

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

Pr **SYMTUZA**[®]

(darunavir/cobicistat/emtricitabine/tenofovir alafenamide) Tablets

Read this carefully before you start taking **SYMTUZA**[®] 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 **SYMTUZA**[®].

Serious Warnings and Precautions

“Flare-ups” of Hepatitis B Virus infection can occur if you also have hepatitis B and stop taking **SYMTUZA**[®]. In these cases, your infection may return and become worse than it was before. Do not stop taking **SYMTUZA**[®] without your doctor’s advice. If you stop taking **SYMTUZA**[®], tell your doctor right away. Tell your doctor about any new, unusual or worsening symptoms that you notice after stopping treatment. After you stop taking **SYMTUZA**[®], your doctor will still need to check your health and take blood tests to check your liver. **SYMTUZA**[®] is not approved for the treatment of hepatitis B virus infection.

What is **SYMTUZA**[®] used for?

- **SYMTUZA**[®] is used to treat human immunodeficiency virus (HIV) infection. HIV is the virus that causes AIDS (Acquired Immune Deficiency Syndrome).
- **SYMTUZA**[®] is for adults and children 12 years of age and older and who weigh at least 40 kg (88 lbs).

How does **SYMTUZA**[®] work?

SYMTUZA[®] works by reducing the amount of HIV in your blood (called “viral load”). HIV infection affects the immune system. The immune system helps fight infection. Reducing the amount of HIV may improve your immune system (your body’s natural defences).

SYMTUZA[®] does not cure HIV infection or AIDS. At present, there is no cure for HIV infection. People taking **SYMTUZA**[®] may still develop infections or other conditions associated with HIV infection. Because of this, it is very important for you to remain under the care of a doctor.

What are the ingredients in **SYMTUZA**[®]?

Each **SYMTUZA**[®] tablet contains:

Medicinal ingredients:

Darunavir (800 mg) as ethanolate, Cobicistat (150 mg), Emtricitabine (200 mg) and Tenofovir alafenamide (10 mg) as hemifumarate.

Non-medicinal ingredients:

Tablet core: colloidal silicon dioxide, croscarmellose sodium, magnesium stearate, microcrystalline cellulose.

Film-coating: polyethylene glycol (macrogol), polyvinyl alcohol (partially hydrolyzed), talc, titanium dioxide, yellow ferric oxide.

SYMTUZA® tablets are yellow to yellowish brown, capsule-shaped, debossed on one side with “8121” and the number “JG” on the other side.

SYMTUZA® comes in the following dosage forms:

Film-coated tablet: 800 mg darunavir ethanolate / 150 mg cobicistat/ 200 mg emtricitabine/ 10 mg tenofovir alafenamide hemifumarate (see “**What are the ingredients in SYMTUZA®?**”).

Do not use SYMTUZA® if:

- you are taking any medication that is listed in this leaflet under “**Drugs that should not be taken with SYMTUZA®**”.
- you are allergic to SYMTUZA® or any of its ingredients, including non-medicinal ingredients or components of the container (see “**What are the ingredients in SYMTUZA®?**”).
- Have severe liver problems.

