

♦**Tibella**®

Tibolone Tablets

Read this carefully before you start taking **Tibella** 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 **Tibella**.

Serious Warnings and Precautions

Tibella use may increase your chance of having a stroke, breast cancer, or cancer of the lining of the uterus (called endometrial cancer). Talk to your healthcare professional about your medical history before you start taking Tibella. Get regular check-ups while you are taking this medicine.

The Women's Health Initiative (WHI) trial was a large clinical study. This study assessed the benefits and risks of two oral therapies (combined estrogen plus progestin and estrogen-alone) compared with placebo (a pill with no active ingredients) in postmenopausal women.

In postmenopausal women taking oral combined estrogen plus progestin, the WHI trial indicated an increased risk of:

- myocardial infarction (heart attack),
- stroke,
- breast cancer,
- pulmonary emboli (blood clots in the lungs), and deep vein thrombosis (blood clots in the large veins).

In postmenopausal women taking oral estrogen-alone, who had a prior surgery to remove the uterus (called a hysterectomy), the WHI trial indicated an increased risk of:

- stroke, and
- deep vein thrombosis.

Therefore, you should highly consider the following:

- There is an increased risk of developing invasive breast cancer, heart attack, stroke and pulmonary emboli and deep vein thrombosis with the use of estrogen plus progestin therapy.
- There is an increased risk of stroke and blood clots in the large veins with the use of estrogen-alone therapy.
- Estrogens with or without progestins should not be used for the prevention of heart disease or stroke.
- Estrogens with or without progestin should be used at **the lowest effective dose** and for **the shortest period of time** possible.

What is Tibella used for?

Tibella is a **hormone replacement therapy (HRT)**. It is used to treat some symptoms that occur when the level of estrogen produced by a woman's body drops after menopause. These symptoms can include hot flashes, flushing and night sweats.

Tibella is used over a short term in women when more than 12 months have passed since their last period (called postmenopausal). Only women with an intact uterus should take Tibella.

How does Tibella work?

There are different types of HRTs. These include medicines that contain:

- Estrogen alone,
- A combination of estrogen and progesterone (called combined HRT), or
- Tibolone. This is the active ingredient in Tibella.

Tibella is different from other HRTs, as it does not contain actual hormones. Instead, your body breaks down tibolone to make three substances that act like estrogen, progesterone and testosterone. These substances act on different tissues in the body to help treat symptoms of menopause.

What are the ingredients in Tibella?

Medicinal ingredients: tibolone.

Non-medicinal ingredients: ascorbyl palmitate, lactose monohydrate, magnesium stearate, mannitol, potato starch.

Tibella comes in the following dosage form: tablet, 2.5 mg.

Do not use Tibella if:

- You have or have had liver disease, and blood tests to measure how your liver is working have not returned to normal;
- You have or may have cancer that is sensitive to estrogens. An example is endometrial cancer;
- You have an overgrowth of the lining of the uterus for which you may or may not have received treatment. This is called endometrial hyperplasia;
- You have or have had breast cancer, or you are suspected of having it;
- You have unexplained bleeding from the vagina;
- You are pregnant or think you may be pregnant;
- You are breastfeeding;
- You have recently had a heart attack, stroke, angina, a blockage or narrowing of the arteries around the heart (called coronary heart disease), mini-stroke (called a transient ischemic attack);
- You have or have had a deep vein thrombosis or a pulmonary embolism or you have inflammation of a vein caused by a blood clot (called thrombophlebitis);
- You have a blood clotting disorder. Examples are protein C, protein S, or anti-thrombin deficiency;
- You have vision problems that are caused by low blood flow to the eye;

- You have been diagnosed with porphyria. This is a disease of blood pigment that is passed down in families (inherited);
- You are allergic to tibolone or to any of the non-medicinal ingredients in the drug, or components of its container.

