

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

P^rTIBSOVO[®]

Ivosidenib Tablets

Read this carefully before you start taking **TIBSOVO** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **TIBSOVO**.

Serious Warnings and Precautions

Differentiation syndrome in patients with acute myeloid leukemia (AML):

TIBSOVO can cause a serious condition known as **differentiation syndrome** in patients with AML. This is a condition that affects your blood cells and may be life-threatening if not treated.

Seek urgent medical attention if you have any of the following symptoms after taking TIBSOVO:

- fever
- cough
- trouble breathing
- rash
- decreased urination
- dizziness or light-headedness
- rapid weight gain
- swelling of your arms or legs

These may be signs of differentiation syndrome. Differentiation syndrome in patients with AML happened up to 33 days after starting TIBSOVO.

A patient alert card is included in the packaging for TIBSOVO that tells you and your healthcare professionals about differentiation syndrome as well as the symptoms that you may experience. Carry this card with you at all times. Be sure to keep it in a safe place. Show this card to any healthcare professional involved in your care so that they know you are taking TIBSOVO.

Heart Problems:

TIBSOVO can cause a serious heart condition known as QTc interval prolongation. This can cause irregular heartbeats and life-threatening arrhythmias (abnormal electrical activity of the heart that affects its heartbeat or rhythm).

Seek urgent medical help immediately if you feel dizzy, light headed, abnormal heartbeat (palpitations) or faint after taking TIBSOVO.

Tell your health professionals you are taking TIBSOVO before starting any new medicines as these may increase the risk of an abnormal heartbeat.

Your health professional will check the electrical activity of your heart before and during treatment with TIBSOVO.

If necessary, your health professional may lower, temporarily hold, or permanently stop your treatment with TIBSOVO.

What is TIBSOVO used for?

TIBSOVO is used to treat adults with:

- acute myeloid leukemia (AML). This is a cancer of the white blood cells.
 - For these patients, TIBSOVO is used with another anti-cancer medicine called “azacitidine”.
- bile duct cancer (also known as “cholangiocarcinoma”). This is a cancer of the bile ducts (tubes that carry bile from your liver to your intestine)
 - TIBSOVO is used on its own to treat patients whose bile duct cancer has spread to other parts of the body (metastatic cancer) and who have been treated with at least one prior medicine.

TIBSOVO is only used in patients whose AML or bile duct cancer is related to a change (mutation) in the IDH1 protein.

How does TIBSOVO work?

TIBSOVO contains ivosidenib. It is a medicine used to treat specific cancers that contain a mutated (changed) gene that makes a protein called IDH1. This protein helps make energy for cells. When the IDH1 gene is mutated, the IDH1 protein is changed and does not function properly. This results in changes in the cell which can lead to cancer. TIBSOVO blocks the mutated form of the IDH1 protein and helps to slow or stop the cancer from growing.

What are the ingredients in TIBSOVO?

Medicinal ingredient: Ivosidenib

Non-medicinal ingredients: Colloidal silica (anhydrous), Croscarmellose sodium, Hypromellose acetate succinate, Magnesium stearate, Microcrystalline cellulose, Sodium lauryl sulfate, Hypromellose, Indigo carmine aluminum lake, Lactose monohydrate, Titanium dioxide, Triacetin.

TIBSOVO comes in the following dosage forms:

Tablets: 250 mg

Do not use TIBSOVO if:

- you are **allergic** to **ivosidenib** or any of the **other ingredients** of this medicine.
- you are already taking medicines such as:
 - St. John’s wort (a herbal product used for depression and anxiety).
 - rifampicin (used for treating bacterial infections).
 - medicines used to treat epilepsy (a condition where you have recurring seizures) like carbamazepine, phenobarbital, phenytoin.
- you have a heart problem that you were born with called “congenital long QTc syndrome”. This is a condition that causes fast and irregular heartbeats.
- you have a familial history of sudden death or an abnormal or irregular heartbeat in the lower chambers of the heart.
- you have a severe abnormal electrical activity of the heart that affects its rhythm. This is a condition called ‘QTc prolongation’.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take TIBSOVO. Talk about any health conditions or problems you may have, including if you:

