

## PATIENT MEDICATION INFORMATION

### READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

#### PrMAR-AMITRIPTYLINE

#### Amitriptyline Hydrochloride Tablets

Read this carefully before you start taking **MAR-AMITRIPTYLINE** 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 **MAR-AMITRIPTYLINE**.

#### Serious Warnings and Precautions

**To help avoid side effects and ensure proper use, before you take MAR-AMITRIPTYLINE, talk to your healthcare professional if you:**

- Are taking any other medication that may cause heart problems or affect your heart rhythm.
- Have electrolytes levels that are either too low or too high such as a low level of potassium, calcium or magnesium, or a high level of potassium in your blood. Your healthcare professional will need to treat this before you start taking MAR-AMITRIPTYLINE.
- Have a history of heart problems such as
  - changes in heart rhythm,
  - a slow heartbeat (bradycardia),
  - heart disease, including a condition called heart failure (a condition where your heart cannot pump the blood in your body as well as it should)

A heart problem called “prolonged QT interval” (which is shown on your electrocardiogram, ECG) and problems with the heart rhythm (rapid or irregular heartbeat) have been reported in people taking MAR-AMITRIPTYLINE.

MAR-AMITRIPTYLINE may also reveal a hidden heart problem you did not know you had, a problem called “Brugada Syndrome”. Before you start taking MAR-AMITRIPTYLINE, tell your healthcare professional if you have unexplained fainting or a family history of “Brugada Syndrome” or unexplained sudden death before 45 years of age, as this could indicate you may have “Brugada Syndrome”. You should not take MAR-AMITRIPTYLINE if you have or are suspected to have “Brugada Syndrome”.

These problems can be serious and cause sudden death. Get immediate medical help if you experience dizziness, fainting, a rapid heartbeat or heart palpitations while taking MAR-AMITRIPTYLINE.

- have a history of trouble emptying your bladder (urinary retention), an enlarged prostate gland, increased pressure in the eye or glaucoma as MAR-AMITRIPTYLINE can make these conditions worse.
- have thyroid problems or are taking thyroid medication. Heart rhythm problems may

develop when MAR-AMITRIPTYLINE is taken with thyroid medicines.

- have a history of seizures or fits. MAR-AMITRIPTYLINE can make you more likely to have seizures or fits.

#### **New or worsened emotional or behavioural problems:**

- When you first start taking MAR-AMITRIPTYLINE or when your dose is adjusted, you may feel worse instead of better. You may feel new or worsened feelings of agitation, hostility, anxiety, or impulsivity.
- During your treatment with MAR-AMITRIPTYLINE, it is important that you and your healthcare professional talk regularly about how you are feeling. They will closely monitor you for signs of new or worsened emotions or behaviours while you are taking MAR-AMITRIPTYLINE.
- You may find it helpful to tell a relative or close friend that you are depressed. Ask them to read this leaflet. You might ask them to tell you if they:
  - think your depression is getting worse, or
  - are worried about changes in your behaviour.
- If your depression worsens or you experience changes in your behaviour, tell your healthcare professional right away. Do not stop taking your medicine as it takes time for MAR-AMITRIPTYLINE to work.

#### **Self-harm or Suicide**

- Antidepressants, such as MAR-AMITRIPTYLINE, can increase the risk of suicidal thoughts or actions.
- If you have thoughts of harming or killing yourself at any time, tell your healthcare professional or go to a hospital right away. You will be closely observed by your healthcare professional in this situation.

#### **What is MAR-AMITRIPTYLINE used for?**

MAR-AMITRIPTYLINE is used in adults to treat depression.

#### **How does MAR-AMITRIPTYLINE work?**

MAR-AMITRIPTYLINE is an antidepressant that belongs to a group of medicines known as tricyclic antidepressants. It is not known exactly how MAR-AMITRIPTYLINE works. It is thought to increase the concentration of certain chemicals in the brain which can help with the symptoms of depression.

#### **What are the ingredients in MAR-AMITRIPTYLINE?**

Medicinal ingredients: amitriptyline hydrochloride

Non-medicinal ingredients: colloidal anhydrous silica, crospovidone, hypromellose, lactose monohydrate, microcrystalline cellulose, dried maize starch, magnesium stearate, polyethylene glycol, talc, and titanium dioxide.

