

PART III: CONSUMER INFORMATION

Pr SUSTIVA[®]
(efavirenz, USP)

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

ABOUT THIS MEDICATION

What is SUSTIVA?

- SUSTIVA is the brand name for the active ingredient efavirenz.
- SUSTIVA belongs to a class of anti-HIV medicines known as "non-nucleoside reverse transcriptase inhibitors" (NNRTIs or non-nukes).

What the medication is used for:

- Your doctor has prescribed SUSTIVA for you because you have been infected with HIV. SUSTIVA must always be taken in combination with other anti-HIV medicines (frequently referred to as "combination therapy").
- When taken with other anti-HIV medicines, SUSTIVA has been shown to reduce viral load and increase the number of CD4 cells (a type of immune cell in blood). SUSTIVA may not have these effects in every patient.

Does SUSTIVA cure HIV or AIDS?

- SUSTIVA is not a cure for HIV nor Acquired Immunodeficiency Syndrome (AIDS). People taking SUSTIVA may still develop infections or other illnesses associated with HIV.
- It is very important that you remain under the constant care of your doctor while taking SUSTIVA.

Does SUSTIVA reduce the risk of passing HIV to others?

- SUSTIVA has not been shown to reduce the risk of passing HIV to others through sexual contact or blood contamination. It is important to continue to practice safe sex and not use or share dirty needles.

What it does:

- SUSTIVA fights Human Immunodeficiency Virus (HIV) infection by reducing the amount of virus in the blood (called "viral load").

When it should not be used:

- Do not take SUSTIVA if you know you are allergic to any of the ingredients in the SUSTIVA capsules (see **What the nonmedicinal ingredients are**).
- SUSTIVA should not be taken with some other medicines that are listed in this pamphlet (see the section entitled “**Drugs that may interact with SUSTIVA**”).

What the medicinal ingredient is:

Efavirenz

What the nonmedicinal ingredients are:

- SUSTIVA capsules also contain the following other inactive ingredients: sodium starch glycolate, lactose monohydrate, sodium lauryl sulfate and magnesium stearate. The capsule shell contains as excipients: gelatin, sodium lauryl sulfate, titanium dioxide and/or yellow iron oxide and may contain silicon dioxide. The capsules are printed with ink containing carmine, FD&C Blue No. 2 and titanium dioxide.

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What dosage forms it comes in:

- Each SUSTIVA capsule contains either 50 mg or 200 mg of efavirenz.

WARNINGS AND PRECAUTIONS

BEFORE TAKING SUSTIVA

What should I tell my doctor before I start SUSTIVA?

- Inform your doctor about any past or present medical problems, including liver disease, hepatitis, allergies, severe kidney failure, seizures or mental illness.
- Inform your doctor if you have ever had a previous life-threatening skin reaction (e.g., Stevens-Johnson syndrome).
- Inform your doctor about any medications (prescription and nonprescription), herbal products, vitamins, nutritional supplements that you are currently taking or are planning to take.
- Also inform your doctor about any recreational (street, illicit) drugs that you are currently taking or are planning to take. The effect of combining recreational (street, illicit) drugs or alcohol with SUSTIVA has not been studied. Because they may interact with each other, speak with your doctor or other healthcare provider before you

combine these drugs.

- Inform your doctor if you have or have had a heart rhythm disorder such as an irregular heartbeat, prolongation of the QT interval or any risk factors for Torsade de Pointes (dangerous fluttering of the heart).

What should I consider concerning contraception, pregnancy, or breastfeeding?

- Tell your doctor if you are pregnant or planning to become pregnant. Birth defects have been reported in the offsprings of animals and women treated with SUSTIVA during pregnancy. It is not known whether SUSTIVA caused these defects. Women should not become pregnant while taking SUSTIVA and for 12 weeks after stopping it. If you are pregnant, you should take SUSTIVA only if you and your doctor decide that the possible benefit to you is greater than the possible risk to your foetus. If you take SUSTIVA while you are pregnant, talk to your doctor about how you can be included in the antiretroviral pregnancy registry.
- It is currently recommended that women living with HIV should not breastfeed because HIV infection can be passed on the baby in breast milk. If you are breastfeeding or thinking about breastfeeding you **should discuss it with your doctor as soon as possible**.
- A reliable form of barrier contraception must always be used even if you or your partner are using other methods of contraception such as the pill or other hormonal therapy (e.g., implants, injections). SUSTIVA may remain in your blood for a time after therapy is stopped. Therefore, you should continue use of a reliable form of contraception for 12 weeks after stopping treatment with SUSTIVA.

