doctor or pharmacist. Especially inform the doctor or pharmacist if you are taking: other medicines used to treat cancer, other myelosuppressive medicines or valproic acid.

☒ 2.4 Taking Temo with food and drink
Take the capsules on an empty stomach, for example: at least an hour before you plan to eat breakfast. Swallow the capsule/s whole with a glass of water.

☒ 2.5 Pregnancy, breastfeeding and fertility
If you are pregnant, think you might be pregnant or are planning on becoming pregnant, consult your doctor or pharmacist before taking this medicine. This is because you must not use **Temo** during pregnancy unless explicitly instructed to do so by your doctor. Female patients or female partners of patients must avoid pregnancy during treatment and for 6 months following treatment completion.
Male and female patients taking **Temo** must use effective contraceptive means (see also "Fertility in men" below).
You must stop breastfeeding during treatment with **Temo**.
Male fertility:
Temo may cause permanent infertility. Men treated with **Temo** should use effective contraceptive means and not impregnate their partner for up to 6 months after stopping treatment. It is recommended to seek advice on conservation of sperm before starting the treatment.

☒ 2.6 Driving and use of machinery
Temo may make you feel tired or sleepy. In this case, do not drive or operate any tools or machinery or ride a bicycle until you see how this medicine affects you (see section 4 "Side effects").

☒ 2.7 Important information about some of the ingredients of Temo
Temo contains lactose (a type of sugar). If you have been told by your doctor that you have an intolerance to certain sugars, refer to your doctor before taking the medicine.

☒ 2.8 Children and adolescents
Do not give this medicine to children under 3 years of age as it has not been studied. **Temo** is intended for the treatment of children from 3 years of age for different types of brain tumors (such as glioblastoma multiforme and anaplastic astrocytoma), that recur or continue to develop after standard treatment. However, the information on children over 3 years of age is limited.

3. HOW SHOULD YOU USE TEMO?
Always take **Temo** exactly as prescribed by the doctor. It is very important to check with your doctor or pharmacist if you are unsure. Mistakes in how you take the medicine might have severe repercussions on your health.

Do not exceed the recommended dose.
This medicine is not intended for infants and children under 3 years of age.
Your doctor will decide on the exact dose of **Temo** you should take, based on body size (height, weight), and whether or not you have been treated with chemotherapy in the past. You may be asked to take an additional medicine before or after taking **Temo** in order to prevent or control nausea and vomiting.

How to take this medicine (for all patients):
Take your prescribed **Temo** dose once a day on an empty stomach, for example, at least one hour before breakfast. It is preferable to take the dose at the same time every day. Swallow the capsule whole with a glass of water.
Do not open, crush or chew the capsule. If a capsule has been damaged, avoid contact of the capsule's powder with the skin and mucous membrane (eyes, nose).
Depending on the dosage that will be determined for you, you may need to swallow more than one capsule at a time, and you may need to swallow capsules of different dosages together (dosages – the amount of active ingredient in the capsule, in milligrams). The color of the stripes and the writing on the capsules is different for the different dosages (see details in the following table).

Strength	Color of stripes and writing
TEMO 5 mg	"T 5mg" written in green
TEMO 20 mg	"T 20mg" written in orange
TEMO 100 mg	"T 100mg" written in pink
TEMO 140 mg	"T 140mg" written in blue
TEMO 250 mg	"T 250mg" written in black

Make sure that you fully understand and remember the following points:
- The number of capsules you have to take every "dosing day". Ask your doctor or pharmacist to write it down (including the color of the stripes).
- What your dosing days are – the days on which you take the medicine.

Confirm the dosage with your doctor every time you start a new treatment cycle, since it might be different than the previous treatment cycle.