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

- have fibroids inside your uterus;
- have endometriosis (growth of the uterine lining outside your uterus);
- have a history of endometrial hyperplasia;
- have an increased risk of getting an estrogen-sensitive cancer including if you have a mother, sister or grandmother who has had breast cancer;
- have high blood pressure;
- have a liver disorder, such as a benign liver tumor;
- have diabetes;
- have gallstones;
- have migraine or severe headaches;
- have a disease of the immune system that affects many organs of the body. This is called systemic lupus erythematosus;
- have epilepsy;
- have asthma;
- have a disease affecting the eardrum and hearing called otosclerosis;
- have a very high level of fat called triglyceride in your blood;
- have swelling due to heart or kidney problems;
- have kidney problems;
- have been told that you have a condition called hereditary angioedema or if you have had episodes of rapid swelling of the hands, feet, face, lips, eyes, tongue, throat (airway blockage), or digestive tract;
- have a history of bone disease (this includes certain metabolic conditions or cancers that can affect blood levels of calcium and phosphorus);
- have lactose intolerance, such as one of the following rare inherited diseases:
 - Galactose intolerance
 - Lapp lactase deficiency
 - Glucose-galactose malabsorption

Because lactose is a non-medicinal ingredient in Tibella.

Other warnings you should know about:

Tibella has benefits and risks. Consider them when deciding to start taking Tibella or to carry on taking it. You should talk with your healthcare professional regularly about whether you still need treatment with HRT.

Tibella is not for use to prevent pregnancy.

Premature menopause: This is when menopause occurs in a woman who is under 40 years of age. It can happen because the ovaries stop working or they have been removed during surgery. Little is known about using HRT or Tibella to treat premature menopause. If you are under 40 years old and are in menopause, talk to your healthcare professional about the risks and benefits of using Tibella.

Endometrial hyperplasia and endometrial cancer: There have been reports and studies of endometrial hyperplasia or endometrial cancer in women using Tibella. The risk of endometrial cancer increases the longer you use this medicine.

Breast cancer: There is a risk for breast cancer in women taking HRT or Tibella for many years. The risk increases the longer you take HRT and returns to normal within about 5 years after stopping HRT.

Regarding breast cancer, the WHI trial showed:

- an increased risk of breast cancer in postmenopausal women taking combined estrogen plus progestin.
- No difference in the risk of breast cancer in postmenopausal women with a previous hysterectomy taking estrogen-alone.

If you have had breast cancer, you should not take estrogens with or without progestins.

If you have a family history of breast cancer or have had breast lumps, breast biopsies or abnormal mammograms (breast x-rays), talk to your healthcare professional before starting HRT.

Check your breasts often. See your healthcare professional if you notice any changes, such as:

- Dimpling or sinking of the skin;
- Changes in the nipple; or
- Any lumps you can see or feel.

The increased risk of breast cancer in patients taking estrogen-alone or tibolone is lower than in patients using combined (estrogen-progestogen) HRT.

Ovarian cancer: Ovarian cancer is rare. Women who take estrogen-only or combined HRT for 5 or more years have a slightly higher chance of ovarian cancer.

The risk for ovarian cancer in patients using Tibella is similar to other types of HRT.

Heart disease (heart attack) and stroke: The WHI trial showed:

- an increased risk of stroke and coronary heart disease in postmenopausal women taking combined estrogen plus progestin.
- an increased risk of stroke, but no difference in the risk of coronary heart disease in postmenopausal women with a previous hysterectomy taking estrogen-alone.

Heart disease: There is no evidence that HRT or Tibella will prevent a heart attack.

There is no evidence to suggest that the risk of heart attack with Tibella is different than with other HRT.

Stroke: There is an increase in the risk of stroke in patients taking HRT or Tibella. This risk is mostly in women over the age of 60 who are in menopause.

Abnormal blood clotting (including pulmonary embolism and deep vein thrombosis)

Other HRTs may increase the risk of blood clots in the veins, especially during the 1st year of taking it. It is unknown if Tibella increases the risk in the same way.

The WHI trial showed:

- an increased risk of pulmonary emboli and deep vein thrombosis in postmenopausal women taking combined estrogen plus progestin.
- an increased risk of deep vein thrombosis, but no difference in the risk of pulmonary emboli in postmenopausal women with previous hysterectomy taking estrogen-alone.

