

Pharmacist: Tear at perforations and give to patients

<p style="text-align: center;">Patient Information</p>
<p style="text-align: center;">Temozolomide Capsules</p> <p style="text-align: center;">(TEM-oh-ZOE-loe-mide)</p>
<p>What is the most important information I should know about temozolomide capsules?</p> <p>Temozolomide capsules may cause birth defects.</p> <p>Females and female partners of male patients who take temozolomide capsules:</p> <ul style="list-style-type: none">○ Avoid becoming pregnant while taking temozolomide capsules.○ Females who can become pregnant should use an effective form of birth control (contraception) during treatment and for at least 6 months after your last dose of temozolomide capsules. Your doctor should do a pregnancy test to make sure that you are not pregnant before you start taking temozolomide capsules.○ Tell your doctor right away if you become pregnant or think you are pregnant during treatment with temozolomide capsules. <p>Males taking temozolomide capsules and have a female partner who is pregnant or who can become pregnant:</p> <ul style="list-style-type: none">○ Use a condom for birth control (contraception) during treatment and for at least 3 months after taking your final dose of temozolomide capsules.○ Do not donate semen during treatment and for at least 3 months after your final dose of temozolomide capsules. <p>See the section “What are the possible side effects of temozolomide capsules?” for more information about side effects.</p>
<p>What is temozolomide capsule?</p> <p>Temozolomide capsule is a prescription medicine used to treat adults with certain brain cancer tumors.</p> <p>It is not known if temozolomide capsule is safe and effective in children.</p>
<p>Who should not take temozolomide capsules?</p> <p>Do not take temozolomide capsule if you:</p> <ul style="list-style-type: none">• have had an allergic reaction to temozolomide or any of the other ingredients in temozolomide capsules. See the end of this leaflet for a list of ingredients in temozolomide capsules. Symptoms of an allergic reaction with temozolomide capsules may include: a red itchy rash, or a severe allergic reaction, such as trouble breathing, swelling of the face, throat, or tongue, or severe skin reaction. If you are not sure, ask your doctor.• have had an allergic reaction to dacarbazine (DTIC), another cancer medicine.
<p>What should I tell my doctor before taking temozolomide capsules?</p>

Tell your doctor about all of your medical conditions, including if you:

- have kidney problems
- have liver problems
- are pregnant or plan to become pregnant. See **“What is the most important information I should know about temozolomide capsules?”**
- are breast-feeding or plan to breastfeed. It is not known if temozolomide passes into your breast milk. **Do not** breastfeed during treatment and for at least 1 week after your last dose of temozolomide capsules.

Tell your doctor about all the medicines you take, including prescription and non-prescription medicines, vitamins, and herbal supplements. Especially tell your doctor if you take a medicine that contains valproic acid.

Know the medicines you take. Keep a list of them and show it to your doctor and pharmacist when you get a new medicine.

How should I take temozolomide capsules?

Temozolomide capsules may be taken by mouth as a capsule.

Your doctor will decide the best way for you to take temozolomide capsules. Take temozolomide capsules exactly as prescribed by your doctor.

There are 2 common dosing schedules for taking temozolomide capsules depending on the type of brain cancer tumor that you have.

- People with certain brain cancer tumors take or receive temozolomide capsules:
 - 1 time each day for 42 days in a row (possibly 49 days depending on side effects) along with receiving radiation treatment. **This is 1 cycle of treatment.**
 - After this, your doctor may prescribe 6 more cycles of temozolomide capsules as “maintenance” treatment. For each of these cycles, you take or receive temozolomide capsules 1 time each day for 5 days in a row and then you stop taking it for the next 23 days. **This is a 28-day maintenance treatment cycle.**
- People with certain other brain cancer tumors take or receive temozolomide capsules:
 - 1 time each day for 5 days in a row only, and then stop taking it for the next 23 days. **This is 1 cycle of treatment (28 days).**
 - Your doctor will watch your progress on temozolomide capsules and decide how long you should take it. You might take temozolomide capsules until your tumor gets worse or for possibly up to 2 years.
- If your doctor prescribes a treatment regimen that is different from the information in this leaflet, make sure you follow the instructions given to you by your doctor.

- Your doctor may change your dose of temozolomide capsules, or tell you to stop temozolomide capsules for a short period of time or permanently if you have certain side effects.
- Your doctor will decide how many treatment cycles of temozolomide capsules that you will receive, depending on how you respond to and tolerate treatment.