Can children take SUSTIVA?

- SUSTIVA has not been studied in children below 3 years of age.
- SUSTIVA can be taken by children 3 years or older and who are able to swallow capsules. Your child's doctor will determine the right dose based on your child's weight.

Do not drive or operate machinery until you have determined your response to SUSTIVA, as this may make you sleepy or dizzy.

SUSTIVA can cause abnormal blood test results. Your doctor may perform blood tests and will interpret the results.

To find out how to take SUSTIVA please read carefully the following section “**WHILE TAKING SUSTIVA**”.

INTERACTIONS WITH THIS MEDICATION

Drugs that may interact with SUSTIVA

SUSTIVA may affect the dosing of other medications including ones for treating HIV infection. For this reason it is very important to:

- Let all healthcare providers know that you are taking SUSTIVA.
- Inform your doctor and pharmacist about all medications that you are currently taking including those obtained over-the-counter without a prescription and complementary medications (vitamins, nutritional supplements, etc.) and herbal products, particularly St. John’s Wort.
- Consult your doctor or pharmacist before you start any new medication.
- Consult your doctor or pharmacist before you stop any medications that you are currently taking.

Bring all your medications when you see your doctor. Or make a list of their names, how much you take, and how often you take them. This will give your doctor a complete picture of the medications you are taking. Then he or she can decide the best approach for your situation.

You must not take the following medications if you are taking SUSTIVA. Taking these medications with SUSTIVA could create the potential for serious and/or life-threatening side effects:

- CISAPRIDE****
- MIDAZOLAM**
- TRIAZOLAM (e.g, HALCION*)**
- ERGOT MEDICATIONS (e.g, CAFERGOT*)**
- PIMOZIDE (e.g, ORAP*)**
- ZEPATIER**

ST. JOHN’S WORT (*Hypericum perforatum*)

You must not take products containing St. John’s wort (*Hypericum perforatum*) with SUSTIVA as this may stop SUSTIVA from working properly and may lead to resistance to SUSTIVA or resistance to the class of non-nucleoside reverse transcriptase inhibitors (NNRTIs).

* CISAPRIDE is not marketed in Canada

The following drugs may interact with SUSTIVA and your doctor will determine whether they can be used or not or may make dosage changes for SUSTIVA or the other product, or substitute other products, as indicated below:

- SUSTIVA may be taken with many of the medications commonly used in people with HIV

infection. These include the protease inhibitors, such as nelfinavir (Viracept*) and indinavir (Crixivan*), and nucleoside analogue reverse transcriptase inhibitors (NRTIs).

- **Use of SUSTIVA with saquinavir (Invirase*) is not recommended if you are taking saquinavir as your only protease inhibitor.**
- **VORICONAZOLE (VFEND*)** should not be taken at standard doses with SUSTIVA since it may lose its effect or increase the chance of side effects from SUSTIVA. Some doses of voriconazole can be taken at the same time as a lower dose of SUSTIVA, but your doctor will decide if this is appropriate.
- Tegretol* (carbamazepine), Sporanox* (itraconazole), Posanol* (posaconazole) and REYATAZ (atazanavir sulfate), if this is not the first time you are receiving treatment for your HIV infection, may need to be replaced with another medicine when taken with SUSTIVA.
- SUSTIVA reduces the blood levels of clarithromycin (Biaxin*) and is associated with a higher incidence of rash; your doctor may consider giving you an alternative antibiotic.
- If you are taking SUSTIVA and REYATAZ (atazanavir sulfate), you should also be taking Norvir* (ritonavir).
- Antimalarials such as atovaquone/proguanil, when taken with SUSTIVA, may reduce the amount of atovaquone/proguanil in your blood which may reduce the anti-malarial activity of these medicines. Atovaquone/proguanil should not be taken with SUSTIVA; your doctor should consider alternatives to these antimalarial medicines.
- Drugs that may interact with SUSTIVA to affect the electrical activity of your heart which include but may not be limited to macrolide antibiotics (such as clarithromycin) and antimalarials (artemether/lumefantrine).
- Use of EPCLUSA (sofosbuvir/velpatasvir), VOSEVI (sofosbuvir/ velpatasvir/voxilaprevir), and MAVIRET (glecaprevir/pibrentasvir) is not recommended when taking SUSTIVA.
- SUSTIVA may interact with etonogestrel contraceptive implants. This means your implant might not work and you could get pregnant. You should use a barrier birth control method like a condom. Talk to your healthcare professional for advice on additional birth control methods.

