Patient package insert in accordance with the pharmacists' regulations (preparations) - 1986

This medicine is to be supplied upon physician's prescription only

Atripla®

Film-coated tablets

Composition:

Active ingredients:
Each tablet contains 600 mg of efavirenz, 200 mg of emtricitabine and 245 mg of tenofovir disoproxil (as fumarate).

Non active ingredients and allergens: see section 6: "*Additional information"*.

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you. This leaflet contains essential information about this medicine. If you have any further questions, ask your doctor or pharmacist. Keep this leaflet. You may need to read it again. This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if it seems to you that their illness issimilar to yours. If you experience any side effects, talk to your doctor or pharmacist. Even if you experience any side effects that are not listed in this leaflet (see section 4).

1. What is Atripla intended for?

Atripla can be used alone as a complete regimen, or in combination with other antiretroviral medicines to treat HIV-1 infection in adults.

Therapeutic group: Antiviral for systemic use, antivirals for treatment of HIV infections, combinations.

HIV infection destroys CD4+ T cells, which are important to the immune system. The immune system helps fight infection. After a large number of T cells are destroyed, acquired immune deficiency syndrome (AIDS) develops.

Atripla helps block HIV-1 reverse transcriptase enzyme, a viral chemical in your body that is needed for HIV-1 to multiply. Atripla lowers the amount of HIV-1 in the blood (viral load). Atripla may also help to increase the number of T cells (CD4+ cells), allowing your immune system to improve. Lowering the amount of HIV-1 in the blood lowers the chance of death or infections that happen when your immune system is weak (opportunistic infections).

Atripla does not cure HIV-1 infection or AIDS and you may continue to experience illnesses associated with HIV-1 infection, including opportunistic infections. You should remain under the care of a physician when using Atripla.

Atripla has not been shown to lower your chance of passing HIV-1 to other people through sexual contact, sharing needles, or being exposed to your blood.

- Do not share needles or other injection equipment.
- Do not share personal items that can have blood or body fluids on them, like toothbrushes or razor blades.
- Do not have any kind of sex without protection. Always practice safer sex by using a latex or polyurethane condom or other barrier to reduce the chance of sexual contact with semen, vaginal secretions, or blood.

Atripla contains three active substances that are used to treat human immunodeficiency virus (HIV) infection:
- Efavirenz is a non-nucleoside reverse transcriptase inhibitor (NNRTI)
- Emtricitabine is a nucleoside reverse transcriptase inhibitor (NRTI)
- Tenofovir is a nucleotide reverse transcriptase inhibitor (NtRTI)

2. Before taking Atripla

☒ **Do not use this medicine if:**
- **you are hypersensitive (allergic)** to the active ingredients: efavirenz, emtricitabine, tenofovir disoproxil or any of the other ingredients of Atripla (listed in section 6).
-
- **you have severe liver disease.**

- **you have a heart condition, such as an abnormal electrical signal called prolongation of the QT interval that puts you at high risk for severe heart rhythm problems (Torsade de Pointes).**

- any member of your family (parents, grandparents, brothers or sisters) has died suddenly due to a heart problem or was born with heart problems.

- your doctor has told you that you have high or low levels of electrolytes such as potassium or magnesium in your blood.

- you are breast-feeding. **Women should not get pregnant during treatment with Atripla and for 12 weeks thereafter.** Your doctor may require you to take a pregnancy test to ensure you are not pregnant before starting treatment with Atripla.

- **you are currently taking** any of the following medicines (see also "Other Medicines and Atripla"):
    - **astemizole or terfenadine** (used to treat hay fever or other allergies)
    - **bepridil** (used to treat heart disease)
    - **cisapride** (used to treat heartburn)
    - **elbasvir/grazoprevir** (used to treat hepatitis C)
    - **ergot alkaloids** (for example, ergotamine, dihydroergotamine, ergonovine, and methylergonovine) (used to treat migraines and cluster headaches)
    - **midazolam or triazolam** (used to help you sleep)
    - **pimozide, imipramine, amitriptyline or clomipramine** (used to treat certain mental conditions)
    - **St. John's wort** (*Hypericum perforatum*) (a herbal remedy used for depression and anxiety)
    - **voriconazole** (used to treat fungal infections)
    - **flecainide, metoprolol** (used to treat irregular heart beat)
    - **certain antibiotics** (macrolides, fluoroquinolones, imidazole)
    - **triazole antifungal agents**
    - **certain antimalarial agents**
    - **methadone** (used to treat opiate addiction)

→**If you are taking any of these medicines, tell your doctor immediately.** Taking these medicines with Atripla could cause serious or life-threatening side effects or stop these medicines from working properly.