Temozolomide capsules:

- Take temozolomide capsules exactly as your doctor tells you to.
- Temozolomide capsules come in different strengths. Each strength has a different color cap. Your doctor may prescribe more than 1 strength of temozolomide capsules for you, so it is important that you understand how to take your medicine the right way. Be sure that you understand exactly how many capsules you need to take on each day of your treatment, and what strengths to take. **This may be different whenever you start a new cycle.**
- **Do not** take more temozolomide capsules than prescribed.
- Talk to your doctor or pharmacist before taking your dose if you are not sure how much temozolomide capsules to take. This will help to prevent taking too much temozolomide capsules and decrease your chances of getting serious side effects.
- Take each day's dose of temozolomide capsules at one time, with a full glass of water.
- **Swallow temozolomide capsules whole.** Do not chew, open, or split the capsules.
- Take temozolomide capsules at the same time each day.
- Take temozolomide capsules the same way each time, either with food or without food.
- If temozolomide capsules are accidentally opened or damaged, be careful not to breathe in (inhale) the powder from the capsules or get the powder on your skin or mucous membranes (for example, in your nose or mouth). If contact with any of these areas happens, flush the area with water.
- To help reduce nausea and vomiting, try to take temozolomide capsules on an empty stomach or at bedtime. Your doctor may prescribe medicine to help prevent or treat nausea, or other medicines to reduce side effects with temozolomide capsules.
- See your doctor regularly to check your progress. Your doctor will check you for side effects.
- If you take more temozolomide capsules than prescribed, call your doctor or get emergency medical help right away.

What are the possible side effects of temozolomide capsules?

Temozolomide capsules can cause serious side effects, including:

- See “**What is the most important information I should know about temozolomide capsules?**”
- **Decreased blood cell counts.** Temozolomide capsules can affect your bone marrow

and cause you to have decreased blood cell counts. Decreased white blood cell count, red blood cell count and platelet count are common with temozolomide capsules but it can also be severe and lead to death.

- Your doctor will do blood tests regularly to check your blood cell counts before you start and during treatment with temozolomide capsules.
- Your doctor may need to change the dose of temozolomide capsules, or when you get it depending on your blood cell counts.
- **People who are age 70 or older and women have a higher risk for developing decreased blood cell counts during treatment with temozolomide capsules.**
- **Secondary cancers.** Blood problems such as myelodysplastic syndrome (MDS) and new cancers (secondary cancers), including a certain kind of leukemia, can happen in people who take temozolomide capsules. Your doctor will monitor you for this.
- **Pneumocystis pneumonia (PCP).** PCP is an infection that people can get when their immune system is weak. Temozolomide capsules decreases white blood cells, which makes your immune system weaker and can increase your risk of getting PCP.
 - People who are taking steroid medicines or who stay on temozolomide capsules for a longer period of time may have an increased risk of getting PCP infection.
 - Anyone who takes temozolomide capsules will be watched carefully by their doctor for low blood cell counts and this infection.
 - Tell your doctor if you have any of the following signs and symptoms of PCP infection: shortness of breath, or fever, chills, dry cough.
- **Liver problems. Liver problems can happen with temozolomide capsules and can sometimes be severe and lead to death.** Your doctor will do blood tests to check your liver function before you start taking temozolomide capsules, during treatment, and about 2 to 4 weeks after your last dose of temozolomide capsules.

Common side effects of temozolomide capsules include:

- hair loss
- feeling tired
- nausea and vomiting.
- headache
- constipation
- loss of appetite
- convulsions
- rash
- diarrhea
- unable to move (paralysis) on one side of the body
- weakness
- fever
- dizziness
- coordination problems
- viral infection
- memory loss
- sleep problems

Temozolomide capsules can affect fertility in males and may affect your ability to father a child. Talk with your doctor if fertility is a concern for you.

These are not all the possible side effects with temozolomide capsules. For more information, ask your doctor or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store temozolomide capsules?

- Store temozolomide capsules at 77°F (controlled room temperature). Storage at 59°F to 86°F (15°C to 30°C) is permitted occasionally.
- Temozolomide capsules comes in a child-resistant package.
- **Keep temozolomide capsules and all medicines out of the reach of children.**

General information about the safe and effective use of temozolomide capsules.

Medicines are sometimes prescribed for purposes other than those listed in the Patient Information leaflet. Do not use temozolomide capsules for a condition for which it was not prescribed. Do not give temozolomide capsules to other people, even if they have the same symptoms that you have. It may harm them.

