IMPORTANT: PLEASE READ

PART III: CONSUMER INFORMATION

[Pr]APO-QUETIAPINE XR

quetiapine fumarate extended-release tablets

This leaflet is part III of a three-part "Product Monograph" published when APO-QUETIAPINE XR was approved for sale in Canada and is designed specifically for Consumers/Care givers. This leaflet is a summary and will not tell you everything about APO-QUETIAPINE XR. Contact your doctor or pharmacist if you have any questions about the drug.

Before taking APO-QUETIAPINE XR, read this leaflet carefully. Keep this leaflet until you have taken all of your APO-QUETIAPINE XR tablets.

ABOUT THIS MEDICATION

What the medication is used for:

APO-QUETIAPINE XR (quetiapine fumarate extended-release tablets) is used to:

- Treat the symptoms of schizophrenia, such as hallucinations (hearing or seeing things which are not there), fixed false beliefs, unusual suspiciousness or emotional withdrawal. Patients may also feel depressed, anxious or tense.
- Treat the symptoms of mania associated with bipolar disorder, such as racing thoughts, irritability, aggressiveness, agitation, impulsive behaviour or excessively elevated mood.
- Treat the symptoms of depression associated with bipolar disorder, such as sadness, feeling guilty, lack of energy, loss of appetite and/or sleep disturbance.
- Treat symptoms of patients with depression who have failed treatment with currently available antidepressant medications due to lack of appropriate response and/or due to side effect issues. APO-QUETIAPINE XR is a new treatment for depression and belongs to a class of drug known as 'atypical antipyschotic'. It is important to discuss with your doctor about your depressive symptoms and possible side effects.

You may find it helpful to tell a friend or relative that you are suffering from these symptoms, and ask them to read this leaflet. You might ask them to tell you if they think your symptoms are getting worse, or if they are worried about any other changes in your behaviour.

Your doctor may have prescribed APO-QUETIAPINE XR for another reason. Ask your doctor if you have any questions about why APO-QUETIAPINE XR has been prescribed for you.

APO-QUETIAPINE XR is not a cure for your condition but it can help manage your symptoms and help you feel better.

What it does:

APO-QUETIAPINE XR is a medication that belongs to a class of medicines called "atypical antipsychotics".

Illnesses that affect the brain, such as schizophrenia, bipolar disorder and major depressive disorder, may be due to certain chemicals in the brain being out of balance. These imbalances may cause some of the symptoms you may be experiencing. Doctors and scientists are not sure what causes these imbalances to occur. APO-QUETIAPINE XR is thought to work by regulating the imbalance of chemicals in the brain.

When it should not be used:

Do not take APO-QUETIAPINE XR if you have had an allergic reaction to APO-QUETIAPINE XR or any of the ingredients listed in the "nonmedicinal ingredients" section of this leaflet.

What the medicinal ingredient is:

APO-QUETIAPINE XR contains the active ingredient quetiapine fumarate.

What the nonmedicinal ingredients are:

The inactive ingredients in APO-QUETIAPINE XR are: lactose monohydrate, hydroxypropyl methylcellulose, sodium chloride, povidone K30, Silicified microcrystalline cellulose, magnesium stearate, and purified talc. The coating of the tablet contains hydroxypropyl methylcellulose (200 mg, 300 mg, 400 mg), polyvinyl alcohol (50 mg, 150 mg), polyethylene glycol, talc (50 mg, 150 mg), titanium dioxide, iron oxide red (50 mg), iron oxide yellow (50 mg, 200 mg, 300 mg).

What dosage forms it comes in:

APO-QUETIAPINE XR comes in five tablet strengths: 50 mg (capsule shape, peach colour), 150 mg (capsule shape, white colour), 200 mg (capsule shape, yellow colour), 300 mg (capsule shape, light yellow colour) and 400 mg (capsule shape, white colour). The following letters are marked on each tablet "AB1" (50 mg), "AB2" (150 mg), FV3"(200 mg), "FV4" (300 mg) and "FV5" (400 mg). These letters are easy to read on the tablets, and if you see them you know you are taking the right medicine.

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions

Studies with various medications of the group to which APO-QUETIAPINE XR belongs, including quetiapine fumarate immediate-release tablets, when used in elderly patients with dementia have been associated with an increased rate of death. APO-QUETIAPINE XR is not indicated in elderly patients with dementia.

