PART III: CONSUMER INFORMATION

PrTARKA®
trandolapril/verapamil hydrochloride sustained-release tablets

This leaflet is PART III of a three-part "Product Monograph" published when TARKA® was approved for sale in Canada and is designed specifically for consumers. This leaflet is a summary and will not tell you everything about TARKA®. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:

TARKA® lowers high blood pressure.

What it does:

TARKA® contains a combination of 2 drugs, trandolapril and verapamil hydrochloride:

- Trandolapril is an angiotensin converting enzyme (ACE) inhibitor. You can recognize ACE inhibitors because their medicinal ingredient ends in '-PRIL'. It lowers blood pressure.

- Verapamil hydrochloride is a calcium channel blocker. It changes the amount of calcium getting into the muscle cells of your heart and blood vessels. This can change the strength and speed at which your heart beats. It also opens up the blood vessels so that blood can be pumped around your body more easily. This helps to lower your blood pressure.

This medicine does not cure high blood pressure. It helps to control it. Therefore, it is important to continue taking TARKA® regularly even if you feel fine.

When it should not be used:

Do not take TARKA® if you:

- Are allergic to trandolapril, verapamil hydrochloride or to any non-medicinal ingredient in the formulation.
- Have experienced an allergic reaction (angioedema) with swelling of the hands, feet, or ankles, face, lips, tongue, throat, or sudden difficulty breathing or swallowing, to any ACE inhibitor or without a known cause. Be sure to tell your doctor, nurse, or pharmacist that this has happened to you.
- Have been diagnosed with hereditary angioedema: an increased risk of getting an allergic reaction that is passed down through families. This can be triggered by different factors, such as surgery, flu, or dental procedures.
- Are using PrEntresto™ (sacubitril/valsartan), a medicine to treat heart failure. There is an increased risk of serious allergic reaction which causes swelling of the face or throat (angioedema) when taken with TARKA®. **You must wait at least 36 hours after your last dose of TARKA® before starting PrEntresto™. You must wait at least 36 hours after your last dose of PrEntresto™ before starting TARKA®.**
- Are already taking a blood pressure-lowering medicine that contains aliskiren (such as Rasilez®), or an angiotensin receptor blocker (ARB) which is another medicine to treat your high blood pressure [you can recognize ARBs because their medicinal ingredient ends in "-**SARTAN**".]; or another ACE inhibitor **and** you have one of the following conditions:
  - diabetes;
  - kidney disease;
  - high potassium levels;
  - heart failure combined with low blood pressure.
- Have narrowing of the arteries to one or both kidneys (renal artery stenosis).
- Have hypotension (low blood pressure).
- Are pregnant or intend to become pregnant. Taking TARKA® during pregnancy can cause injury and even death to your baby.
- Are breastfeeding. TARKA® passes into breast milk.
- Have certain serious heart conditions.
- Have slow heartbeat or irregular heartbeat.
- Are on dialysis.
- Have liver cirrhosis (scarring of the liver).
- Have severe kidney disease.
- Are being given beta-blockers (heart medicine) by IV.
- Are using ivabradine.
- Are less than 18 years old.
- You have one of the following rare hereditary diseases:
  - Galactose intolerance
  - Lapp lactase deficiency
  - Glucose-galactose malabsorption

  because lactose is a non-medicinal ingredient in TARKA®.
- Are using flibanserin, a medicine to treat low sexual desire disorder in women. **You must wait at least 2 weeks after your last dose of TARKA® before starting flibanserin. You must wait at least 2 days after your last dose of flibanserin before starting TARKA®.**

What the medicinal ingredients are:

trandolapril and verapamil hydrochloride

What the non-medicinal ingredients are:

colloidal anhydrous silica, docusate sodium, ferric oxide, ferrous/ferric oxide, hydrated ferric oxide, hydroxypropyl cellulose, hydroxypropyl methylcellulose, lactose monohydrate, macrogol 400, macrogol 6000, magnesium stearate, microcrystalline cellulose, povidone, purified water, sodium alginate, sodium stearyl fumarate, starch, talc, titanium dioxide.

What dosage forms it comes in:

TARKA® is available as sustained-release tablets in the following strength combinations of trandolapril/verapamil hydrochloride:

2 mg/240 mg; 4 mg/240 mg.

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions – Pregnancy

- TARKA® should not be used during pregnancy. If you discover that you are pregnant while taking TARKA®, stop the medication and contact your doctor, nurse, or pharmacist as soon as possible.