Tests and follow-up
During the course of treatment you must undergo blood tests frequently in order to monitor the status of your blood cells.
In addition, a liver function test will be performed before and during the course of treatment, since there is a risk of liver damage that may even be life-threatening (see section 2).
In case of vomiting after taking the medicine, do not take another dose that same day.
If you took more Temo than you should have
If you accidently took more **Temo** capsules than you were told to, refer to your doctor, pharmacist or nurse immediately.
If you forgot to take Temo
Take the forgotten dosage as soon as possible during the same day. If a full day of treatment has passed, check with your doctor. Do not take a double dose to make up for a forgotten dose, unless the doctor instructed you to do so.
Do not take medicines in the dark! Check the label and the dose each time you take a medicine. Wear glasses if you need them.
If you have any further questions regarding the use of this medicine, ask your doctor, pharmacist or nurse.

4. SIDE EFFECTS
As with any medicine, the use of this medicine may cause side effects in some users.
Refer to your doctor immediately if you have any of the following signs**:**
- A severe allergic (hypersensitivity) reaction (hives, wheezing or other breathing difficulties)
- Uncontrolled bleeding
- Epileptic seizures (convulsions)
- Fever
- Severe headache that does not go away

Treatment with **Temo** may cause a reduction in the counts of certain kinds of blood cells. This may cause you increased bruising or bleeding, anemia (a shortage of red blood cells), fever, and reduced resistance to infections. The reduction in blood cell counts usually lasts a short while. In certain cases, it may be prolonged and may lead to a very severe form of anemia (aplastic anemia). Your doctor will regularly check your blood to detect changes, and decide if any treatment is needed. In some cases, the dosage of **Temo** will be reduced or the treatment will be stopped.

Side effects from clinical studies:
Temo in combination treatment with radiotherapy in newly diagnosed glioblastoma patients
Patients receiving **Temo** in combination with radiotherapy may experience different side effects than patients taking **Temo** alone. The following side effects may occur, and may require medical attention:

Very common (effects that occur in more than one in ten users): loss of appetite, headache, constipation (difficulty passing stools), nausea, vomiting, rash, hair loss, tiredness.

Common (effects that may affect up to 1 in 10 users): oral infections, wound infection, a reduction in the number of blood cells (neutropenia, thrombocytopenia, lymphocytopenia, leukopenia), increased blood sugar levels, weight loss, 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, diarrhea, stomach or abdominal pain, heartburn, upset stomach, difficulty swallowing, dry mouth, skin irritation or redness, dry skin, itchiness, muscle weakness, joint pain, muscle pains, frequent urination, difficulty holding in urine, allergic reaction, fever, radiation injury, facial swelling, pain, abnormal taste, abnormal liver function test results.

Uncommon (effects that may affect up to 1 in 100 users): flu-like symptoms, red spots under the skin, low potassium level in the blood, weight gain, mood swings, hallucinations and memory impairment, partial paralysis, impaired coordination, impaired sensations, partial loss of vision, dryness or pain in the eyes, deafness, middle ear infection, ringing in the ears, earaches, palpitations (when you can feel your heartbeats), blood clot in the lung, hypertension, pneumonia, inflammation of the sinuses, bronchitis, a cold or the flu, swollen abdomen, difficulty controlling bowel movements, hemorrhoids, peeling skin, increased skin sensitivity to sunlight, change in skin color, 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, change in tongue color, changes in sense of smell, thirst, tooth disorder.

Temo monotherapy treatment in patients with recurring or progressive glioma or malignant melanoma
The following side effects may occur and require medical attention:

Very common (effects that occur in more than one in ten users): reduced number of blood cells (neutropenia or lymphocytopenia, thrombocytopenia), loss of appetite, headache, vomiting, nausea, constipation (difficulty passing stools), tiredness.

Common (effects that may affect up to 1 in 10 users): weight loss, sleepiness, dizziness, tingling sensation, shortness of breath, diarrhea, abdominal pain, upset stomach, rash, itching, hair loss, red spots under the skin, fever, weakness, shivering, feeling unwell, pain, changes in sense of taste.

Uncommon (effects that may affect up to 1 in 100 users): reduced blood cell counts (pancytopenia, anemia, leukopenia).

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

Very rare (effects that may affect up to 1 in 10,000 users): skin redness, urticaria (hives), skin eruptions, allergic reactions.