Before starting APO-QUETIAPINE XR, be sure to tell your

doctor:

- If you have had an allergic reaction to any medicine which you have taken previously to treat your condition, or if you think you might be sensitive or allergic to any of the ingredients in APO-QUETIAPINE XR.
- About any other medications - prescription, non-prescription or alternative - that you are taking or plan to take. Certain medications can seriously affect the way other medications work.
- If you are pregnant or plan to become pregnant while taking APO-QUETIAPINE XR.
- If you are breast-feeding or are planning on breast-feeding while taking APO-QUETIAPINE XR. You should not breast-feed while taking APO-QUETIAPINE XR.
- If you drink alcohol or use street drugs.
- If you have a history of alcohol or drug abuse.
- If you have any health problems.
- If you have low or high blood pressure or have had a stroke.
- If you or a family member have a history of any problems with the way your heart beats or have a history of heart disease or heart problems or if you are taking any medicines that may have an impact on the way your heart beats.
- If you have a history of seizures (fit).
- If you have diabetes, a family history of diabetes or high blood sugar during pregnancy.
- If you have a history of liver or kidney problems.
- If you know that you had a low white blood cell count in the past which may or may not have been caused by other medicines.
- If you exercise vigorously or work in hot or sunny places.
- If you have risk factors for developing blood clots such as: a family history of blood clots, age over 65, smoking, obesity, recent major surgery (such as hip or knee replacement), immobility due to air travel or other reason, or take oral contraceptives ("The Pill").
- If you suffer or have ever suffered from severe constipation, obstruction of the bowel or any other condition which has affected your large bowel.
- If you have or have had a condition where you stop breathing for short periods during your normal nightly sleep (called "sleep apnea") and are taking medicines that slow down normal activity of the brain ("depressants") or breathing.
- If you have or have had a condition where your bladder does not empty or does not empty completely (urinary retention), have an enlarged prostate, a blockage in your intestines, or increased pressure inside your eyes. These conditions are sometimes caused by medicines called "anticholinergics".

Tell your doctor as soon as possible if you have:

- Fever, flu-like symptoms, sore throat, or any other infection, as this could be a result of a very low white blood cell count, which may require APO-QUETIAPINE XR to be stopped and/or treatment to be given.
- Constipation along with persistent stomach pain, or constipation which has not responded to treatment, as this may lead to a more serious blockage of the bowel.

In clinical studies with quetiapine fumarate extended-release tablets and other drugs of this type, an increased risk of death has been reported in elderly patients with dementia and behavioural disturbances. APO-QUETIAPINE XR is not approved for this use.

Pancreatitis (inflammation of the pancreas) has been reported in some patients. Many of these patients also had factors which are known to be associated with pancreatitis such as increased triglyceride (a fatty substance in the blood) levels, gallstones and alcohol consumption.

Cardiomyopathy (weakening of the heart muscle) and myocarditis (inflammation of the heart) have been reported in some patients, however, it is not known if APO-QUETIAPINE XR treatment is related to these problems.

If you already have diabetes, you should be monitored for worsening of your diabetes.

Do not drive or operate machinery until you know your response to this medication, as APO-QUETIAPINE XR can cause drowsiness.

Thoughts of suicide and worsening of your depression or other mental illnesses:
If you are depressed and/or have other mental illnesses you may sometimes have thoughts of harming or killing yourself. These may be increased when first starting treatment, since these medicines all take time to work, usually about two weeks but sometimes longer.

If you have thoughts of harming or killing yourself at any time, contact your doctor or go to a hospital straight away.

You may find it helpful to tell a relative or close friend that you are depressed or have other mental illnesses, and ask them to read this leaflet. You might ask them to tell you if they think your depression or mental illness is getting worse, or if they are worried about changes in your behaviour.

Effects on Newborns:
In some cases, babies born to a mother taking APO-QUETIAPINE XR during pregnancy have experienced symptoms of withdrawal that are severe and require the newborn to be hospitalized. Sometimes, the symptoms may resolve on their own. Be prepared to seek immediate emergency medical attention for your newborn if they have

difficulty breathing, are overly sleepy, have muscle stiffness, or floppy muscles (like a rag doll), are shaking, or are having difficulty feeding.

INTERACTIONS WITH THIS MEDICATION

Because certain medications can seriously affect the way other medications work, it is important to tell all doctors, dentists, and pharmacists who are treating you that you are taking APO-QUETIAPINE XR. As well, be sure to tell them about any other medications - prescription, non-prescription or alternative - that you are taking or plan to take.