In addition to the above ingredients, the tablets also contain the following non-medicinal ingredients:

10 mg tablets: Lake of Brilliant Blue (FD & C Blue No.1)

25 mg tablets: Colour Quinoline Yellow (D & C Yellow No. 10)

50 mg tablets: Aluminum Lake (FD & C Yellow No. 6) and Indigo Carmine (FD & C Blue No. 2)

75 mg tablets: Aluminum Lake (FD & C Yellow No. 6)

**MAR-AMITRIPTYLINE comes in the following dosage forms:**

Tablets: 10 mg, 25 mg, 50 mg and 75 mg

**Do not use MAR-AMITRIPTYLINE if you:**

- are allergic to amitriptyline or any of the other ingredients of this medicine.
- have recently experienced a heart attack or heart failure.
- have a severe liver disease.
- are taking a medicine known as monoamine oxidase inhibitors (MAOIs), also used to treat depression.
- have taken a MAOI within the last 14 days.
- are taking cisapride.

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

- have liver problems.
- have dental problems.
- wear contact lenses.
- have a tumour (cancer) of the adrenal gland (such as pheochromocytoma or neuroblastoma).
- have bipolar disorder.
- have schizophrenia.
- have or have had a blood disease such as low platelet or white blood cell counts.
- have pylorus stenosis (narrowing of the gastric outlet) and paralytic ileus (blocked intestine).
- have diabetes as you might need an adjustment of your antidiabetic medicine.
- are dehydrated or suffer from excessive sweating, vomiting or diarrhea, or an eating disorder.
- are undergoing electroconvulsive therapy (ECT) to treat mental health problems.
- are taking warfarin or similar medicines, used to thin the blood.
- are taking other anticholinergic medicines (certain medicines used to treat asthma, chronic obstructive pulmonary disease, stomach and gut problems, and Parkinson's disease).
- have been told you have enzymes that do not work well (such as "CYP2D6 poor metabolizer" or "CYP2C19 poor metabolizer").
- had a recent bone fracture or were told you have osteoporosis or risk factors for osteoporosis.

- are 65 years of age or older.

**Other warnings you should know about:**

**Pregnancy:** Before taking MAR-AMITRIPTYLINE, tell your healthcare professional if you are pregnant, think you might be pregnant or are planning to become pregnant. You should not take MAR-AMITRIPTYLINE if you are pregnant unless you and your healthcare professional have discussed the risks and decided that you should. Tell your healthcare professional right away if you become pregnant while taking MAR-AMITRIPTYLINE.

Babies born to mothers that took medicines similar to MAR-AMITRIPTYLINE while they were pregnant have experienced withdrawal symptoms after birth. Get immediate medical help for your baby if you took MAR-AMITRIPTYLINE while you were pregnant, and they have any of the following symptoms:

- breathing problems, bluish skin
- seizures or fits
- body temperature changes
- stiff or floppy muscles
- jitteriness, irritability, lethargy
- drowsiness
- constant crying

**Breastfeeding:** Tell your healthcare professional if you are breastfeeding or planning to breastfeed. MAR-AMITRIPTYLINE is released into breast milk. It is not known if this is safe for your baby. You and your healthcare professional should decide if you should breastfeed or take MAR-AMITRIPTYLINE. You should not do both.

**Cavities:** Long term use of MAR-AMITRIPTYLINE can cause dental cavities.

**Withdrawal symptoms:** Do NOT stop taking MAR-AMITRIPTYLINE without talking to your healthcare professional. You may need to lower your dose gradually and careful monitoring by your healthcare professional is required. Stopping MAR-AMITRIPTYLINE suddenly may cause withdrawal symptoms including restlessness, nausea, headache, malaise (general discomfort), sleep disturbance, irritability and changes in behavior.

**Bone Fracture:** Taking MAR-AMITRIPTYLINE may increase your risk of breaking a bone if you are elderly, have osteoporosis, or have other major risk factors for breaking a bone. You should take extra care to avoid falls, especially if you get dizzy or have low blood pressure.