This leaflet summarizes the most important information about temozolomide capsules. If you would like more information, talk with your doctor. You can ask your pharmacist or doctor for information about temozolomide capsules that is written for health professionals.

For more information, go to www.accordhealthcare.us or call Accord Healthcare at 1-866-941-7875.

What are the ingredients in temozolomide capsules?

Temozolomide capsules:

Active ingredient: temozolomide.

Inactive ingredients: lactose anhydrous, colloidal anhydrous silica, sodium starch glycolate, tartaric acid, stearic acid.

The body of the capsules is made of gelatin and is white. The body of 250 mg capsule contain additionally sodium lauryl sulfate. The cap is also made of gelatin, and the colors vary based on the dosage strength. The capsule body and cap are imprinted with pharmaceutical branding ink, which contains black iron oxide, potassium hydroxide and shellac.

Temozolomide capsules 5 mg: The green cap contains gelatin, titanium dioxide, iron oxide yellow and FD&C Blue 2.

Temozolomide capsules 20 mg: The yellow cap contains gelatin, iron oxide yellow and titanium dioxide.

Temozolomide capsules 100 mg: The pink cap contains gelatin, titanium dioxide and iron oxide red.

Temozolomide capsules 140 mg: The transparent blue cap contains gelatin and FD&C Blue 2.

Temozolomide capsules 180 mg: The maroon cap contains gelatin, iron oxide red, iron oxide yellow and titanium dioxide.

Temozolomide capsules 250 mg: The white cap contains gelatin, titanium dioxide and sodium lauryl sulfate.

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Durham, NC 27703,
USA.

Manufactured By:

Intas Pharmaceuticals Limited,
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This Patient Information has been approved by the U.S. Food and Drug Administration.

Temozolomide Capsules

PHARMACIST:

Dispense enclosed Patient Package Insert to each patient.

PHARMACIST INFORMATION SHEET

IMPORTANT DISPENSING INFORMATION

For every patient, dispense temozolomide capsules in a separate vial or in its original package, making sure each container lists the strength per capsule and that patients take the appropriate number of capsules from each package or vial. Please see the dispensing instructions below for more information.

What is temozolomide capsule? *[See Full Prescribing Information, Indications and Usage (1).]*

Temozolomide is an oral alkylating agent for the treatment of newly diagnosed glioblastoma multiforme and refractory anaplastic astrocytoma.

How is temozolomide capsules dosed? *[See Full Prescribing Information, Recommended Dosage and Dosage Modifications for Newly Diagnosed Glioblastoma (2.1), Recommended Dosage and Dosage Modifications for Refractory Anaplastic Astrocytoma (2.2).]*

The physician calculates the daily dose of temozolomide capsules for a given patient based on the patient's body surface area (BSA). Round off the resulting dose to the nearest 5 mg. An example of the dosing may be as follows: the initial daily dose of temozolomide capsules in milligrams is the BSA multiplied by mg/m²/day (e.g., a patient with a BSA of 1.84 is 1.84 x 75 mg = 138, or 140 mg/day). Adjust the dose for subsequent cycles according to nadir neutrophil and platelet counts in the previous cycle and at the time of initiating the next cycle.

How might the dose of temozolomide capsules be modified for Refractory Anaplastic Astrocytoma? *[See Full Prescribing Information, Recommended Dosage and Dosage Modifications for Refractory Anaplastic Astrocytoma (2.2).]*

The initial dose is 150 mg/m² orally once daily for 5 consecutive days per 28-day treatment cycle. Increase the temozolomide capsules dose to 200 mg/m²/day for 5 consecutive days per 28-day treatment cycle if both the nadir and day of dosing (Day 29, Day 1 of next cycle) absolute neutrophil counts (ANC) are greater than or equal to 1.5 x 10⁹/L (1500/μL) and both the nadir and Day 29, Day 1 of next cycle platelet counts are greater than or equal to 100 x 10⁹/L (100,000/μL). During treatment, obtain a complete blood count on Day 22 (21 days after the first dose), and weekly until the ANC is above 1.5 x 10⁹/L (1500/μL) and the platelet count exceeds 100 x 10⁹/L (100,000/μL). Do not start the next cycle of temozolomide capsules until the ANC and platelet count exceed these levels. If the ANC falls to less than 1.0 x 10⁹/L (1000/μL) or the platelet count is less than 50 x 10⁹/L (50,000/μL) during any cycle, reduce the dose for the next cycle by

50 mg/m². Permanently discontinue temozolomide capsules in patients who are unable to tolerate a dose of 100 mg/m² per day.