A study done using a database from the United Kingdom showed that the risk for deep vein thrombosis in women using Tibella is lower than in women using other types of HRTs. In this database, there was only a small number of women who were using tibolone. Thus, there may be only a slightly higher risk for deep vein thrombosis in these women.

You are more likely to get a blood clot in your veins as you get older. Talk to your healthcare professional if any of the below situations apply to you. Blood clots can be life-threatening or cause serious disability:

- You use estrogens;
- You are unable to walk for a long time because of a major surgery, injury or illness;
- You are overweight and your BMI is greater than 30;
- You have any blood clotting problem that needs long-term treatment with a medicine used to prevent blood clots;
- If any of your close relatives has ever had a blood clot in the leg, lung or another organ;
- You smoke;
- You have systemic lupus erythematosus;
- You have cancer.

If you are going to have a surgery, tell your healthcare professional that you are taking Tibella. You may need to stop taking Tibella about 4 - 6 weeks before the operation to reduce the risk of a blood clot. Ask your healthcare professional when you can start taking Tibella again.

Gallbladder disease: The use of estrogens by postmenopausal women has been associated with an increased risk of gallbladder disease that needs surgery.

Dementia: The Women's Health Initiative Memory Study (WHIMS) was a sub-study of the WHI trial. The WHIMS study showed:

- an increased risk of dementia (loss of memory and intellectual function) in postmenopausal women age 65 and over who were taking oral combined estrogen plus progestin.
- no difference in the risk of dementia in postmenopausal women aged 65 and over who had previously had a hysterectomy and were taking oral estrogen-alone.

Physical exam, tests, and check-ups:

Before you start taking Tibella, you will need to have examinations and tests. These will include a physical exam, a Pap smear and a breast exam. Your healthcare professional will ask you about your personal and your family's health history. You will also have your blood pressure taken as well as blood tests and a mammogram.

While you are taking Tibella, check your breasts often and get regular check-ups with your healthcare professional.

Your first check-up should be within 3 to 6 months of starting Tibella. Thereafter, these should be scheduled at least once a year. These check-ups will help to identify any side effects you may have. Your visits may include a blood pressure check, a breast exam, a Pap smear, and pelvic exam. You will also have repeat mammograms and blood tests. Your healthcare professional will decide when these are necessary and will interpret the results.

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

Serious Drug Interactions

The following medicines may have serious interactions with Tibella:

- Medicines to prevent blood clots like warfarin. Tibella may increase the effects of these medicines and could lead to bleeding.
- St. John's wort (*Hypericum perforatum*). This is an herbal product that is often used to treat depression. If used with Tibella, you may experience bleeding from the uterus.

The following may also interact with Tibella:

- Medicines for epilepsy (such as phenobarbitone, phenytoin and carbamazepine);
- Medicines for tuberculosis (such as rifampicin);
- Medicines for diabetes;
- Medicines to treat high blood pressure;
- The medicine, midazolam, which is used for anesthesia.

How to take Tibella: Always take this medicine exactly as your healthcare professional has told you.

Take Tibella:

- with water or another drink,
- at the same time each day;
- by swallowing whole. Do **NOT** break or chew tablets;
- until the pack is empty. Start a new pack the next day without missing any days.

You may start taking Tibella straight away:

- If you have had your ovaries surgically removed, or
- It has been at least 12 months since your last period, or
- You are being treated with medicines for endometriosis known as gonadotrophin releasing hormone (GnRH) analogues.

If you are switching from another type of HRT: your healthcare professional will tell you when to start taking Tibella.

Usual dose: One (2.5 mg) tablet per day.

Your healthcare professional may interrupt or stop your treatment with Tibella. This will depend on your condition and how you are feeling.

Overdose:

Signs of an overdose may include feeling sick or vomiting. Vaginal bleeding may also occur after a few days.

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

Missed Dose:

If you forgot to take a tablet, take it as soon as you remember. But, if it is almost time for your next dose, skip the missed tablet and continue with your next scheduled tablet.

Do not take two tablets at the same time.

What are possible side effects from using Tibella?

These are not all the possible side effects you may feel when taking Tibella. If you experience any side effects not listed here, contact your healthcare professional.