- have heart problems or have a family history of heart problems.
- have been told by your healthcare professional before that you have abnormal levels of electrolytes (such as sodium, potassium, calcium or magnesium).
- are taking certain medicines that can affect the heart such as:
 - medicines used to treat abnormal heartbeats (anti-arrhythmics),
 - medicines used to treat bacterial infections (antibiotics) or fungal infections (antifungals)
 - medicines used to prevent nausea and vomiting.
- have kidney problems.
- have liver problems.
- suffer from a lactose intolerance. This is because TIBSOVO contains lactose.
- are pregnant, may become pregnant, or have a partner who is pregnant. TIBSOVO may harm your unborn baby.
 - Women who might become pregnant or men with partners who might become pregnant must use effective birth control to avoid pregnancy during treatment with TIBSOVO and for at least 1 month after the last dose.
 - **Talk to your healthcare professional about the right birth control method for you and your partner.**
 - Tell your healthcare professional right away if you are pregnant, become pregnant, think you may be pregnant or want to get pregnant, while taking TIBSOVO.
- are breast-feeding. Do NOT breastfeed during treatment with TIBSOVO and for at least 1 month after the last dose. It is not known if TIBSOVO passes into breast milk.

Other warnings you should know about:

Children and adolescents:

TIBSOVO is NOT for use in patients under the age of 18 years of age. There is no information on its use in this age group.

Check-ups and testing:

You will have regular visits with your healthcare professional during treatment with TIBSOVO to monitor your health. They will:

- do blood tests before you start and during treatment with TIBSOVO.
- check for signs and symptoms of heart problems.

Your healthcare professional will check the electrical activity of your heart before and during treatment with TIBSOVO.

- You will be given an electrocardiogram (ECG – a recording of the electrical activity of your heart) to monitor your heartbeat before you start treatment with TIBSOVO, once a week for the first three weeks of treatment, and then monthly thereafter.
- Additional ECGs may be given as if required, by your healthcare professional.
- If you start taking certain medicines that can affect your heart, you will be given an ECG before starting and during treatment with the new medicine, as needed.

Driving and using machines:

TIBSOVO may affect your ability to drive or use any tools or machines. If you feel unwell after taking

TIBSOVO, do not drive or use any tools or machines until you feel well again.

Pregnancy, breast-feeding and fertility:

TIBSOVO is NOT recommended to be used in women who are pregnant. TIBSOVO may harm the unborn baby.

Women who are able to get pregnant should have a pregnancy test done before starting treatment with TIBSOVO and should avoid becoming pregnant during treatment.

Tell your healthcare professional right away if you are pregnant, become pregnant, think you may be pregnant or want to get pregnant, during your treatment with TIBSOVO.

Women who might become pregnant or men with partners who might become pregnant must use effective birth control to avoid pregnancy during treatment with TIBSOVO and for at least 1 month after the last dose.

- TIBSOVO may stop hormonal birth control drugs from working properly.
- If you or your partner use birth control pills, contraceptive patches, implants or other hormonal birth control drugs, you must also use a barrier method (such as condoms or a diaphragm) to avoid becoming pregnant.
- Talk to your healthcare professional about the right birth control method for you and your partner.

Do NOT breastfeed during treatment with TIBSOVO and for at least 1 month after the last dose. It is not known if TIBSOVO passes into breast milk.

It is not known if TIBSOVO impacts your ability to have children (fertility). Talk to your healthcare professional if you are concerned about your fertility while taking TIBSOVO.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with TIBSOVO:

- antibiotics used for bacterial infections like erythromycin, clarithromycin, ciprofloxacin, levofloxacin.
- warfarin (used to prevent blood clots).
- medicines used for fungal infections like itraconazole, ketoconazole, fluconazole, isavuconazole, posaconazole, voriconazole.
- medicines that affect your heartbeat (anti-arrhythmics) like diltiazem, verapamil, quinidine.
- medicines used to stop nausea and vomiting (anti-emetics) like aprepitant, ondansetron, tropisetron, granisetron.
- medicines used after organ transplants (immunosuppressants) like ciclosporin, everolimus, sirolimus, tacrolimus).
- medicines used to treat HIV (human immunodeficiency virus) like ritonavir.
- alfentanil (used for anaesthesia in surgery).
- fentanyl (used for severe pain).
- pimozide (used for schizophrenia).