Patients should continue taking temozolomide capsules until their physician determines that their disease has progressed or until unacceptable side effects or toxicities occur. In the clinical trial, treatment could be continued for a maximum of 2 years, but the optimum duration of therapy is not known. Physicians may alter the treatment regimen for a given patient.

Dosing for Patients with Newly Diagnosed Glioblastoma Multiforme [*See Full Prescribing Information, Recommended Dosage and Dosage Modifications for Newly Diagnosed Glioblastoma (2.1).*]

Concomitant Phase Treatment Schedule

Administer temozolomide capsules orally at 75 mg/m² daily for 42 days concomitant with focal radiotherapy (60 Gy administered in 30 fractions), followed by maintenance temozolomide capsules for 6 cycles. No dose reductions are recommended; however, dose interruptions may occur based on patient tolerance. Continue the temozolomide capsules dose throughout the 42-day concomitant period up to 49 days if all of the following conditions are met: absolute neutrophil count greater than or equal to 1.5 x 10⁹/L, platelet count greater than or equal to 100 x 10⁹/L, and nonhematological adverse reactions less than or equal to Grade 1 (except for alopecia, nausea and vomiting). During treatment, obtain a complete blood count weekly. Interrupt or discontinue temozolomide dosing during the concomitant phase according to the hematological and nonhematological toxicity criteria [*see Table 1 in the Full Prescribing Information, Recommended Dosage and Dosage Modifications for Newly Diagnosed Glioblastoma (2.1)*]. *Pneumocystis pneumonia* (PCP) prophylaxis is required during the concomitant administration of temozolomide capsules and radiotherapy, and should be continued in patients who develop lymphocytopenia until resolution to Grade 1 or less.

Maintenance Phase Treatment Schedule

Four weeks after completing the temozolomide capsules and radiotherapy phase, administer temozolomide capsules for an additional 6 cycles of maintenance treatment. Dosage in Cycle 1 (maintenance) is 150 mg/m² once daily for 5 days followed by 23 days without treatment. At the start of Cycle 2, escalate the dose to 200 mg/m², if the nonhematologic adverse reactions for Cycle 1 are Grade less than or equal to 2 (except for alopecia, nausea and vomiting), absolute neutrophil count (ANC) is greater than or equal to 1.5 x 10⁹/L, and the platelet count is greater than or equal to 100 x 10⁹/L. If the dose was not escalated at Cycle 2, do not escalate the dose in subsequent cycles. Maintain the dose at 200 mg/m² per day for the first 5 days of each subsequent cycle except if toxicity occurs.

During treatment, obtain a complete blood count on Day 22 (21 days after the first dose) and weekly until the ANC is above 1.5 x 10⁹/L (1500/ μ L) and the platelet count exceeds

100 x 10⁹/L (100,000/ μ L). Do not start the next cycle of temozolomide capsules until the ANC and platelet count exceed these levels. Base dose reductions during the next cycle on the lowest blood counts and worst nonhematologic adverse reactions during the previous cycle. Apply dose reductions or discontinuations during the maintenance phase [see Table 2 in the Full Prescribing Information, Recommended Dosage and Dosage Modifications for Newly Diagnosed Glioblastoma (2.1)].

How is temozolomide capsules taken? [See Full Prescribing Information, Preparation and Administration, Temozolomide capsules (2.3).]

Advise patients to take each day's dose with a full glass of water, preferably on an empty stomach or at bedtime. Taking the medication on an empty stomach or at bedtime may help ease nausea. If patients are also taking anti-nausea or other medications to relieve the side effects associated with temozolomide capsules, advise them to take these medications prior to and/or following administration of temozolomide capsules. Advise patients that temozolomide capsules should be swallowed whole and **NEVER CHEWED**. Advise patients that they **SHOULD NOT** open or split the capsules. If capsules are accidentally opened or damaged, advise patients to take rigorous precautions with the capsule contents to avoid inhalation or contact with the skin or mucous membranes. In case of powder contact, advise the patients to wash their hands. Advise patients to keep this medication away from children.

What should the patient avoid during treatment with temozolomide capsules? [See Full Prescribing Information, Use in Specific Populations, Pregnancy (8.1), Lactation (8.2), Females and Males of Reproductive Potential (8.3).]