**MAR-AMITRIPTYLINE can cause serious side effects, including:**

- **Angle-closure glaucoma:** MAR-AMITRIPTYLINE can cause angle-closure glaucoma (sudden eye pain). Having your eyes examined before you take MAR-AMITRIPTYLINE could help identify if you are at risk of having angle-closure glaucoma. Talk to your healthcare professional rightaway if you have:
  - eye pain;
  - changes in vision;
  - swelling or redness in or around the eye.

- **Serious skin reactions:** Cases of Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS), which can be serious or life-threatening, have been reported with MAR-AMITRIPTYLINE. Get immediate medical help if you experience:
  - fever
  - severe rash
  - peeling skin
  - swelling of the face
  - swollen lymph glands
  - flu-like feeling
  - yellow skin or eyes
  - shortness of breath
  - swelling of the legs
  - dry cough
  - chest pain or discomfort
  - feeling thirsty
  - urinating less often, less urine or dark urine
- **Serotonin toxicity (also known as Serotonin syndrome) or Neuroleptic malignant syndrome:** MAR-AMITRIPTYLINE can cause serotonin toxicity or neuroleptic malignant syndrome, rare but potentially life-threatening conditions. They can cause serious changes in how your brain, muscles and digestive system work. You may develop serotonin toxicity or neuroleptic malignant syndrome if you take MAR-AMITRIPTYLINE with certain medications used to treat depression, migraine or other mental health problems such as schizophrenia.

Symptoms of serotonin toxicity or neuroleptic malignant syndrome include:

  - fever, sweating, shivering, diarrhea, nausea, vomiting;
  - muscle shakes, jerks, twitches or stiffness, changes in reflexes, loss of coordination;
  - fast heartbeat, changes in blood pressure;
  - confusion, agitation, restlessness, hallucinations, mood changes, unconsciousness, and coma.

See the [Serious side effects and what to do about them table](#), below, for more information on these and other serious side effects.

**Driving and Using Machines:** MAR-AMITRIPTYLINE can affect your ability to drive and operate machinery. Do not drive or operate machinery until you know how MAR-AMITRIPTYLINE affects you.

**Blood tests and monitoring:** MAR-AMITRIPTYLINE can cause abnormal blood test results. Your healthcare professional will decide when to perform blood tests and will interpret the results. Your healthcare professional will also monitor your blood pressure and the health of your heart while you are taking MAR-AMITRIPTYLINE.

**Surgery:** If you have a planned surgery, talk to your healthcare professional as soon as possible. They may ask you to stop taking MAR-AMITRIPTYLINE.

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

#### Serious Drug Interactions

- **Do not** take MAR-AMITRIPTYLINE if you are taking a monoamine oxidase inhibitor (MAOI), or if you have taken one in the last 14 days as this can cause serious side effects.
- **Do not** take MAR-AMITRIPTYLINE if you are taking cisapride\*, as this can cause serious side effects.
- Taking MAR-AMITRIPTYLINE and thyroid medication can cause heart rhythm problems.

#### The following may interact with MAR-AMITRIPTYLINE:

- alcohol. You should avoid drinking alcohol while taking MAR-AMITRIPTYLINE.
- medicines such as adrenaline, ephedrine, isoprenaline, noradrenaline, phenylephrine and phenylpropanolamine which may be found in cough and cold medication and anesthetics used in surgery.
- other medicines used to treat depression such as other tricyclic antidepressants and selective serotonin reuptake inhibitors (SSRIs) like fluoxetine, fluvoxamine, sertraline, and paroxetine.
- bupropion, used to treat depression or for smoking cessation.
- ozanimod, used to treat multiple sclerosis or ulcerative colitis.
- triptans, used to treat migraine.
- anticholinergic drugs such as certain medicines used to treat asthma, chronic obstructive pulmonary disease, Parkinson's disease and stomach and gut problems, like atropine and hyoscyamine\*.
- cimetidine, used to treat stomach ulcers.
- sedatives used to treat anxiety and sleep disorders.
- pitolisant, used to treat excessive daytime sleepiness.
- modafinil, used to treat excessive sleepiness.
- disulfiram\*, used to treat alcoholism.
- medicines used to treat schizophrenia and other mental health problems, such as pimozide, sertindole\*, fluphenazine, thioridazine\* and haloperidol.
- high blood pressure medications such as calcium-channel blockers (e.g. diltiazem and verapamil), guanethidine\*, betanidine\*, reserpine\*, clonidine and methyldopa.
- medicines used to treat irregular heartbeat such as quinidine\*, propafenone, flecainide,

disopyramide, amiodarone, procainamide and sotalol.