Special warnings relating to the use of this medicine
Talk to your doctor or pharmacist before taking Atripla.

- **You can still pass on HIV** when taking this medicine, although the risk lowered by effective antiretroviral therapy. Discuss with your doctor the precautions needed to avoid infecting other people. This medicine is not a cure for HIV infection. While taking Atripla you may still develop infections or other illnesses associated with HIV infection.

- You must remain under the care of your doctor while taking Atripla.

- **Before starting the treatment with Atripla, tell your physician if:**
  - **You are taking other medicines** that contain efavirenz, emtricitabine, tenofovir disoproxil, tenofovir alafenamide, or lamivudine or adefovir dipivoxil. Atripla should not be taken with any of these medicines.

  - **You have or have had kidney disease,** or if tests have shown problems with your kidneys. Atripla is not recommended if you have moderate to severe kidney disease. (See also section 2, "*Tests and Follow-up*").

    Atripla may affect your kidneys. Before starting treatment, your doctor may order blood tests to assess kidney function. Your doctor may also order blood tests during treatment to monitor your kidneys.

    Atripla is not usually taken with other medicines that can damage your kidneys (see section 2, "*Other Medicines and Atripla*"). If this is unavoidable, your doctor will monitor your kidney function once a week.

  - **If you have a heart disorder, such as abnormal electrical signal called prolongation of the QT interval.**

  - **You have a history of mental illness**, including depression, or of substance or alcohol abuse. Tell your doctor immediately if you feel depressed, have suicidal thoughts or have strange thoughts (see section 4, "*Side Effects*").

  - **You have a history of convulsions (fits or seizures)** or if you are being treated with anticonvulsant therapy such as carbamazepine, phenobarbital and phenytoin. If you are taking any of these medicines, your doctor may need to check the level of anticonvulsant medicine in your blood to ensure that it is not affected while taking Atripla. Your doctor may give you a different anticonvulsant.

  - **You have a history of liver disease, including chronic active hepatitis**. Patients with liver disease including chronic hepatitis B or C, who are treated with combination antiretrovirals, have a higher risk of severe and potentially life threatening liver problems. Your doctor may conduct blood tests in order to check how well your liver is working or may switch you to another medicine. **If you have severe liver disease, do not take Atripla**. (See also section 2, "*Tests and Follow-up*").

    If you have hepatitis B infection, your doctor will carefully consider the best treatment regimen for you. Tenofovir disoproxil and emtricitabine, two of the active substances in Atripla, show some activity against hepatitis B virus although emtricitabine is not approved for the treatment of hepatitis B infection. Symptoms of your hepatitis may become worse after discontinuation of Atripla. Your doctor may then conduct blood tests at regular intervals in order to check how well your liver is working. (See also section 2, "*Tests and Follow-up*").

  - Independent of a history of liver disease, your doctor will consider regular blood tests to check how your liver is working.

  - **If you are over 65.** Insufficient numbers of patients over 65 years of age have been studied. If you are over 65 years of age and are prescribed Atripla, your doctor will monitor you carefully.

- **Once you start taking Atripla, look out for**:

  - **Signs of dizziness, difficulty sleeping, drowsiness, difficulty concentrating or abnormal dreaming.** These side effects may start in the first 1 or 2 days of treatment and usually go away after the first 2 to 4 weeks.

  - **Any signs of skin rash.** Rashes may be caused by Atripla. If you see any signs of a severe rash with blistering or fever, stop taking Atripla and tell your doctor at once. If you had a rash while taking another NNRTI, you may be at higher risk of getting a rash with Atripla.