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

- Have lactic acidosis (high levels of acid in the blood). See “**Serious side effects and what to do about them**” table for symptoms. Contact your doctor right away if you get these side effects.
- Have hepatitis B and/or C or severe liver problems (hepatotoxicity) including enlarged or fatty liver. See “**Serious side effects and what to do about them**” table for symptoms. Cases leading to death have been reported.
- If you have hepatitis B virus (HBV) infection at the same time and take SYMTUZA®. Do not stop taking SYMTUZA®. Your HBV infection may get worse (flare-up) and symptoms worsen if you stop taking SYMTUZA® (see “**Serious Warnings and Precautions**” box and “**Serious side effects and what to do about them**” table). Worsening of hepatitis may be life-threatening for patients with advanced liver disease or cirrhosis.
- Have a history of pancreatitis (swelling of the pancreas). See the “**Serious side effects and what to do about them**” table for symptoms.
- Have kidney problems. Kidney problems, including kidney failure, have occurred. Your kidney problems could get worse if you take SYMTUZA® with some medicines such as non-steroidal anti-inflammatory drugs.
- Have a history of bone fracture, bone loss or osteoporosis.
- Have diabetes. In general, anti-HIV medicines, such as SYMTUZA®, might increase sugar levels in the blood. Some patients have diabetes before starting treatment with SYMTUZA®, which gets worse. Some patients get diabetes during treatment with SYMTUZA®. Some patients will need changes in their diabetes medicine. Some patients may need new diabetes medicine. See “**Serious side effects and what to do about them**” table.
- Have hemophilia. SYMTUZA®, might increase the risk of bleeding.
- Are allergic to sulfa medicines.
- Notice any symptoms of infection. Tell your doctor right away if you have high fever, joint or muscle pain, redness, rash, swelling, or fatigue.

Other warnings you should know about:

If you are pregnant or plan to become pregnant:

It is not known if SYMTUZA[®] can harm your unborn child. Talk to your doctor. You should not take SYMTUZA[®] during pregnancy.

Pregnancy Registry: There is a pregnancy registry for women who take antiviral medicines during pregnancy. This registry collects information about your health and your baby's health. If you become pregnant while taking SYMTUZA[®], talk with your doctor about taking part in this registry.

If you are breast-feeding or plan to breast-feed:

Do not breast-feed if you have HIV because of the chance of passing the HIV virus to your baby. Do not breast-feed if you take SYMTUZA[®]. One of the ingredients of SYMTUZA[®], emtricitabine, can be passed to your baby in your breast milk and may cause harm to your baby. It is not known if the other components can be passed to your baby in breast milk. If you are a woman who has or will have a baby, talk with your doctor about the best way to feed your baby.

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 SYMTUZA[®]:

Drugs that must not be taken with SYMTUZA[®] (contraindicated)

Type of Drug	Examples of Generic Names (Brand Names)
Alpha1-Adrenoreceptor Antagonists (to treat enlarged prostate)	alfuzosin
Antiarrhythmics/Antianginals (to treat abnormal heart rhythms)	amiodarone (CORDARONE), dronedarone (MULTAQ), ivabradine (LANCORA), lidocaine (when given by injection)
Anticoagulants (to prevent the clotting of red blood cells)	apixaban (ELIQUIS), rivaroxaban (XARELTO)
Anti-convulsants (to prevent seizures)	carbamazepine (TEGRETOL), phenobarbital phenytoin (DILANTIN)
Anti-gout (to treat gout and familial Mediterranean fever)	colchicine
Antimycobacterial (to treat tuberculosis)	rifampin (RIFADIN, RIFATER, RIFAMATE, ROFACT)
Ergot Derivatives (to treat migraine and headaches)	dihydroergotamine (MIGRANAL), ergonovine, ergotamine (CAFERGOT)
Hepatitis C Virus Direct-Acting Antivirals (to treat hepatitis C infection)	elbasvir/grazoprevir
Herbal products (to improve mood)	St. John's Wort (<i>HYPERICUM PERFORATUM</i>)
Drugs used to lower cholesterol	lovastatin (MEVACOR), simvastatin (ZOCOR), lomitapide (JUXTAPID)
Inhaled Beta-Agonists (to treat asthma and/or chronic obstructive pulmonary disease)	salmeterol (ADV AIR)
Neuroleptics (to treat psychiatric conditions)	lurasidone, pimozide (ORAP)
PDE-5 Inhibitor (to treat pulmonary arterial hypertension)	sildenafil (REVATIO)

Type of Drug	Examples of Generic Names (Brand Names)
Platelet Aggregation Inhibitor (to prevent blood clots)	ticagrelor (BRILINTA)
Sedatives/Hypnotics (to treat trouble with sleeping and/or anxiety)	triazolam (HALCION)
Opioid antagonist (to treat opioid-induced constipation)	naloxegol (MOVANTIK)