- astemizole\* and terfenadine\*, used to treat allergies and hayfever.
- diuretics or “water pills” such as furosemide.
- medicines used to treat bacterial infections such as erythromycin, clarithromycin, tacrolimus, rifampicin\* and ciprofloxacin.
- medicines used to treat malaria such as quinine, halofantrine\* and chloroquine.
- medicines used to treat fungal infections such as ketoconazole, itraconazole, fluconazole and terbinafine.
- domperidone used to treat nausea and vomiting and increase milk supply in breastfeeding mothers.
- medicines used to treat nausea and vomiting in cancer patients such as ondansetron.
- medicines used to treat cancer such as sunitinib and vorinostat.
- medicines used to treat breathing problems like asthma and COPD such as salmeterol.
- opioids such as morphine, tramadol, buprenorphine, and methadone, used to treat pain and opioid drug dependence.
- warfarin or similar medicines, used to thin the blood.
- baclofen, used to treat muscle spasms.
- nitrates, used to treat angina (chest pain).
- phenytoin, carbamazepine, topiramate, valproic acid, used to treat seizures or fits.
- methylphenidate, used to treat ADHD.
- protease inhibitors such as ritonavir, used to treat HIV and COVID-19.
- oral contraceptives, used to prevent pregnancy.
- St. John’s Wort (*hypericum perforatum*) – a herbal remedy used for depression.
- grapefruit juice.

\* Product is not or no longer marketed in Canada.

### **How to take MAR-AMITRIPTYLINE:**

- Always take MAR-AMITRIPTYLINE exactly as your healthcare professional has told you. Check with your healthcare professional if you are not sure.
- MAR-AMITRIPTYLINE can be taken with or without food.
- Swallow the tablets whole with water. Do not chew them.

Even if you feel better, do not stop taking MAR-AMITRIPTYLINE without first talking to your healthcare professional. Stopping MAR-AMITRIPTYLINE suddenly can cause serious withdrawal symptoms.

### **Usual dose:**

**Adults:** The recommended initial dose is 25 mg three times a day.

Depending on your response to MAR-AMITRIPTYLINE, your healthcare professional may gradually increase your dose to 150 mg per day divided in two doses.

The usual maintenance dose is 50 to 100 mg per day.

**Overdose:**

Signs of an overdose may include:

- temporary confusion
- drowsiness
- low body temperature (hypothermia)
- heart rhythm problems such as an irregular heartbeat
- heart failure
- abnormal eye movement
- convulsions
- severe low blood pressure
- constipation
- coma

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

**Missed Dose:**

If you forget to take MAR-AMITRIPTYLINE, take it as soon as you remember. If it is almost time for your next dose, skip the missed dose. Do NOT take two doses at the same time to make up for a missed dose.

**What are possible side effects from using MAR-AMITRIPTYLINE?**

These are not all the possible side effects you may have when taking MAR-AMITRIPTYLINE. If you experience any side effects not listed here, tell your healthcare professional.

Side effects may include:

- nausea, vomiting
- stomach pain
- constipation
- diarrhea
- drowsiness
- dizziness
- fatigue
- restlessness
- headache
- dry mouth, sore mouth
- unpleasant taste in the mouth
- black tongue
- itching
- changes in weight (loss or gain)
- weakness