  - **Any signs of inflammation or infection.** In some patients with advanced HIV infection (AIDS) and a history of opportunistic infection, signs and symptoms of inflammation from previous infections may occur soon after anti HIV treatment is started. It is believed that these symptoms are due to improvement in the body's immune response, enabling the body to fight infections that may have been present with no obvious symptoms. If you notice any symptoms of infection, please tell your doctor at once.

    In addition to the opportunistic infections, autoimmune disorders (a condition that occurs when the immune system attacks healthy body tissue) may also occur after you start taking medicines for the treatment of your HIV infection. Autoimmune disorders may occur many months after the start of treatment. If you notice any symptoms of infection or other symptoms such as muscle weakness, weakness beginning in the hands and feet and moving up towards the trunk of the body, palpitations, tremor or hyperactivity, please inform your doctor immediately to seek necessary treatment.

  - **Bone problems**. Some patients taking combination antiretroviral therapy may develop a bone disease called osteonecrosis (death of bone tissue caused by loss of blood supply to the bone). The length of combination antiretroviral therapy, corticosteroid use, alcohol consumption, severe immunosuppression, higher body mass index, among others, may be some of the many risk factors for developing this disease. Signs of osteonecrosis are joint stiffness, aches and pains (especially of the hip, knee and shoulder) and difficulty in movement. If you notice any of these symptoms please inform your doctor.

    Bone problems (manifesting as persistent or worsening bone pain and sometimes resulting in fractures) may also occur due to damage to kidney tubule cells (see section 4, "Side Effects"). Tell your doctor if you have bone pain or fractures.

  - Tenofovir disoproxil (a component of Atripla) may also cause loss of bone mass. Overall, the effects of tenofovir disoproxil on long-term bone health and future fracture risk in adult patients are uncertain. Tell your doctor if you know you suffer from osteoporosis. Patients with osteoporosis are at a higher risk of fractures.

Children and adolescents

This medicine is not intended for children and adolescents under 18 years of age.
There is no information on the safety and efficacy of this medicine in children and adolescents under 18 years of age.

Tests and Follow-up:

- Atripla may affect your kidneys. Before starting treatment, your doctor may order blood tests to assess kidney function. Your doctor may also order blood tests during treatment to monitor your kidneys. Atripla is not usually taken with other medicines that can damage your kidneys (see section 2, "*Before using Atripla*"). If this is unavoidable, your doctor will monitor your kidney function once a week.

- Patients with liver disease including chronic hepatitis B or C, who are treated with combination

antiretrovirals, have a higher risk of severe and potentially life threatening liver problems. Your doctor may conduct blood tests in order to check how well your liver is working or may switch you to another medicine. If you have severe liver disease, do not take Atripla (see section 2, "*Before using Atripla*").

- If you have hepatitis B infection, your doctor will carefully consider the best treatment regimen for you. Tenofovir disoproxil and emtricitabine, two of the active substances in Atripla, show some activity against hepatitis B virus although emtricitabine is not approved for the treatment of hepatitis B infection. Symptoms of your hepatitis may become worse after discontinuation of Atripla. Your doctor may then conduct blood tests at regular intervals in order to check how well your liver is working (see also section 3, "*If you stop taking Atripla*").

- Independent of a history of liver disease, your doctor will consider regular blood tests to check how your liver is working.

Other medicines and Atripla

You must not take Atripla with certain medicines. These are listed under *Do not use this medicine if*, at the start of section 2. They include some common medicines and some herbal preparations (including St. John's wort) which can cause serious interactions.

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines, including medicines obtained without a prescription, vitamins, herbal remedies or dietary supplements.

Also, Atripla should not be taken with any other medicines that contain efavirenz (unless recommended by your doctor), emtricitabine, tenofovir disoproxil, tenofovir alafenamide, or lamivudine or adefovir dipivoxil.