You should not drink alcohol while taking APO-QUETIAPINE XR, as the combination could increase the effects of the alcohol.

You should tell your doctor if you are taking or about to stop taking medications for anxiety, depression, epilepsy (such as phenytoin or carbamazepine), high blood pressure, or to help you sleep.

Dopamine agonists, e.g. levodopa (antiparkinsonian agent), may decrease the effect of APO-QUETIAPINE XR.

Medications known to interact with APO-QUETIAPINE XR include carbamazepine (anticonvulsant), phenytoin (anticonvulsant), ketoconazole (antifungal), and protease inhibitors (for treating Human Immunodeficiency Virus).

You should tell your doctor if you are taking erythromycin (antibiotic), clarithromycin (antibiotic), nefazodone, thioridazine (antipsychotic), diltiazem or verapamil (blood pressure medications), medications that can cause constipation or medicines called "anticholinergics" that may affect your ability to empty your bladder. You should also tell your doctor if you are taking medicines that have an impact on the way and how slow your heart beats, for example drugs that can cause an imbalance in electrolytes (low levels of potassium or magnesium) such as diuretics (water pills) or certain antibiotics (drugs to treat infections).

Effect on Urine Drug Screens:

APO-QUETIAPINE XR may cause positive results for methadone or certain drugs for depression called tricyclic antidepressants (TCAs) when some test methods are used, even though you may not be taking these drugs. Confirmation of the results by more specific tests is recommended.

PROPER USE OF THIS MEDICATION

APO-QUETIAPINE XR is not recommended for use in patients under 18 years old.

USUAL DOSE:

Adult
In order for APO-QUETIAPINE XR to help you feel better, it is very important to take it every day exactly as your doctor tells you to. Take the exact number of tablets your doctor has prescribed at the right time every day.

Recommended Dose:

Schizophrenia and Bipolar Mania:
The usual titration schedule is day 1: 300 mg, day 2: 600 mg and up to 800 mg from day 3 onwards taken once daily. The maximum dose is 800 mg per day.

Bipolar Depression:
The usual titration schedule is day 1: 50 mg, day 2: 100 mg, day 3: 200 mg and day 4 and onwards: 300 mg taken once daily. Your doctor may further increase the dose depending on your response and tolerability. The maximum dose is 600 mg per day.

Major Depressive Disorder:
The usual titration schedule is 50 mg on days 1 and 2 and 150 mg on day 3. Your doctor may adjust the dose upwards or downwards within the recommended dose range of 50-300 mg per day during the course of your treatment depending on your response and tolerability.

It takes time to feel better and you should expect some symptoms to improve slowly over the first few weeks of treatment. Do not stop taking APO-QUETIAPINE XR, or change the times of day you take APO-QUETIAPINE XR without talking to your doctor first.

If you stop taking APO-QUETIAPINE XR abruptly you may experience withdrawal symptoms such as insomnia (inability to sleep), nausea and vomiting.

To make sure you are getting the most benefit from APO-QUETIAPINE XR, you must:

- Continue taking APO-QUETIAPINE XR everyday and
- Keep your doctor well informed of how you are feeling, both good and bad.

By doing these two things, you and your doctor together will be able to make sure that you are getting the best dose of APO-QUETIAPINE XR for you.

You may take APO-QUETIAPINE XR with or without food. **Tablets should be swallowed whole. Do not split, crush or chew.**

Do not give APO-QUETIAPINE XR to anyone else. Your doctor has prescribed APO-QUETIAPINE XR for you only.

Switching from quetiapine fumarate immediate-release tablets to APO-QUETIAPINE XR:

If you are currently being treated with divided doses of quetiapine fumarate immediate-release tablets your doctor may switch you to APO-QUETIAPINE XR at an equal total daily dose taken once daily.

OVERDOSE:

In case of drug overdose, contact a health care practitioner, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

In case of APO-QUETIAPINE XR overdose or if you think you or anyone else are experiencing severe episodes of any of the side effects of APO-QUETIAPINE XR (especially drowsiness, including also rapid heart beat, lightheadedness and/or dizziness, especially when standing up quickly or getting out of bed), call your doctor or poison control centre or go to the nearest hospital emergency room right away. Make sure to bring your medication bottle with you.

MISSED DOSE:

APO-QUETIAPINE XR should be taken at the same time each day. If you miss a dose from the previous day, you should take your next regular dose of APO-QUETIAPINE XR the next day at the normal time.