Additional side effects:
Cases of elevations of liver enzymes have been commonly reported. Cases of increased bilirubin, problems in bile flow (cholestasis), hepatitis and liver damage, 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. **Refer to your doctor immediately** if these side effects appear.
Very rare cases of lung side effects, including cases of non-infectious pneumonia, have been observed with **Temo**. Patients usually experience shortness of breath and cough. If you notice these symptoms, refer to your doctor.
In very rare cases, patients taking **Temo** and similar medicines might be at risk of developing secondary cancers, including leukemia.
New or recurring cytomegalovirus infections and reactivated hepatitis B virus infections have been uncommonly reported.
Cases of brain infections cause by the herpes virus (meningoencephalitis herpetic), including fatal cases, have been uncommonly reported.
Cases of diabetes insipidus have been uncommonly reported. Signs of diabetes insipidus include passing a lot of urine and a feeling of thirst.

If a side effect appears, if one of the side effects worsens or if you suffer from a side effect not mentioned in this leaflet, consult your doctor.

Reporting of side effects:
Side effects can be reported to the Ministry of Health by clicking on the link "Report Side Effects of Drug Treatment" found on the Ministry of Health homepage (www.health.gov.il) which directs to the online form for reporting side effects, or by entering the link:
https://forms.gov.il/globaldata/getsequence/getsequence.aspx?formType=AdversEffectMedic@moh.gov.il
Additionally, you can report to Perrigo via the following address: www.perrigo-pharma.co.il

5. HOW SHOULD THE MEDICINE BE STORED?
- Store this medicine out of the reach and sight of children, preferably in a locked cabinet. Accidental swallowing can be lethal for children.
- Do not use the medicine after the expiry date (exp. date) that appears on the package. The expiry date refers to the last day of that month
- Storage conditions: Store below 25°C. Can be used for 3 weeks after first opening, but not later than the expiry date.
- Do not dispose of medicines via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer in use. These measures will help to protect the environment.

6. PACKAGE CONTENTS AND FURTHER INFORMATION

6.1 What does Temo contain?
In addition to the active ingredient Temozolomide the medicine also contains:
Lactose anhydrous, Sodium starch glycolate (type A), Stearic acid, Tartaric acid, Silica colloidal anhydrous, Gelatin, Titanium dioxide (E 171).
Each 5 mg capsule contains: 87.30 mg lactose and 0.21 mg sodium.
Each 20 mg capsule contains: 72.30 mg lactose and 0.21 mg sodium.
Each 100 mg capsule contains: 83.60 mg lactose and 0.42 mg sodium.
Each 140 mg capsule contains: 117.04 mg lactose and 0.59 mg sodium.
Each 250 mg capsule contains: 209.00 mg lactose and 1.05 mg sodium.

6.2 What Temo looks like and contents of the package
Temo 5 mg: white opaque gelatin capsule with two stripes and "T 5mg" written in green.
Temo 20 mg: white opaque gelatin capsule with two stripes and "T 20mg" written in orange.
Temo 100 mg: white opaque gelatin capsule with two stripes and "T 100mg" written in pink.
Temo 140 mg: white opaque gelatin capsule with two stripes and "T 140mg" written in blue.
Temo 250 mg: white opaque gelatin capsule with two stripes and "T 250mg" written in black.
The capsules contain a white-beige to light pink powder.
- Registration holder and address: Perrigo Israel Agencies Ltd., 1 Rakefet St., Shoham 6085000.
- Manufacturer and address: Haupt Pharma Amareg GmbH, Regensburg, Germany.
- This leaflet was checked and approved by the Ministry of Health in May 2015 and was updated in accordance with the Ministry of Health's instructions in May 2018.
- Registration number of the medicine in the National Drug Registry of the Ministry of Health:
  Temo 5 mg:14524.33256
  Temo 20 mg:14525.33257
  Temo 100 mg:14526.33258
  Temo 140 mg:14527.33259
  Temo 250 mg:14529.33261

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