Tell your doctor if you are taking other medicines which may damage your kidneys. Some examples include:
- aminoglycosides, vancomycin (medicines for bacterial infections)
- foscarnet, ganciclovir, cidofovir (medicines for viral infections)
- amphotericin B, pentamidine (medicines for fungal infections)
- interleukin-2 (to treat cancer)
- non-steroidal anti-inflammatory drugs (NSAIDs, to relieve bone or muscle pains)

Atripla may interact with other medicines, including herbal preparations such as Ginkgo biloba extracts. As a result, the amounts of Atripla or other medicines in your blood may be affected. This may stop your medicines from working properly, or may make any side effects worse. In some cases, your doctor may need to adjust your dose or check your blood levels.

! It is important to tell your doctor or pharmacist if you are taking any of the following:
- **Medicines containing didanosine (for HIV infection): Taking Atripla with other antiviral medicines that** contain didanosine can raise the levels of didanosine in your blood and may reduce CD4 cell counts. Inflammation of the pancreas and lactic acidosis (excess lactic acid in the blood), which sometimes caused death, have been reported rarely when medicines containing tenofovir disoproxil and didanosine were taken together. Your doctor will carefully consider whether to treat you with medicines containing tenofovir and didanosine.
- **Other medicines used for HIV infection:** The following protease inhibitors: darunavir, indinavir, lopinavir/ritonavir, ritonavir, or ritonavir boosted atazanavir or saquinavir. Your doctor may consider giving you an alternative medicine or changing the dose of the protease inhibitors. Also, tell your doctor if you are taking maraviroc.
- **Medicines used to treat infection with the hepatitis C virus:** elbasvir/grazoprevir, glecaprevir/pibrentasvir, sofosbuvir/velpatasvir, sofosbuvir/velpatasvir/voxilaprevir.

- **Medicines used to lower blood fats (also called statins):** Atorvastatin, pravastatin, simvastatin. Atripla can reduce the amount of statins in your blood. Your doctor will check your cholesterol levels and will consider changing the dose of your statin, if needed.
- **Medicines used to treat convulsions/seizures (anticonvulsants):** Carbamazepine, phenytoin, phenobarbital. Atripla can reduce the amount of the anticonvulsant in your blood. Carbamazepine can reduce the amount of efavirenz, one of the components of Atripla, in your blood. Your doctor may need to consider giving you a different anticonvulsant.
- **Medicines used to treat bacterial infections,** including tuberculosis and AIDS-related mycobacterium avium complex: Clarithromycin, rifabutin, rifampicin. Your doctor may need to consider changing your dose or giving you an alternative antibiotic. In addition, your doctor may consider giving you an additional dose of efavirenz to treat your HIV infection.
- **Medicines used to treat fungal infections (antifungals):** Itraconazole or posaconazole. Atripla can reduce the amount of itraconazole or posaconazole in your blood. Your doctor may need to consider giving you a different antifungal.
- **Medicines used to treat malaria:** Atovaquone/proguanil or artemether/lumefantrine. Atripla may reduce the amount of atovaquone/proguanil or artemether/lumefantrine in your blood.
- **Hormonal contraceptive, such as birth control pills, an injected contraceptive (for example, Depo-Provera), or a contraceptive implant (for example, Implanon):** You must also use a reliable barrier method of contraception (see *Pregnancy and breast-feeding*). Atripla may make hormonal contraceptives less likely to work. Pregnancies have occurred in women taking efavirenz, a component of Atripla, while using a contraceptive implant, although it has not been established that the efavirenz therapy caused the contraceptive to fail.
- **Sertraline**, a medicine used to treat depression, as your doctor may need to change your dose of sertraline.
- **Bupropion**, a medicine used to treat depression or to help you stop smoking, as your doctor may need to change your dose of bupropion.
- **Diltiazem or similar medicines (called calcium channel blockers):** When you start taking Atripla, your doctor may need to adjust your dose of the calcium channel blocker.
- **Medicines used to prevent organ transplant rejection (also called immunosuppressants)**, such as cyclosporine, sirolimus or tacrolimus. When you start or stop taking Atripla your doctor will closely monitor your plasma levels of the immunosuppressant and may need to adjust its dose.
- **Warfarin or acenocoumarol** (medicines used to reduce clotting of the blood): Your doctor may need to adjust your dose of warfarin or acenocoumarol.
- **Ginkgo biloba extracts** (herbal preparation).
- **Metamizole,** a medicine used to treat pain and fever**.**

For further information please speak to a doctor or pharmacist.