BEFORE you use TARKA® talk to your doctor, nurse or pharmacist if you:

- Are allergic to any drug used to lower blood pressure.
- Have recently received or are planning to get allergy shots for bee or wasp stings.
- Have narrowing of an artery or a heart valve.
- Have had a heart attack or stroke.
- Have heart failure.
- Have diabetes, liver, heart, or kidney disease.
- Are on LDL apheresis (a treatment to remove LDL cholesterol from the blood).
- Are dehydrated or suffer from excessive vomiting, diarrhea, or sweating.
- Are taking a salt substitute that contains potassium, potassium supplements, a potassium-sparing diuretic (a specific kind of "water pill"), or co-trimoxazole also known as trimethoprim/ sulfamethoxazole (a type of antibiotic).
- Are on a low-salt diet.
- Are taking a medicine that contains aliskiren, such as Rasilez®, used to lower high blood pressure. The combination with TARKA® is not recommended.
- Are taking an angiotensin receptor blocker (ARB). You can recognize an ARB because its medicinal ingredient ends in "-SARTAN". The combination of TARKA® is not recommended.
- Are receiving gold (sodium aurothiomalate) injections.
- Are taking any of the following medicines, the risk of angioedema may be increased:
  - Medicines used to prevent organ transplant rejection and for cancer.
- Are taking medicines called neutral endopeptidase (NEP) inhibitors.
- Are taking an antibiotic containing trimethoprim and sulfamethoxazole.
- Have neuromuscular disease (myasthenia gravis, Lambert-Eaton syndrome or Duchenne muscular dystrophy.
- Have collagen vascular disease (Lupus, scleroderma)
- Are taking flibanserin.

You may become sensitive to the sun while taking TARKA®. Exposure to sunlight should be minimized until you know how you respond.

If you are going to have surgery and will be given an anesthetic, be sure to tell your doctor or dentist that you are taking TARKA®.

TARKA® contains sodium. If you are on a low-salt diet tell your doctor, nurse or pharmacist you are taking TARKA®.

Driving and using machines: Before you perform tasks which may require special attention, wait until you know how you respond to TARKA®. Dizziness, lightheadedness, or fainting can especially occur after the first dose and when the dose is increased.

INTERACTIONS WITH THIS MEDICATION

As with most medicines, interactions with other drugs are possible. Tell your doctor, nurse, or pharmacist about all the medicines you take, including drugs prescribed by other doctors, vitamins, minerals, natural supplements, or alternative medicines.

The following may interact with TARKA®:

- Agents increasing serum potassium, such as a salt substitute that contains potassium, potassium supplements, a potassium-sparing diuretic (a specific kind of "water pill", examples include spironolactone, triamterene or amiloride), or co-trimoxazole also known as trimethoprim/ sulfamethoxazole (a type of antibiotic); cyclosporine, an immunosuppressant medicine used to prevent organ transplant rejection; and heparin, a medicine used to thin blood to prevent clots.
- Allopurinol used to treat gout.
- Antidiabetic drugs, including insulin and oral medicines.
- Gold for the treatment of rheumatoid arthritis.
- Lithium used to treat bipolar disease.
- Drugs belonging to the class of mTOR inhibitors which are most often used to avoid rejection of transplanted organs (e.g., sirolimus, everolimus).
- Ivabradine.
- A drug containing the combination of sacubitril/valsartan.
- Nonsteroidal anti-inflammatory drugs (NSAIDs), used to reduce pain and swelling. Examples include ibuprofen, naproxen, and celecoxib.
- Blood pressure-lowering drugs, such as beta-blockers (e.g. propranolol, metoprolol, atenolol, timolol, and intravenous beta-blockers), including diuretics ("water pills"), aliskiren-containing products (e.g. Rasilez®), or angiotensin receptor blockers (ARBs).
- Corticosteroids used to treat joint pain and swelling;
- drugs used for the treatment of abnormal heartbeats (arrhythmia) such as disopyramide, procainamide, flecainide, quinidine, prazosin, terazosin, digoxin, digitoxin;
- dabigatran (a blood thinner)
- antibiotics such as erythromycin, telithromycin, rifampicin;
- some drugs used to treat migraine headaches (e.g. almotriptan);
- some drugs used to treat epilepsy or other neurological conditions (e.g. carbamazepine, phenobarbital, phenytoin);

- some drugs used to treat stomach ulcers (e.g. cimetidine);
- some drugs used to treat certain forms of arthritis or gout (e.g. sulfinpyrazone, allopurinol, colchicine);
- some drugs used to treat lung conditions such as asthma (e.g. theophylline);
- any of the group of medicines known as major tranquilizers, or antidepressants of the tricyclic group (e.g. lorazepam, imipramine);
- any of the group of medicines known as benzodiazepines or other anti-anxiety treatment (e.g. buspirone, midazolame);
- anti-cancer medications (e.g. cisplatin, doxorubicin);
- any medication that can affect your immune system (e.g. corticosteroids, cyclosporine, sirolimus, tacrolimus);
- any neuromuscular blocking agent (e.g. atracurium);
- some cholesterol lowering drugs (e.g., simvastatin, atorvastatin, lovastatin);
- some HIV-antiviral medication (e.g. ritonavir);
- alcohol;
- St. John's Wort;
- low density lipoprotein apheresis (dextran sulphate);
- hymenoptera (bees, wasps) venom;
- inhalation anesthetics.
- Co-trimoxazole (trimethoprim/ sulfamethoxazole).
- Neutral endopeptidase (NEP) inhibitors.