Drugs that should not be taken with SYMTUZA®:

- Any other medicines to treat HIV-1 infection.
- Any other medicines that contain protease inhibitors (PREZISTA®, PREZCOBIX®, REYATAZ, CRIVAN, INVIRASE, KALETRA).
- Any other medicines that contain tenofovir (GENVOYA, ATRIPLA, COMPLERA, ODEFSY, STRIBILD, TRUVADA, VEMLIDY, VIREAD).
- Any other medicines that contain emtricitabine or lamivudine (ATRIPLA, COMPLERA, EMTRIVA, GENVOYA, ODEFSY, STRIBILD, TRUVADA; 3TC, COMBIVIR, HEPTOVIR, KIVEXA, TRIUMEQ, TRIZIVIR).
- Any other medicines containing ritonavir or cobicistat (NORVIR, KALETRA, HOLKIRA PAK, PREZCOBIX®, TYBOST, STRIBILD).
- adefovir (HEPSERA).
- medications that may affect your kidneys and have not been discussed with your doctor.

Drugs that interact with SYMTUZA® and where the dose of SYMTUZA® or the dose of the other drug should be changed or more instruction from your doctor is needed:

- Tell your doctor if you are taking hormonal contraceptives. SYMTUZA® might reduce the effectiveness of this type of birth control and/or increase their side effects. Additional or other methods of non-hormonal birth control, such as a condom, are recommended.
- Tell your doctor if you are taking any of the following medicines.

Type of Drug	Examples of Generic Names (Brand Names)
Antiarrhythmics/Antianginals (for the heart)	digoxin, disopyramide, flecainide, mexiletine, propafenone
Anticancer Agents (to treat cancer)	dasatinib (SPRYCEL), nilotinib (TASIGNA), vinblastine, vincristine, everolimus (AFINITOR), irinotecan
Anticoagulants (to prevent the clotting of red blood cells)	dabigatran etexilate (PRADAXA), edoxaban (LIXIANA), warfarin (COUMADIN)
Anticonvulsants (to treat epilepsy and prevent seizures)	clonazepam (CLONAPAM), ethosuximide (ZARONTIN), oxcarbazepine (TRILEPTAL)
Antidepressants (to treat depression, anxiety, or panic disorder)	amitriptyline, desipramine, imipramine, nortriptyline, paroxetine (PAXIL), sertraline (ZOLOFT), trazodone (OLEPTRO)
Anti-infectives (to treat bacterial infections)	clarithromycin (BIAXIN), erythromycin (ERYC)
Antifungals (to treat fungal infections)	fluconazole (DIFLUCAN), ketoconazole (NIZORAL®), itraconazole (SPORANOX®), isavuconazole, posaconazole (POSANOL), voriconazole (VFEND)
Anti-gout (to treat gout and familial Mediterranean fever)	colchicine
Antimycobacterials (to treat bacterial infections)	rifabutin (MYCOBUTIN)