There are no dietary restrictions for patients taking temozolomide capsules. Temozolomide capsules may affect testicular function and may cause birth defects. Advise male patients to exercise adequate birth control measures. Advise female patients to avoid becoming pregnant while receiving this drug. Advise pregnant women of the potential risk to the fetus. Advise females of reproductive potential to use effective contraception during treatment and for at least 6 months after the last dose. Advise males of reproductive potential to use condoms during treatment and for at least 3 months after the last dose. Advise male patients not to donate semen during treatment with temozolomide capsules and for at least 3 months after the final dose. It is not known whether temozolomide is excreted into breast milk. Because of the potential for serious adverse reactions in breastfed children, advise women not to breastfeed while taking temozolomide capsules and for at least 1 week after the last dose.

What are the side effects of temozolomide capsules? [See Full Prescribing Information, Adverse Reactions (6).]

Alopecia, fatigue, nausea, and vomiting are the most common side effects associated with temozolomide capsules. Noncumulative myelosuppression is the dose-limiting toxicity. Patients should be evaluated periodically by their physician to monitor blood counts.

Other commonly reported side effects reported by patients taking temozolomide capsules are headache, constipation, anorexia, and convulsions.

How is temozolomide capsules supplied? [See Full Prescribing Information, How Supplied/Storage and Handling (16).]

Temozolomide capsules are available in 5-mg, 20-mg, 100-mg, 140-mg, 180-mg, and 250-mg strengths. The capsules contain a white capsule body with a color cap, and the colors vary based on the dosage strength.

<u>Temozolomide Capsule Strength</u>	<u>Color</u>
5 mg	Green Cap
20 mg	Yellow Cap
100 mg	Pink Cap
140 mg	Transparent Blue Cap
180 mg	Maroon Cap
250 mg	White Cap

The 5-mg, 20-mg, 100-mg, 140-mg, and 180-mg capsule strengths are available in 5 count, and 14 count packages. The 250-mg capsule strength is available in 5 count package.

How is temozolomide capsules dispensed?

Dispense each strength of temozolomide capsules in a separate vial or in its original package (one strength per one container). Follow the instructions below: Based on the dose prescribed, determine the number of each strength of temozolomide capsules needed for the full 42-or 5-day cycle as prescribed by the physician. For example, in a 5-day cycle, 275 mg/day would be dispensed as five 250-mg capsules, five 20-mg capsules and five 5-mg capsules. Label each container with the appropriate number of capsules to be taken each day. Dispense to the patient, making sure each container lists the strength (mg) per capsule and that he or she understands to take the appropriate number of capsules of temozolomide capsules from each package or vial to equal the total daily dose prescribed by the physician.

How can temozolomide capsules be ordered?

Temozolomide capsules can be ordered from your wholesaler. It is important to understand if temozolomide capsules are being used as part of a 42-day regimen or as part of a 5-day course. Remember to order enough temozolomide capsules for the appropriate cycle. For example:

- a 5-day course of 360 mg/day would require the following to be ordered: two 5-count packages of 180-mg capsules.
- a 42-day course of 140 mg/day would require the following to be ordered: three 14-count packages of 140-mg capsules.

<u>Temozolomide Capsules</u>	<u>NDC Number</u>
<i>Amber Glass Bottles:</i>	
5-mg capsules (5 count)	16729-048-53
5-mg capsules (14 count)	16729-048-54

20-mg capsules (5 count)	16729-049-53
20-mg capsules (14 count)	16729-049-54
100-mg capsules (5 count)	16729-050-53
100-mg capsules (14 count)	16729-050-54
140-mg capsules (5 count)	16729-129-53
140-mg capsules (14 count)	16729-129-54
180-mg capsules (5 count)	16729-130-53
180-mg capsules (14 count)	16729-130-54
250-mg capsules (5 count)	16729-051-53
<i>Sachet Packs (Carton Contains Individual Sachet with One Capsule each):</i>	
5-mg capsules (5 count)	16729-048-31
5-mg capsules (14 count)	16729-048-04
20-mg capsules (5 count)	16729-049-31
20-mg capsules (14 count)	16729-049-04
100-mg capsules (5 count)	16729-050-31
100-mg capsules (14 count)	16729-050-04
140-mg capsules (5 count)	16729-129-31
140-mg capsules (14 count)	16729-129-04
180-mg capsules (5 count)	16729-130-31
180-mg capsules (14 count)	16729-130-04
250-mg capsules (5 count)	16729-051-31

References:

“OSHA Hazardous Drugs.” *OSHA*. <http://www.osha.gov/SLTC/hazardousdrugs/index>.

Manufactured For:

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