Grapefruit juice: You should not drink Grapefruit juice if you are taking TARKA®.

PROPER USE OF THIS MEDICATION

Take TARKA® exactly as prescribed. It is recommended to take your dose at about the same time every day.

Usual Adult Dose:

Dosage must be individualized. Your doctor will adjust the individual amounts of trandolapril and verapamil hydrochloride. Once the proper doses are achieved, your doctor may switch you to TARKA®, as it may be more convenient to take only one pill. TARKA® should be taken once-a-day at the same time every day.

The usual adult dose for verapamil hydrochloride monotherapy is 180 to 240 mg/day.

The usual maintenance dose for trandolapril monotherapy is 1 to 2 mg once daily. The recommended initial dose is 1 mg once daily.

Take TARKA® with food to help it work better. TARKA® sustained-release tablets should be swallowed whole. Do not divide, crush or chew TARKA®.

Overdose:

If you think you have taken too much TARKA® contact your doctor, nurse, pharmacist, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

Missed Dose:

If you forget to take one tablet, take another as soon as you remember, unless it is almost time for your next dose. If it is, do not take the missed tablet at all.

Never double-up on a missed dose.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Side effects may include:

- dizziness
- drowsiness, fatigue, weakness, tiredness, difficulty in sleeping,
- cough, dry mouth,
- headache
- abdominal pain
- constipation, diarrhea
- feeling sick (nausea)
- nasal congestion,
- flushing of the face or neck,
- ache or pains in the joints of muscles,
- swollen ankles,
- mild skin rash or itching,
- tingling or pickling of the skin,
- hair loss,
- impotence,
- blurred vision,
- taste disturbance

If any of these affect you severely, tell your doctor, nurse or pharmacist.

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

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom/effect		Talk with your doctor, nurse or pharmacist		Stop taking drug and seek immediate medical help
		Only if severe	In all cases	
Common	**Low Blood Pressure:** dizziness, fainting, lightheadedness. May occur when you go from lying or sitting to standing up.	√		
	Increased levels of potassium in the blood: irregular heartbeat, muscle weakness and generally feeling unwell		√	
Uncommon	Chest pain, faint pulse, irregular heartbeats, shortness of breath			√
	Fever and chills	√		
	Angioedema and Severe Allergic Reactions: swelling of the face, eyes, or tongue, difficulty swallowing, wheezing, hives and generalized itching, rash, fever, abdominal cramps, chest discomfort or tightness, difficulty breathing, unconsciousness.			√
	Kidney Disorder: change in frequency of urination, nausea, vomiting, swelling of extremities, fatigue		√	
	Liver Disorder (Jaundice): yellowing of the skin or eyes, dark urine, abdominal pain, nausea, vomiting, loss of appetite		√	

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom/effect		Talk with your doctor, nurse or pharmacist		Stop taking drug and seek immediate medical help
		Only if severe	In all cases	
	Electrolyte Imbalance: weakness, drowsiness, muscle pain or cramps, irregular heartbeat		√	
Rare	**Decreased Platelets:** bruising, bleeding, fatigue and weakness		√	
	Decreased White Blood Cells: infections, fatigue, fever, aches, pains, and flu-like symptoms		√	
Unknown	**Ileus (blocked intestines):** abdominal discomfort, constipation, nausea and vomiting, especially after meals excessive burping	√		
	Seizures: fits with uncontrolled movements			√
	Bronchospasm: Sudden worsening of shortness of breath and wheezing			√

This is not a complete list of side effects. For any unexpected effects while taking TARKA®, contact your doctor or pharmacist.

HOW TO STORE IT

Keep TARKA® an all other medicines out of reach and sight of children.

TARKA® sustained-release tablets should be stored at 15° to 25°C, protected from light and moisture.

Do not take your tablets after the expiry date shown on the label.

It is important to keep the TARKA® sustained-release tablets in the original package.

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

MORE INFORMATION

The most recent version of this document plus the full Product Monograph, prepared for health professionals can be found at:

www.mylan.ca
or by contacting the sponsor, BGP Pharma ULC, Etobicoke, Ontario, M8Z 2S6 at:
1-844-596-9526

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PrEntresto™ and Rasilez® are products of Novartis Pharmaceuticals Canada Inc.