Here are some tips that can help you remember to take each dose of APO-QUETIAPINE XR:

- Take your APO-QUETIAPINE XR at the same time every day.
- Take APO-QUETIAPINE XR during daily events which will help you remember to take your medicine as well, e.g., mealtime or bedtime.
- Use a pill container that will separate your APO-QUETIAPINE XR doses by the day of the week.
- Use a calendar to note the day and time after you have taken each dose to help you keep track of when you need to take your APO-QUETIAPINE XR.
- Keep a written reminder to take your APO-QUETIAPINE XR that can be easily seen, e.g., on a mirror or on the refrigerator.
- Have a family member or friend remind you to take your medication.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Like any medication, APO-QUETIAPINE XR may produce side effects in some people.

Increases in blood glucose (sugar) and hyperglycaemia (high blood sugar) have been observed with APO-QUETIAPINE XR. Also, occasional cases of diabetes have been reported. Your doctor may take blood tests to check your blood sugar before starting APO-QUETIAPINE XR. They may continue to monitor your blood sugar for as long as you are being treated.

Light-headedness and dizziness (symptoms of postural hypotension) and drowsiness are among the most common side effects you may experience while taking APO-QUETIAPINE XR, particularly during the first week of treatment or after an increase in dose. The dizziness and drowsiness are usually mild and should go away with time. To help prevent these feelings, be careful to move slowly when you are getting up from a sitting or lying position. Dizziness and drowsiness may lead to falls.

Low blood pressure in standing position is common, which may result in dizziness or feeling faint (may lead to falls).

As feelings of drowsiness are also common at the start of treatment, or when your dose is increased, if you have to drive, operate machinery or do anything else that requires you to be fully alert, use extra caution until you are sure APO-QUETIAPINE XR does not cause you to be drowsy.

Dry mouth and weight gain have also been reported very commonly in patients taking APO-QUETIAPINE XR. Your doctor may take your body weight before starting APO-QUETIAPINE XR and continue to monitor it for as long as you are being treated.

Discontinuation symptoms which occur upon stopping APO-QUETIAPINE XR have been reported very commonly and include insomnia (inability to sleep), nausea, headache, diarrhea, vomiting, dizziness and irritability. Gradual withdrawal over a period of at least one to 2 weeks is advisable.

Other common side effects may include: headache, rapid heart beat, feeling like your heart is pounding, racing or has skipped beats, shortness of breath, constipation, indigestion, feeling weak, swelling of arms and legs, fever, upset stomach or abdominal pain, vomiting (mainly in the elderly), blurred vision, abnormal dreams and nightmares, irritability, feeling more hungry, disturbance in speech and language, and changes in laboratory tests for liver and thyroid functions.

There have been uncommon cases of difficulty swallowing, fainting (may lead to falls), stuffy nose, difficulty in passing urine, and a slower than normal heart rate which may occur when starting treatment and which may be associated with low blood pressure and fainting.

There have also been reports, in a small number of patients, of changes to the lens of the eye. Although it is not known whether or not these changes are caused by APO-QUETIAPINE XR, your doctor may advise you that a

specific type of eye exam is recommended in order to maximize safe use of this drug.

In rare cases, there have been reports of decreased body temperature (hypothermia), a combination of fever, flu-like symptoms, sore throat, or any other infection with very low white blood cell count (a condition called agranulocytosis), bowel obstruction, and walking, talking, eating or other activities while asleep.

In very rare cases, this type of medicine can interfere with your body's ability to control body temperature. Therefore, take care to avoid becoming overheated or dehydrated (for example with vigorous exercise, or exposure to extreme heat) while taking APO-QUETIAPINE XR.

Side effects that are of unknown frequency (cannot be estimated from available data) include symptoms of withdrawal in newborn babies of mothers that have used APO-QUETIAPINE XR during their pregnancy.