The following medicine should not be taken with SUSTIVA since it contains efavirenz, the active ingredient in SUSTIVA:

- ATRIPLA (efavirenz, emtricitabine, tenofovir disoproxil fumarate) unless your doctor decides a

dose adjustment is needed (e.g. with rifampin).

- Your doctor may need to adjust the dose of either SUSTIVA or the following medications when taken with SUSTIVA:
 - Crixivan* (indinavir)
 - Methadone
 - Zoloft* (sertraline)
 - Wellbutrin SR, Wellbutrin XL, or Zyban (bupropion)
 - Kaletra* (lopinavir/ritonavir) Lopinavir and ritonavir combination should not be taken once daily with SUSTIVA. Your doctor may suggest an alternate dosing regimen.
 - Celsentri* (maraviroc)
 - Mycobutin* (rifabutin)
 - The cholesterol-lowering medicines Lipitor* (atorvastatin), Pravachol* (pravastatin), and Zocor* (simvastatin)
 - Rifadin* (rifampin) or the rifampin-containing medicines Rofact* and Rifater*
 - Calcium channel blockers such as Cardizem* or Tiazac* (diltiazem), Covera HS, Isoptin SR or Tarka (verapamil), and others.
 - Immunosuppressants such as Neoral* (cyclosporin), Advagraf* or Prograf* (tacrolimus), Rapamune* or Torisel* (sirolimus)
 - Hepatitis C antiviral agents
 - Antimalarials such as Coartem*♦ and Riamet*♦ (artemether/lumefantrine) *Anthelmintics* such as Biltricide* (praziquantel). Your doctor may have to consider increasing the dose of praziquantel.

♦ Not marketed in Canada

- The effect of combining alcohol or recreational (street, illicit) drugs with SUSTIVA has not been studied. Because they may interact with each other, speak with your doctor or other healthcare provider before you combine these drugs.

PROPER USE OF THIS MEDICATION

WHILE TAKING SUSTIVA

Usual Dose

- The dose of SUSTIVA for adults and children weighing more than 40 kg (88 lbs) is 600 mg once-a-day (three 200 mg capsules taken together).
- The dose for children weighing 40 kg or less is determined by the weight of the child and is taken once daily. SUSTIVA capsules should only be administered to children if they have the ability to

- reliably swallow capsules.
- You should take SUSTIVA on an empty stomach, preferably at bedtime. Taking SUSTIVA with food increases the level of efavirenz in the blood and may increase the possibility of side effects.
- Your doctor or pharmacist will give you instructions for proper dosage.

What should I remember to do or avoid while taking SUSTIVA?

- Swallow SUSTIVA with water.
- Do not chew the capsules.
- Taking SUSTIVA at bedtime may improve the tolerability of the nervous system side effects.
- It is important to take SUSTIVA as your doctor prescribes. Do not change the dose on your own.
- SUSTIVA should not be used alone to treat HIV. SUSTIVA should always be taken with other anti-HIV medications in order to prevent the virus from becoming resistant to your drug treatment.
- You should not stop taking SUSTIVA without first consulting with your doctor.
- If you are unsure of what to do or need help in planning the best times to take your medications, ask your doctor or other healthcare provider.
- If you think it would be useful, ask a friend or family member to remind you to take your medications.
- When your SUSTIVA supply starts to run low, get more from your doctor or pharmacist. This is very important because the amount of virus may start to increase if SUSTIVA is stopped for even a short time. The virus may then become harder to treat.
- Remember, SUSTIVA has been prescribed just for you. Never give your medications to others to try.
- Do not use your current supply of SUSTIVA after the end of the month and year shown by the “expiry date” on the bottle.

Overdose:

In case of drug overdosage, contact a healthcare practitioner (e.g., doctor), hospital emergency department or regional poison control centre, even if there are no symptoms.