Using Atripla with food
You should take Atripla on an empty stomach.

Using Atripla and alcohol consumption
Taking Atripla with alcohol or with other medications causing similar side effects as Atripla, such as drowsiness, may increase those side effects.

Pregnancy and breast-feeding
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Women should not get pregnant during treatment with Atripla and for 12 weeks thereafter. Your doctor may require you to take a pregnancy test to ensure you are not pregnant before starting treatment with Atripla.

If you could get pregnant while receiving Atripla, you need to use a reliable form of barrier contraception (for example, a condom) with other methods of contraception including oral (pill) or other hormonal

contraceptives (for example, implants, injection). Efavirenz, one of the active components of Atripla, may remain in your blood for a time after therapy is stopped. Therefore, you should continue to use contraceptive measures, as above, for 12 weeks after you stop taking Atripla.

Tell your doctor immediately if you are pregnant or intend to become pregnant. If you are pregnant, you should take Atripla only if you and your doctor decide it is clearly needed.

Serious birth defects have been seen in unborn animals and in the babies of women treated with efavirenz during pregnancy.

Ask your doctor or pharmacist for advice before taking any medicine.

If you have taken Atripla during your pregnancy, your doctor may request regular blood tests and other diagnostic tests to monitor the development of your child. In children whose mothers took NRTIs during pregnancy, the benefit from the protection against HIV outweighed the risk of side effects.

Do not breast-feed during treatment with Atripla. Both HIV and the ingredients of Atripla may pass through breast milk and cause serious harm to your baby.

Driving and using machines:
Atripla may cause dizziness, impaired concentration and drowsiness. If you are affected, do not drive and do not use any tools or machines.

Important information about some of the ingredients of Atripla:
This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

3. How to take Atripla?

Always take Atripla exactly as your doctor has prescribed to you.
Check with your doctor or pharmacist if you are not sure regarding the dosage and treatment regimen.

The dosage and treatment regimen will be determined by the doctor only.

Dosage:
Never change the dose on your own. Do not stop this medicine unless your doctor tells you to stop.
The usual prescribed dose is one Atripla tablet a day. Atripla should be taken on an empty stomach (commonly defined as 1 hour before or 2 hours after a meal) preferably at bedtime. This may make some side effects (for example, dizziness, drowsiness) less troublesome. Swallow Atripla whole with water. There is no information available regarding the crushing/splitting of the product. Do not chew, crush or split the tablet.

Atripla must be taken every day.

If your doctor decides to stop one of the components of Atripla, you may be given efavirenz, emtricitabine and/or tenofovir disoproxil separately or with other medicines for the treatment of your HIV infection.
Do not exceed the recommended dose.
This medicine is to be taken at specific time intervals as determined by the attending doctor.
Do not miss a dose of Atripla.

If you have accidentally taken a higher dosage than normal:
If you accidentally take too many Atripla tablets you may be at increased risk of experiencing possible side effects with this medicine (see section 4, "*Side effects*"). Contact your physician or nearest emergency

department immediately for advice. Keep the tablet bottle with you so that you can easily describe what you have taken.

If a child has accidently swallowed some of this medicine, go immediately to a doctor or the nearest emergency department and bring the medicine packaging with you.

Do not induce vomiting unless explicitly instructed to do so by a physician!

If you forget to take the medicine

It is important not to miss a dose of Atripla.

If you so miss a dose of Atripla within 12 hours of when it is usually taken, take it as soon as you remember. Take the next dose at the specified time.

If it is almost time (less than 12 hours left) for your next dose anyway, do not take the dose you forgot to take, wait and take the next dose at the specified time. Do not take a double dose to make up for a forgotten tablet.

If you throw up the tablet (within 1 hour after taking Atripla), you should take another tablet. Do not wait until your next dose is due. You do not need to take another tablet if you were sick more than 1 hour after taking Atripla.

If you stop taking Atripla:

Don't stop taking Atripla without talking to your doctor even if you feel improvement in you general health. Stopping Atripla can seriously affect your response to future treatment. If Atripla is stopped, speak to your doctor before you restart taking Atripla tablets. Your doctor may consider giving you the components of Atripla separately if you are having problems or need your dose adjusted.