- increased sweating

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	
<b>RARE</b>			
<b>Mania:</b> elevated or irritated mood, decreased need for sleep, racing thoughts, uneasiness, excessive physical activity		√	
<b>VERY RARE</b>			
<b>Serotonin Toxicity (also called serotonin syndrome) or Neuroleptic Malignant Syndrome:</b> Reactions which may cause feelings of agitation or restlessness, muscle twitching, involuntary eye movements, flushing, heavy sweating, high body temperature (>38°C), or rigid muscles.			√
<b>UNKNOWN FREQUENCY</b>			
<b>Allergic reaction:</b> rash, hives, swelling of the face, lips and tongue or throat, difficulty swallowing or breathing.			√
<b>Angle-closure glaucoma:</b> increased pressure in the eye, pupil dilation, blurred vision, eye pain		√	
<b>Bone marrow depression:</b> easy bruising, bleeding, nose bleeds, bleeding gums, red spots on the skin, fever and chills, rash, extreme fatigue, pale skin and lips			√
<b>Difficulty passing urine</b>	√		
<b>Drug reaction with eosinophilia and systemic symptoms (DRESS)</b> (serious			√

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	
skin reaction that may affect more than one organ): fever, severe rash, swollen lymph glands, flu-like feeling, yellow skin or eyes, shortness of breath, dry cough, chest pain or discomfort, urinate less often, less urine			
<b>QT interval prolongation and Brugada Syndrome (serious and potentially life-threatening electrical problems with the heart):</b> dizziness, fainting, fast heartbeat, palpitations, abnormal heart rate, seizures (fits)			√
<b>Gastrointestinal disorders:</b> Heart burn, diarrhoea, black tongue, constipation, dry mouth, unpleasant taste, swollen salivary gland, bowel obstruction, change in weight (loss or gain)	√		
<b>Heart attack:</b> chest pain, tightness or pressure that may spread to your neck, jaw or back, pain in the arm or shoulder, nausea, indigestion, shortness of breath, cold sweat, fatigue, dizziness			√
<b>Heart problems (enlarged heart, heart disease):</b> weakness, fatigue, shortness of breath especially during exercise, light-headedness, chest pain, palpitations, fainting, swelling in your feet, ankles and legs		√	
<b>High blood pressure:</b> headache, fatigue, vision problems		√	
<b>Hyponatremia (low sodium in the blood):</b> lethargy, confusion, muscular twitching, achy, stiff or uncoordinated muscles, seizure, coma		√	
<b>Increased or decreased blood sugar:</b> frequent urination, thirst, hunger, shakiness, sweating and chills, irritability, confusion, dizziness	√		

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	
<b>Liver problems:</b> yellowing of the skin or eyes, dark urine, abdominal pain, nausea, vomiting, loss of appetite		√	
<b>Mental health problems:</b> confusion, hallucinations, trouble sleeping, excitement, nightmares, problems with attention, anxiety		√	
<b>Nervous system problems:</b> shaking, numbness and tingling of the hands and feet, clumsiness and lack of coordination, loss of balance, uncontrolled twitching or jerking, slurred speech, ringing in the ears, coma		√	
<b>New or worsened emotional or behavioural problems:</b> feeling angry, aggressive, worried, agitated, hostile or impulsive, feeling violent, feeling like you are not yourself or that you are less inhibited		√	
<b>Photosensitivity:</b> Increased sensitivity of the skin to sun	√		
<b>Reproductive problems:</b> swelling of testicles, impotence in men, increase in breast tissue (in men and women), change in sex drive		√	
<b>Stroke:</b> sudden numbness or weakness in the face, arm or leg, confusion, trouble speaking, blurred vision, trouble walking, dizziness, loss of balance			√
<b>Seizures or fits:</b> uncontrollable shaking with or without loss of consciousness			√
<b>Thoughts of death or suicide:</b> thoughts about hurting or killing yourself or other people			√
<b>Unusual hair loss or thinning</b>		√	
<b>Withdrawal symptoms:</b> nausea, headache, irritability, restlessness, dream and sleep disturbance, generally		√	

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	
feeling unwell, irritability, behavioural changes			

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/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 room temperature (15°C to 30°C). Keep in a tightly closed container. Keep out of reach and sight of children.

### If you want more information about MAR-AMITRIPTYLINE:

- 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>; on the manufacturer's website [www.marcanpharma.com](http://www.marcanpharma.com), or by calling 1-855-627-2261.

This leaflet was prepared by Marcan Pharmaceuticals Inc.

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