The following may also occur with APO-QUETIAPINE XR, and may be seen in routine blood testing:

- Decrease in the amount of white blood cells. These changes will normally disappear when stopping the treatment of APO-QUETIAPINE XR.
- Decrease in the amount of red blood cells. These are the cells that transport oxygen throughout the body.
- Increase in the amount of eosinophils. These are a type of white blood cell sometimes seen in allergic reactions.
- Decrease in platelets (thrombocytopenia), which are cells that help you stop bleeding if you get a cut.
- Increase in the amount of liver enzymes. These changes will normally disappear when continuing the treatment of APO-QUETIAPINE XR.
- Changes in the amount of fatty substances (lipid levels, such as triglycerides and cholesterol) in the blood.
- Increase in the amount of "creatine phosphokinase", a substance in the muscles.
- Increase in the amount of sugar (glucose) in the blood.
- Increase in the amount of hormone prolactin in the blood. Rarely (<0.1% - ≥0.01%) this may lead to swelling of breasts and unexpected production of breast milk in women and in some men, and changes in the regularity of monthly period.
- Changes in the amount of thyroid hormones in your blood. These changes usually do not affect how you feel.
- If you have high levels of prolactin and a condition called hypogonadism you may be at an increased risk of breaking a bone due to osteoporosis. This may occur in both men and women.

One of the most important things for you to do to minimize the risks from side effects, while helping APO-QUETIAPINE XR work for you, is to contact your doctor or pharmacist if you notice any symptom that worries you, even if you think it is not connected with this medicine or is not listed here.

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

Symptom / effect		Talk with your doctor right away		Stop taking drug and seek immediate emergency assistance
		Only if severe	In all cases	
Very Common	Abnormal muscle movements, including difficulty starting muscle movements, shaking, restlessness or muscle stiffness without pain		√	
Common	New or worsening constipation		√	
Uncommon	Involuntary movements, mainly of your face or tongue (Tardive dyskinesia)		√	
	Symptoms of allergic reactions such as skin lumps, bumps or swelling			√
	Restless legs (unpleasant sensations in the legs)		√	
	Seizure (i.e., loss of consciousness with uncontrollable shaking "fit")			√
	Not being able to pass urine (called "urinary retention")			√
Rare	Long-lasting (greater than 4 hours in duration) and painful erection of the penis			√
	Combination of high fever, muscle stiffness, marked increase in blood			√

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

Symptom / effect		Talk with your doctor right away		Stop taking drug and seek immediate emergency assistance
		Only if severe	In all cases	
	pressure and/or heartbeats, and reduced consciousness (called neuroleptic malignant syndrome)			
	Blood clots: swelling, pain and redness in an arm or leg that can be warm to touch. You may develop sudden chest pain, difficulty breathing and heart palpitations		√	
	Liver Disorder, or inflammation of the liver with or without jaundice (a yellowish discolouration of the skin/ palms or whites of your eyes), dark urine, abdominal pain, nausea, vomiting, loss of appetite		√	
Very Rare	Anaphylaxis (severe form of allergic reaction; symptoms may include swelling of the mouth, face, lips or tongue, may include severe difficulty breathing and shock)			√
	Stop breathing for short periods during your normal nightly sleep (called "sleep apnea")			√

This is not a complete list of side effects. For any unexpected effects while taking APO-QUETIAPINE XR, contact your doctor or pharmacist.

HOW TO STORE IT

Store APO-QUETIAPINE XR at room temperature (between 15 - 30°C) and well out of the reach and sight of children.

The expiry date of this medicine is printed on the package label. Do not use the medicine after this date.

If your doctor tells you to stop taking APO-QUETIAPINE XR or you find that it has passed its expiry date, please return any leftover medicine to your pharmacist.

REPORTING SUSPECTED SIDE EFFECTS

You can help improve the safe use of health products for Canadians by reporting serious and unexpected side effects to Health Canada. Your report may help to identify new side effects and change the product safety information:

3 ways to report:

- Online at MedEffect (http://hc-sc.gc.ca/dhp-mps/medeff/index-eng.php);
- By calling 1-866-234-2345 (toll-free);
- By completing a Consumer Side Effect Reporting Form and sending it by:
  - Fax to 1-866-678-6789 (toll-free), or
  - Mail to: Canada Vigilance Program
    Health Canada
    Postal Locator 0701E
    Ottawa, ON
    K1A 0K9

Postage paid labels and the Consumer Side Effect Reporting Form are available at MedEffect (http://hc-sc.gc.ca/dhp-mps/medeff/index-eng.php).

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

For more information, please contact your doctor, pharmacist or other healthcare professional.

This leaflet plus the full product monograph, prepared for health professionals, can be obtained by contacting DISpedia, Apotex's Drug Information Service at: 1-800-667-4708

This leaflet can also be found at: http://www.apotex.ca/products.

This leaflet was prepared by Apotex Inc., Toronto, Ontario, M9L 1T9.

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