Type of Drug	Examples of Generic Names (Brand Names)
Antiplatelets (to prevent the clotting of red blood cells)	clopidogrel (PLAVIX)
Beta-Blockers (to treat heart disease)	carvedilol, metoprolol (BETALOC, LOPRESOR), timolol
Calcium Channel Blockers (to treat heart disease)	amlodipine (CADUET, TWYNSTA), diltiazem (CARDIZEM, TIAZAC) felodipine, nifedipine (ADALAT), verapamil (ISOPTIN, VERELAN)
Corticosteroids (to treat inflammation or asthma)	bethamethasone, budesonide (PULMICORT, RHINOCORT, SYMBICORT), dexamethasone, fluticasone propionate (ADVAIR DISKUS, CUTIVATE, FLONASE, FLOVENT DISKUS), mometasone, prednisone (WINPRED), triamcinolone
Endothelin Receptor Antagonists (to treat pulmonary arterial hypertension)	bosentan (TRACLEER®)
Hormonal Contraceptives	ethinyl estradiol, norethindrone, norgestimate, drospirenone
Eugeroics	modafinil
Hepatitis C Virus direct-acting antivirals (to treat Hepatitis C Virus [HCV])	glecaprevir/pibrentasvir (MAVIRET)
HMG-CoA Reductase Inhibitors (to lower cholesterol levels)	atorvastatin (LIPITOR), pravastatin (PRAVACHOL), rosuvastatin (CRESTOR)
Immunosuppressants (to prevent organ transplant rejection)	cyclosporine (SANDIMMUNE, NEORAL), tacrolimus (PROGRAF), sirolimus (RAPAMUNE), everolimus (AFINITOR)
Narcotic Analgesics (to treat opioid dependence)	buprenorphine/naloxone (SUBOXONE), fentanyl (ABSTRAL, DURAGESIC®), methadone, meperidine, oxycodone tramadol (DURELA, RALIVIA, TRAMACET®, TRIDURAL, ULTRAM®, ZYTRAM XL)
Neuroleptics (to treat psychotic disorders)	perphenazine, risperidone (RISPERDAL®, RISPERDAL CONSTA®), quetiapine (SEROQUEL)
PDE-5 Inhibitors (to treat erectile dysfunction)	sildenafil (VIAGRA), vardenafil (LEVITRA), tadalafil (CIALIS)
Sedatives/Hypnotics (to treat trouble with sleeping and/or anxiety)	bupirone, clorazepate, diazepam (DIAZEMULS, VALIUM), midazolam (taken by injection), flurazepam (DALMANE, SOM-PAM), zolpidem
Antiemetics (to manage symptoms of upper gastrointestinal motility disorders)	domperidone
Urinary antispasmodics (to treat overactive bladder)	fesoterodine solifenacin

This is not a complete list of medicines that you should tell your doctor that you are taking. You can ask your doctor or pharmacist for a list of medicines that can interact with SYMTUZA®. Do not start any new medicines while you are taking SYMTUZA® without first talking with your doctor or pharmacist.

How to take SYMTUZA®:

Always use SYMTUZA® exactly as your doctor has told you. You must check with your doctor or pharmacist if you are not sure.

You should always take SYMTUZA® with food. The type of food is not important.

SYMTUZA[®] cannot work properly without food. Take SYMTUZA[®] within 30 minutes of eating.

Swallow SYMTUZA[®] tablets whole without breaking or crushing. Swallow the tablet with a drink such as water, milk, or a nutritional drink. If you have trouble swallowing SYMTUZA[®], tell your doctor or pharmacist. Your doctor will determine whether SYMTUZA[®] or its individual components are right for you.

Take SYMTUZA[®] at about the same time each day, every day. Talk to your doctor if you need help with making a schedule that works for you.

Do not stop using SYMTUZA[®] without talking to your doctor first.

Even when you feel better.

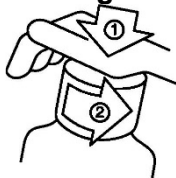
If you have both HIV infection and hepatitis B, it is very important not to stop taking SYMTUZA[®] without talking to your doctor first (see “**Serious Warnings and Precautions**”).

Do not run out of SYMTUZA[®]. Refill your prescription or talk to your doctor before your SYMTUZA[®] is all gone. This is very important because the amount of virus may start to increase if the medicine is stopped for even a short time.

Usual dose:

The dose of SYMTUZA[®] is 1 tablet once a day for adults and adolescents 12 years of age and older, who weigh at least 40 kg.

Removing the child resistant cap



The plastic bottle comes with a child resistant cap and should be opened as follows:

- Push the plastic screw cap down while turning it counter clockwise.
- Remove the unscrewed cap.

Overdose:

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

Missed Dose:

It is important that you do not miss any doses. If you forget to take SYMTUZA[®].

