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 250 mg
Capsules

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

Inactive ingredients and allergens in the medicine - see section 2 "**Important information about some of the ingredients of Temo**" and in section 6 of this leaflet.

Read this entire leaflet carefully before using this medicine.
- This leaflet contains concise information about the medicine. If you have any further questions, refer to the 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 years. The information concerning children over 3 years of age is limited.

1. What is the medicine intended for?
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 medicines called cytotoxic or chemotherapy medicines.

Temo capsules are intended for the treatment of:
- Patients suffering from newly diagnosed glioblastoma multiforme (a unique form of brain tumor) combined with radiation treatment and subsequently as monotherapy treatment.
- In patients 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.
- A first line treatment for patients suffering from advanced metastatic malignant melanoma.

Therapeutic group: Antineoplastic preparation.

2. Before using Temo

Do not use Temo if:
- you are hypersensitive (allergic) to the active ingredient temozolomide or to any of the other ingredients this medicine contains (see section 6 "**Additional Information**" in this leaflet).
- 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.
- 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. The doctor will perform blood tests to make sure you have enough of these blood cells before starting treatment.
- you are pregnant or breastfeeding.

Special warnings regarding the use of Temo
Before treatment with **Temo**, talk to your doctor, pharmacist or nurse
- 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 decide to 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 a 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**.

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.

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 also in section 2 special warnings regarding the use of **Temo**).

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

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.

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 who are able to become pregnant during the treatment with **Temo** should use effective contraceptive precautions during the treatment and for at least 6 months following treatment completion.

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 at least 3 months after stopping treatment. It is recommended to seek advice on conservation of sperm before starting the treatment.

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**").

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.
Temo contains less than 23 mg sodium in each capsule, and therefore is considered "sodium free".

3. How should you use Temo?
Always take **Temo** as instructed by the doctor. Check with the doctor or pharmacist if you are not sure. 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.

Crushing/halving/chewing:
Do not open, crush or chew the capsule.
Temo belongs to the group of medicines called cytotoxic or chemotherapy medicines. Opening the capsules causes a risk of unintended exposure to the medicine by inhalation or contact with the skin or mucous membranes. In order to reduce the risk of unintentional exposure to **Temo**, do not open the capsules. If a capsule has been damaged, avoid contact of the capsule's powder with the skin and mucous membrane (eyes, nose). In case of contact with the powder, wash your hands.

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 doses together (doses – 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 strengths (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 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 dose with your doctor every time you start a new treatment cycle, since it might be different than the previous treatment cycle.
In case of vomiting after taking the medicine, do not take another dose that same day.

If you have accidentally taken a higher dose
If you have accidently taken more **Temo** capsules than you were told, refer immediately to your doctor, pharmacist or nurse.

If you forgot to take Temo
Take the forgotten dose 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. Do not be alarmed when reading the list of side effects .You may not suffer from any of them.

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
- Chills
- Severe headache that does not go away

Treatment with **Temo** may cause a reduction in 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.

Additional side effects that have been reported are listed below:
Very common side effects (effects that may affect more than one in ten users):
- loss of appetite, difficulty speaking, headache
- diarrhea, constipation, nausea, vomiting
- rash, hair loss
- tiredness

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

Uncommon side effects (effects that may affect up to 1 in 100 users):
- brain infections caused by the herpes virus (meningoencephalitis herpetic), including fatal cases
- wound infections
- new or reactivated cytomegalovirus infections
- reactivated hepatitis B virus infections
- secondary cancer including leukemia
- reduced blood cell counts (pancytopenia, anemia, leukopenia)
- red spots under the skin
- diabetes insipidus (symptoms include increased production of urine and feeling thirsty), low potassium level in the blood
- mood swings, hallucinations
- partial paralysis, changes in sense of smell
- hearing impairment, middle ear infection
- palpitations (when you can feel your heartbeat), hot flushes
- swollen stomach, difficulty controlling bowel movements, hemorrhoids, dry mouth
- hepatitis and injury to the liver (including fatal liver failure), biliary obstruction (cholestasis), an increase in bilirubin
- blisters on the body or in the mouth, skin peeling, skin eruption, painful reddening of the skin, a serious rash accompanied by skin swelling (including the palms of your hands and soles of your feet)
- increased skin sensitivity to sunlight, urticaria (hives), increased sweating, change in skin color
- difficulty in urinating
- vaginal bleeding, vaginal irritation, absent or heavy menstrual periods, breast pain, sexual impotence
- shivering, face swelling, change in tongue color, thirst, dental problems
- dry eyes

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 the 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://sideeffects.health.gov.il
Additionally, you can report to the company via the following address: Padagis.co.il

5. How should the medicine be stored?
- Avoid poisoning! This medicine and any other medicine must be kept in a closed place out of the reach and sight of children and/or infants, preferably in a locked cabinet, to avoid poisoning. Accidental swallowing can be lethal for children. Do not induce vomiting unless explicitly instructed to do so by a doctor.
- 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 the noted month.
- 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 the pharmacist how to dispose of medicines no longer in use. These measures will help protect the environment.

6. Additional information
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 **Temo 5** mg capsule contains: 87.30 mg lactose
Each **Temo 20** mg capsule contains: 72.30 mg lactose
Each **Temo 100** mg capsule contains: 83.60 mg lactose
Each **Temo 250** mg capsule contains: 209.00 mg lactose

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 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. The capsules are packaged in a glass bottle that contains 5, 20 capsules.
Not all package sizes may be marketed.

- Registration holder and address: Padagis Israel Agencies Ltd., 1 Rakefet St., Shoham.
- Manufacturer and address: Haupt Pharma Amareg GmbH, Regensburg, Germany.
- Revised in February 2022 according to MOH guidelines.
- Drug registration number at the national medicines registry of the Ministry of Health:
  Temo 5 mg: 145.24.33256
  Temo 20 mg: 145.25.33257
  Temo 100 mg: 145.26.33258
  Temo 250 mg: 145.29.33261

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