- Fatigue;
- Stomach, abdominal, or pelvic pain;
- Nausea or vomiting;
- Gastro-intestinal or stomach upset;
- Changes in appetite;
- Weight changes;
- Breast pain, swelling, painful nipples, or breasts feeling uncomfortable;
- Vaginal symptoms, such as discharge, itching, and irritation;
- Vaginal infections;
- Unnatural hair growth, or hair loss;
- Acne, rash, or itchy skin;
- Change in skin colour (darker or tanned appearance);
- Swollen hands, ankles, feet, or general swelling – a sign of fluid retention;
- Dizziness, headache, migraine, or memory loss;
- Mood changes (persistent sadness, irritability, nervousness);
- Changes in vision including blurred vision;
- Joint or muscle pain;
- Feeling of heart fluttering or pounding;
- Change in sex drive;
- Pain during sexual intercourse;
- Painful or difficult urinating.

You may have **irregular vaginal bleeding** in the first 3 – 6 months of taking Tibella. This is drops of blood or spotting. If it lasts for more than 6 months or continues after you stop taking Tibella, see your healthcare professional as soon as possible.

Tibella can cause abnormal blood test results. Your doctor will decide when to perform blood tests and will interpret the results.

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	
UNCOMMON			
Breast abnormalities (including breast cancer): dimpling or sinking of the skin, changes in the nipple, or any lumps you can see or feel		✓	✓
Stroke (blood clot in the brain): sudden severe headache, vomiting, dizziness, fainting, problems with your vision or speech, weakness or numbness in the face, arm, or leg		✓	✓
Pulmonary embolism (blood clot in the lungs): sharp chest pain, coughing up blood, or sudden shortness of breath		✓	✓
Deep vein thrombosis (blood clot in the legs) or Thrombophlebitis (inflammation of a vein often in the leg): sudden leg swelling or pain; redness, warmth, tenderness and pain in affected area		✓	✓
RARE			
Endometrial hyperplasia: (abnormal growth of the lining of the uterus): menstrual bleeding that is heavier or lasts longer than normal, bleeding after menopause, menstrual cycles that are shorter than 21 days		✓	✓
Severe vaginal bleeding		✓	✓
Coronary artery disease (blockage or narrowing of blood vessels near heart): crushing chest pain, chest heaviness, shortness of breath, pain in your shoulder or arm, sweating		✓	✓
Cancer of the ovaries: abdominal pain or bloating, quickly feeling full after eating, weight loss, pain in pelvis, change in bowel habits, need to urinate often		✓	✓
Endometrial cancer (cancer of the lining of the uterus): vaginal bleeding not associated with a period or after menopause; abnormal blood-tinged discharge from the vagina; pain in the pelvis		✓	✓
Hypertension (high blood pressure): headache, stronger and possibly faster heartbeat, chest pain, dizziness, excessive tiredness, and blurred vision		✓	✓
Liver Disorder: yellowing of the skin or eyes (jaundice), dark urine and pale stools, abdominal pain, nausea, vomiting, loss of appetite		✓	✓
Neuritis (inflammation of a nerve): pain, feeling of pins-and-needles, numbness, loss of reflexes		✓	✓
Cystitis (bladder infection): increased need to urinate, pain in the pelvis or lower back, frequent urination during the night, cloudy urine that may contain blood, burning sensation when passing urine		✓	✓
Erythema multiforme (an allergic skin reaction): raised red or purple skin patches, possibly with blister or crust in the center; possibly swollen lips, mild itching or burning		✓	✓
Erythema nodosum (swelling of the fat cells under the skin): Tender red lumps usually on both shins		✓	✓
Hyperglycemia (high blood sugar): increased thirst, frequent urination, dry skin, headache, blurred vision and fatigue		✓	✓

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to 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/adverse-reaction-reporting.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 health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

Store at 15–30°C in the original package (blister cards in their outer carton) to protect from light and moisture.

Keep out of reach and sight of children.

Do not use after the expiry date stated on the blister and outer box.

If you want more information about Tibella:

- 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.biosynt.com, or by calling 1-888-439-0013.

This leaflet was prepared by BioSynt Pharma Inc.

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