- If you notice **within 12 hours** of the time you usually take SYMTUZA[®], take the tablet immediately, with food. Then take the next dose at your usual time.
- If you notice **after 12 hours, do NOT take the missed dose.** Wait to take the next dose with food at your usual time.
- **Do NOT take a double dose (two doses together).**
- Call your doctor or pharmacist if you are not sure what to do.

Do not take more or less than your prescribed dose of SYMTUZA[®] at any one time

What are possible side effects from using SYMTUZA[®]?

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

The most common side effects with SYMTUZA® include:

- Diarrhea, rash, tiredness (fatigue), swelling of the belly (abdominal distension), feeling sick (nausea), muscle aches (myalgia).

Some side effects are typical for anti-HIV medicines in the same family as SYMTUZA®. These are:

- High blood sugar (hyperglycemia) and diabetes.
- Increases in triglycerides and cholesterol (forms of fat that are found in your blood).
- Changes in your immune system (Immune Reconstitution Inflammatory Syndrome) can happen when you start taking HIV medicines. Sometimes symptoms can be severe, so if you develop high temperature (fever), joint or muscle pain, redness, rash, swelling, abdominal pain, yellowing of the skin and eyes, or fatigue or any new symptoms contact your doctor straight away.
- Bone problems including bone pain, softening or thinning (which may lead to fractures).
- Kidney problems.

Tell your doctor promptly about these or any other unusual symptoms. If the condition persists or worsens, seek medical attention.

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	
<u>UNCOMMON</u> <u>Severe and sometimes life-threatening rash</u> (blisters, peeling skin) which may be accompanied by <ul style="list-style-type: none"> - fever - fatigue - swelling of the face or lymph glands - muscle aches and pain - liver problems 			✓
<u>Liver problems</u> with symptoms such as <ul style="list-style-type: none"> - yellowing of the skin or whites of the eyes - dark (tea coloured) urine - pale coloured stools (bowel movements) - nausea - vomiting - loss of appetite - pain, aching, or - sensitivity on right side below ribs 		✓	
<u>Diabetes</u> with symptoms such as <ul style="list-style-type: none"> - excessive thirst - excessive urination - excessive eating - unexplained weight loss - poor wound healing 		✓	

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	
- infections			
<u>Inflammation of the pancreas</u> with symptoms such as - abdominal pain - nausea and - vomiting		✓	
RARE <u>Lactic acidosis</u> with symptoms such as - feeling very weak or tired, unusual muscle pain - stomach pain with nausea and vomiting - feeling unusually cold especially in arms and legs - feeling dizzy or lightheaded - fast or irregular heartbeat - fast and deep breathing		✓	
VERY RARE Hepatotoxicity (severe liver problems) with hepatomegaly (liver enlargement) and steatosis (fat in the liver) with symptoms such as - jaundice (skin or the white part of eyes turn yellow) - urine turns dark - bowel movements (stools) turn light in color - loss of appetite for several days or longer - feeling sick to your stomach (nausea) - lower stomach pain		✓	
VERY RARE Flare-ups of hepatitis B virus infection following drug discontinuation with symptoms such as - jaundice (skin or the white part of eyes turn yellow) - urine turns dark - bowel movements (stools) turn light in color - loss of appetite for several days or longer - feeling sick to your stomach (nausea) - lower stomach pain		✓	

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

Storage:

Store SYMTUZA® in the original package with desiccant inside the bottle in order to protect the tablets from moisture. Keep the bottle tightly closed. Store between 15 - 30°C.

Keep out of reach and sight of children.

If you want more information about SYMTUZA®:

- Talk to your healthcare professional
- For questions or concerns, contact the manufacturer, Janssen Inc. (www.janssen.com/canada)
- 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.janssen.com/canada, or by contacting the manufacturer at: 1-800-567-3331 or 1-800-387-8781.

This information is also available on the Health Canada Drug and Health Product Register at: <https://hpr-rps.hres.ca>

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