How can you contribute to the success of the treatment?
When your supply of Atripla 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 the medicine is stopped for even a short time. The virus may then become harder to treat.

If you have both HIV infection and hepatitis B, it is especially important not to stop your Atripla treatment without talking to your doctor first. Some patients have had blood tests or symptoms indicating that their hepatitis has got worse after stopping emtricitabine or tenofovir disoproxil (two of the three components of Atripla). If Atripla is stopped your doctor may recommend that you resume hepatitis B treatment. You may require blood tests to check how your liver is working for 4 months after stopping treatment. In some patients with advanced liver disease or cirrhosis, stopping treatment is not recommended as this may lead to worsening of your hepatitis, which may be life-threatening.

→ Tell your doctor immediately about new or unusual symptoms after you stop treatment, particularly symptoms you associate with hepatitis B infection.

Do not take medicines in the dark! Check the label and the dose <u>each time</u> you take your medicine. Wear glasses if you need them.

If you have any further questions on the use of this product, ask a doctor or pharmacist.

4. <u>Side effects</u>

During HIV therapy there may be an increase in weight and in levels of blood lipids and glucose. This is

partly linked to restored health and life style, and in the case of blood lipids sometimes to the HIV medicines themselves. Your doctor will test for these changes.

Like all medicines Atripla can cause side effects in some of the users.
Don't get anxious, while reading the list of side effects. You may not have any of them.

Atripla may cause the following serious side effects:
!Call your doctor immediately if you develop:

- **Lactic acidosis** (excess lactic acid in the blood) is a **rare** (may affect up to 1 in every 1,000 patients) but serious side effect that can be fatal. The following side effects may be signs of lactic acidosis:
  - deep rapid breathing
  - drowsiness
  - feeling sick (nausea), being sick (vomiting) and stomach pain.

→ **If you think you may have lactic acidosis, contact your doctor immediately.**

Other possible serious side effects
The following side effects are **uncommon** (these may affect up to 1 in every 100 patients):

- allergic reaction (hypersensitivity) that may cause severe skin reactions (Stevens-Johnson syndrome, erythema multiforme, see section 2)
- swelling of the face, lips, tongue or throat
- angry behaviour, suicidal thoughts, strange thoughts, paranoia, unable to think clearly, mood being affected, seeing or hearing things that are not really there (hallucinations), suicide attempts, personality change (psychosis), catatonia (a condition in which the patient is rendered motionless and speechless for a period).
- pain in the abdomen (stomach), caused by inflammation of the pancreas
- forgetfulness, confusion, fitting (seizures), incoherent speech, tremor (shaking)
- yellowing of the skin or eyes, itching, or pain in the abdomen (stomach) caused by inflammation of the liver
- damage to kidney tubules

Psychiatric side effects in addition to those listed above include delusions (false beliefs), neurosis. Some patients have committed suicide. These problems tend to occur more often in those who have a history of mental illness. Always notify your doctor immediately if you have these symptoms.

Side effects to the liver: If you are also infected with hepatitis B virus, you may experience a worsening of hepatitis after discontinuation of treatment (see section 3).

The following side effects are **rare** (these may affect up to 1 in every 1,000 patients):

- liver failure, in some cases leading to death or to a need for a liver transplant. Most cases occurred in patients who already had liver disease, but there have been a few reports in patients without any existing liver disease
- inflammation of the kidney, passing a lot of urine and feeling thirsty
- back pain caused by kidney problems, including kidney failure. Your doctor may do blood tests to see if your kidneys are working properly
- softening of the bones (with bone pain and sometimes resulting in fractures) which may occur due to damage to the kidney tubule cells
- fatty liver

→ **If you think that you may have any of these serious side effects, talk to your doctor.**

Most frequent side effects

The following side effects are **very common** (these may affect more than 1 in 10 patients)

- dizziness, headache, diarrhoea, feeling sick (nausea), being sick (vomiting)
- rashes (including red spots or blotches sometimes with blistering and swelling of the skin), which may be allergic reactions
- feeling weak