Missed Dose:

- If you forget to take SUSTIVA, **do not double your next dose**. Take the missed dose as soon as possible, and then carry on with your regular dosing schedule.
- Try not to miss a dose. With anti-HIV

medications, missing doses or not taking them properly may allow the amount of HIV in your body to increase. HIV may then become resistant. This means that the virus changes or mutates causing a medication to lose its effect.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

- SUSTIVA, like all medications, affects different people in different ways. Any medication may have unintended or unwanted effects, so-called side effects. Some people may develop side effects, others may not.
- The most notable side effects of SUSTIVA are rash and nervous system symptoms that include dizziness, insomnia (difficulty falling asleep), drowsiness, reduced ability to concentrate, and abnormal dreaming. These side effects are generally mild to moderate and tend to disappear after you have taken SUSTIVA for a few weeks. Decreasing the dose does not seem to help and is not recommended.
- Some of these side effects such as dizziness will likely be less noticeable if you take SUSTIVA before going to bed. Be sure to tell your doctor if any of these side effects continue or if they bother you.
- A small number of patients have had severe depression, strange thoughts, or angry behavior. Some patients have had thoughts of suicide and a few patients have actually committed suicide. These problems tend to occur more often in patients with a history of mental illness. You should contact your doctor immediately if you think you are having these symptoms, so your doctor can decide whether you should continue to take SUSTIVA.
- Dizziness, trouble concentrating, and drowsiness have been reported with SUSTIVA. If you notice any of these symptoms, you should avoid potentially hazardous tasks such as driving or operating machinery.
- You should consult your doctor if you have a rash since some rashes may be serious. However, most cases of rash disappear without any change in your treatment.
- Rash seems to be more common in children than in adults treated with SUSTIVA.
- Some patients taking SUSTIVA have experienced serious liver problems including liver failure resulting in transplantation or death. Most of these serious side effects occurred in patients with a chronic liver disease such as a hepatitis infection, but there have also been a few reports

- in patients without any existing liver disease.
- Changes in your immune system (Immune Reconstitution Inflammatory Syndrome) can happen when you start taking medicines. Your immune system may get stronger and begin to fight infections that have been hidden in your body for a long time. Autoimmune disease (when the immune system attacks healthy body tissue) may also occur after you start taking medicines for HIV infection. Examples of this include the following conditions: Grave's disease, Guillain-Barre syndrome, polymyositis or autoimmune hepatitis]. Autoimmune disorders may occur many months after the start of treatment. Look for any symptoms such as:
 - fever, redness, rash or swelling
 - fatigue
 - joint or muscle pain
 - numbness or weakness beginning in the hands and feet and moving up towards the trunk of the body
 - palpitations (chest pain) or rapid heart rate
 - bulging eyes, light sensitivity, or vision changes
 - yellowing of the skin
 - difficulty talking, chewing, or swallowing

If you notice any of these symptoms, tell your doctor immediately.

Other side effects

- Other common side effects that have been reported include tiredness, nausea, diarrhea and headache. These may be from SUSTIVA or from other medications that you are taking.
- Tell your doctor or other healthcare provider if you notice these or any other side effects not mentioned in the pamphlet that continue or if they bother you.

Remember do not stop taking SUSTIVA without speaking to your doctor first. He or she may be able to help you manage these side effects without stopping your anti-HIV medications.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM				
Effect/Symptoms		Talk with your doctor or pharmacist immediately		Stop taking drug and seek medical advice immediately
		Only if severe	In all cases	
Common	Serious psychiatric events Symptoms: <ul style="list-style-type: none"> Severe depression Thoughts of suicide Strange thoughts Angry behavior. Catatonia (unable to move or speak normally) 		✓	
Uncommon	Severe skin rash Symptoms: <ul style="list-style-type: none"> Blisters or peeling of the skin Blisters or peeling of the mouth, lips and throat Fever and general ill feeling. 			✓
Rare	Liver failure Symptoms: <ul style="list-style-type: none"> 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. 		✓	

This is not a complete list of side effects. If you have any unexpected effects while taking SUSTIVA, contact your doctor or pharmacist.

HOW TO STORE IT

SUSTIVA should be stored at room temperature (25°C; although a range of 15 – 30°C is permitted).

As with all medications, SUSTIVA should be kept out of the reach and sight of children.

REPORTING SUSPECTED SIDE EFFECTS

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- Report online at www.healthcanada.gc.ca/medeffect
- Call toll-free at 1-866-234-2345
- Complete a Canada Vigilance Reporting Form and:
 - Fax toll-free to 1-866-678-6789, or
 - Mail to: Canada Vigilance Program
Health Canada
Postal Locator 0701C
Ottawa, ON K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reactions reporting guidelines are available on the MedEffect™ Canada Web site at www.healthcanada.gc.ca/medeffect.

Note: Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals can be obtained by contacting the sponsor, Bristol-Myers Squibb Canada, at:
1-866-463-6267.

This leaflet was prepared by Bristol-Myers Squibb Canada.

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