- medicines used for cancer like cyclophosphamide, ifosfamide, paclitaxel.
- methadone (used for morphine or heroin addiction, or severe pain).
- medicines used for type 2 diabetes like pioglitazone, repaglinide.
- omeprazole (used for stomach ulcers and acid reflux).
- furosemide (used for fluid build-up known as edema).
- medicines used for high cholesterol known as statins like atorvastatin, pravastatin, rosuvastatin.
- lamotrigine (used for epilepsy).
- hormonal contraceptives (used for birth control).
- grapefruit and grapefruit juice.

How to take TIBSOVO:

- Always take this medicine exactly as your healthcare professional has told you and check with him if you are not sure.
- Take the tablets orally once a day at about the same time each day.
- Do not eat anything for 2 hours before taking TIBSOVO and until 1 hour after taking TIBSOVO.
- Swallow the tablets whole with water.
- If you vomit after taking your usual dose, do NOT take additional tablets. Take your next dose as usual the following day.
- Your healthcare professional may lower, temporarily hold, or permanently stop your treatment with TIBSOVO if you experience certain side effects.
- Do NOT stop taking TIBSOVO before discussing it with your healthcare professional first.

Usual dose:

- Take two 250 mg tablets (500 mg TIBSOVO) by mouth, once a day, at about the same time each day.
- Your healthcare professional may tell you to take one tablet (250 mg TIBSOVO) if you are taking some other medicines or to help you better tolerate some possible side effects.

Overdose:

If you think you, or a person you are caring for, have taken too much TIBSOVO, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:

- If you miss a dose of TIBSOVO, take the tablets as soon as possible unless the next dose is to be taken within 12 hours.
- Do **NOT** take two doses of TIBSOVO within 12 hours.
- Take the next dose as usual the following day.

What are possible side effects from using TIBSOVO?

These are not all the possible side effects you may feel when taking TIBSOVO. Some of these side effects may occur when taking TIBSOVO or when taking TIBSOVO with azacitidine. If you experience any side effects not listed here, talk to your healthcare professional.

The side effects of TIBSOVO when used in combination with azacitidine in adults with AML include:

- low levels of blood platelets which can lead to bleeding and bruising (thrombocytopenia)
- high levels of white blood cells (leukocytosis)
- low levels of white blood cells (leukopenia)
- difficulty sleeping (insomnia)
- headache
- dizziness
- nerve damage in arms and legs causing pain or numbness, burning and tingling (peripheral neuropathy)

The side effects of TIBSOVO in adults with Cholangiocarcinoma include:

- fatigue
- nausea
- abdominal pain
- diarrhea
- decreased appetite
- a build-up of fluid in the abdomen (ascites)
- low levels of red blood cells (anemia)
- headache
- nerve damage in arms and legs causing pain or numbness, burning and tingling (peripheral neuropathy)
- rash
- increased breakdown product of red blood cells (blood bilirubin) which can cause yellowing of the skin and eyes
- changes in liver function tests (aspartate aminotransferase and alanine aminotransferase increased)
- white blood cell count decreased
- platelet count decreased
- build-up of bile causing yellowing of the skin or eyes (jaundice cholestatic)

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
VERY COMMON			
Differentiation syndrome: fever, cough, trouble breathing, rash, decreased urination, dizziness or light headedness, rapid weight gain, swelling of your arms and legs			✓

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
Heart rhythm problems (QTc interval prolongation): dizzy, lightheaded, faint.			✓
Vomiting		✓	
Neutropenia (low levels of neutrophils, a type of white blood cell that fights infections): fatigue, fever, aches, pains and flu-like symptoms		✓	

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (<https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html>) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your healthcare professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

- Store at room temperature (15°C to 30°C).
- Do not use this medicine after the expiry date which is stated on the bottle label and box.
- Keep out of reach and sight of children.
- Keep the bottle tightly closed in order to protect from moisture.

If you want more information about TIBSOVO:

- Talk to your healthcare professional.
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html>); the manufacturer's website (www.servier.ca), or by calling 1-800-363-6093.

This leaflet was prepared by Servier Canada Inc.

Last Revised JUL 19, 2024