Tests may also show:
- decreases in phosphate levels in the blood
- increased levels of creatine kinase in the blood that may result in muscle pain and weakness

Other possible side effects

The following side effects are **common** (these may affect up to 1 in 10 patients)

- allergic reactions
- disturbances of coordination and balance
- feeling worried or depressed
- difficulty falling asleep, strange dreams, difficulty concentrating, drowsiness
- pain, stomach pain
- digestion problems causing discomfort after meals, feeling bloated, wind (flatulence)
- loss of appetite
- tiredness
- itching
- changes in skin colour including darkening of the skin in patches often starting on hands and soles of feet

Tests may also show:
- low white blood cell count (a reduced white blood cell count can make you more prone to infection)
- liver and pancreas problems
- increased fatty acids (triglycerides), bilirubin or sugar levels in the blood

The following side effects are **uncommon** (these may affect up to 1 in every 100 patients):

- breakdown of muscle, muscle pain or weakness
- anaemia (low red blood cell count)
- a feeling of spinning or tilting (vertigo), whistling, ringing or other persistent noise in the ears
- blurred vision
- chills
- breast enlargement in males
- decreased sexual drive
- flushing
- dry mouth
- increased appetite

Tests may also show:
- decreases in potassium in the blood
- increases in creatinine in the blood
- proteins in urine
- increased cholesterol in the blood

The breakdown of muscle, softening of the bones (with bone pain and sometimes resulting in fractures), muscle pain, muscle weakness and decreases in potassium or phosphate in the blood may occur due to damage to kidney tubule cells.

The following side effects are **rare** (these may affect up to 1 in every 1,000 patients):

- itchy rash to the skin caused by a reaction to sunlight

→ If a side effect has appeared, if any of the side effects worsen or if you suffer from a side effect not mentioned in the leaflet, consult the doctor.

Reporting of side effects

You can report any side effects to the Ministry of Health by clicking on the link "Report side effects due to medical treatment" that is located on the Ministry of Health homepage (www.health.gov.il) which will direct you to the online form for reporting side effects or by clicking on the link: https://sideeffects.health.gov.il. You can also report any side effects directly to the registration holder via email: DrugSafety.Israel@gilead.com.

By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store Atripla

Avoid poisoning! This medicine, and all other medicines, must be stored in a safe place out of the reach of children and/or infants, to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by a physician.

Do not use the medicine after the expiry date (exp. date) which is stated on the carton and bottle. The expiry date refers to the last day of that month.

Storage conditions:
Store Atripla in a cool dry place, at no more than 30°C.
Keep Atripla in its original container and keep the container tightly closed.
After first opening use within 6 weeks.
Even if kept in their original container and stored as recommended, medicines may be kept for a limited period only. Please note the expiry date of the medicine! In case of doubt, consult the pharmacist who dispensed the medicine to you.
Do not store different medications in the same package.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. Additional Information

In addition to the active ingredient this medicine also contains:
Inactive ingredients:
Microcrystalline cellulose (E460), croscarmellose sodium, hydroxypropylcellulose (E463), magnesium stearate (E572), sodium laurilsulfate.
The film coating contains polyvinyl alcohol, titanium dioxide (E171), macrogol 3350, talc, red iron oxide (E172) and iron oxide black (E172).

What does the product look like and what is the nature of container: the carton box contains a plastic bottle with 30 film coated tablets (with a silica gel sachet that must be kept in the bottle to help protect your

tablets). The silica gel desiccant is contained in a separate sachet and should not be swallowed. The tablets are pink, capsule-shaped, debossed with “123” on one side and plain on the other.

Registration Holder:
Gilead Sciences Israel Ltd.
4 HaHarash Street
Hod Hasharon
4524075
Israel

Manufacturer:
Gilead Sciences Ireland UC
IDA Business & Technology Park
Carrigtohill
County Cork
Ireland

Revised in September 2021 according to MoH guidelines.

The medicine’s registration numbers in the national register of medicines at the Ministry of Health: 32932, 32933

For simplicity and ease of reading, this leaflet was phrased in the masculine. Nevertheless, the medicine is intended for both sexes.

Reference: EU label from August 2021.

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