1.3.2 PATIENT INFORMATION LEAFLET

SCHEDULING STATUS

S4

PROPRIETARY NAME AND DOSAGE FORM

TRIBUSS

Film-coated tablet

Read this entire leaflet carefully before you start taking TRIBUSS.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, please ask your doctor or pharmacist. This information does not take the place of talking to your doctor or healthcare provider about your medical conditions or treatment.
- TRIBUSS has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

WHAT TRIBUSS CONTAINS

Each film-coated tablet of TRIBUSS contains 600 mg efavirenz, 300 mg tenofovir disoproxil fumarate and 200 mg emtricitabine.

The other ingredients are:

Black iron oxide (C.I. 77499), croscarmellose sodium, hydroxypropyl cellulose, lactose monohydrate, magnesium stearate, microcrystalline cellulose, polyethylene glycol, polyvinyl alcohol, red iron oxide (C.I. 77491), sodium lauryl sulphate, talc, titanium dioxide (C.I. 77891).

Contains sugar: Lactose monohydrate 120,0 mg

WHAT TRIBUSS IS USED FOR

TRIBUSS contains three medicines, combined in one tablet, that are used to treat human immunodeficiency virus (HIV) infection.

TRIBUSS can be used alone or in combination with other anti-HIV medicines to treat people with HIV infection.

TRIBUSS does not cure HIV infection or AIDS.

The long-term effects of TRIBUSS are not known at this time. People taking TRIBUSS may still get opportunistic infections or other conditions that happen with HIV infection. Opportunistic infections are infections that develop because the immune system is weak. Some of these conditions are pneumonia,

and herpes virus infections**. It is very important that you see your doctor or healthcare provider regularly while taking TRIBUSS.**

TRIBUSS does not lower your chance of passing HIV to other people through sexual contact, sharing needles, or being exposed to your blood.

- **Do not have unprotected sex**. For your health and the health of others, it is important to always practise safe sex by using a latex or polyurethane condom, or other suitable barrier, to lower the chance of sexual contact with semen, vaginal secretions, or blood.
- Never use or share dirty needles or other injection equipment.
- Do not share personal items that can have blood or body fluids on them, like toothbrushes or razor blades.

BEFORE YOU TAKE TRIBUSS

Together with your healthcare provider, you need to decide whether TRIBUSS is right for you.

Do not take TRIBUSS:

- If you are allergic to TRIBUSS (efavirenz, emtricitabine, and tenofovir disoproxil fumarate) or any of its other ingredients (see 'WHAT TRIBUSS CONTAINS', for a complete list of ingredients).
- If you have kidney problems or are undergoing kidney dialysis treatment
- If you are younger than 18 years of age, since safety and efficacy have not been established in paediatric and adolescent patients
- If you had a liver disorder or liver failure attributed to treatment with any of the medicines contained in TRIBUSS.
- If you have liver problems

- If you are pregnant or planning to become pregnant
- If you are breastfeeding your baby
- If you are currently taking any of the following medicines:
  - **bepridil** (used to treat heart disease)
  - **cisapride** (used to treat heart burn)
  - **ergot alkaloids** (used to treat migraines and cluster headaches)
  - **midazolam or triazolam** (used to help you sleep)
  - **pimozide** (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)
  - **terfenadine** (used for the treatment of allergic conditions)

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

Do not take TRIBUSS if you are already taking: lamivudine/zidovudine, lamivudine, abacavir sulphate/lamivudine, abacavir sulphate/lamivudine/zidovudine, tenofovir DF, efavirenz, emtricitabine or adefovir dipivoxil, because these medicines contain the same or similar active ingredients.

Discuss this with your treating doctor if you are unsure.

Take special care with TRIBUSS

- If you have bone problems, including previous bone breaks.
- If you have liver problems including hepatitis B virus infection.
- If you have build up of acid in the body (Lactic acidosis).

- If you have ever had mental illness or are using medicines for a mental illness.
- If you have ever had seizures or are taking medicine for seizures.
- If you are older than 65 years of age.
- If you are taking other medicines, as TRIBUSS may interact with these other medicines (see BEFORE YOU TAKE TRIBUSS).
- If you use medicines that may affect your kidney function, since use of such medicines in combination with TRIBUSS will require careful monitoring of your kidney function. Speak to your doctor about this.
- If you suffer from increased weight gain (obesity).
- If you are pregnant, TRIBUSS should be avoided. As TRIBUSS can cause harm to a baby if used in the first 12 weeks of pregnancy.
- If you develop a skin rash.
- If you have suffered from any inflammatory disorders (IRIS).
- If you have been treated for infections due to a low immune system (opportunistic infections).
- If you have autoimmune disorders, such as Graves disease.

Pregnancy and Breastfeeding

You should not use TRIBUSS if you are pregnant or breastfeeding your baby.

If you are pregnant or breastfeeding your baby while taking TRIBUSS, please consult your doctor, pharmacist or other healthcare provider for advice.

Women taking TRIBUSS should not become pregnant. Serious birth defects have been seen in the babies of women treated with efavirenz (a component of TRIBUSS) during pregnancy. Tell your healthcare provider right away if you are pregnant. (see DO NOT TAKE TRIBUSS)

- Women should not rely only on hormone-based birth control, such as pills, injections or implants, because TRIBUSS may make these contraceptives ineffective. Women must use a

reliable form of barrier contraception, such as a condom or diaphragm, even if they also use other methods of birth control.

- Do not breastfeed if you are taking TRIBUSS. It is not known whether the active ingredients of TRIBUSS are excreted in breast milk. Because of both the potential for HIV transmission and the potential for serious side effects in breastfed babies, it is recommended that mothers should not breastfeed their babies when using TRIBUSS.

Driving and using machinery

Since adverse reactions such as dizziness, impaired concentration, and/or drowsiness have been reported in patients receiving TRIBUSS, you should not drive, use machinery or perform any tasks that require concentration, until you are certain that TRIBUSS does not adversely affect your ability to do so (see POSSIBLE SIDE EFFECTS).

Important information about some of the ingredients of TRIBUSS

TRIBUSS contains LACTOSE MONOHYDRATE, which may have an effect on the control of your blood sugar if you have diabetes mellitus. Patients with the rare hereditary conditions of lactose or galactose intolerance should not take TRIBUSS.

If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking TRIBUSS.

Taking other medicines with TRIBUSS

Always tell your healthcare provider if you are taking any other medicine.

(This includes complementary or traditional medicines.)

The following medicines should not be taken with TRIBUSS:

- Other medicines that contain tenofovir DF, efavirenz, emtricitabine, or lamivudine, either alone or as combination tablets. **TRIBUSS should not be used with those medicines because they contain the same or similar active ingredients as TRIBUSS.**
- Adefovir dipivoxil for the treatment of hepatitis B infection, due to the increased risk of kidney damage if combined with TRIBUSS.
- **Medicines that contain didanosine (another antiretroviral). Tenofovir DF (a component of TRIBUSS) may increase the amount of didanosine in your blood and the risk of side effects.**
- Saquinavir, another antiretroviral.
- Atazanavir sulphate or atazanavir/ritonavir combination tablet. These medicines may increase the amount of tenofovir DF (a component of TRIBUSS) in your blood, which could result in more side effects.
- St. John's wort (*Hypericum perforatum*).
- Cisapride, midazolam, triazolam or ergot derivatives as efavirenz (a component of TRIBUSS) could prevent break down of these medicines and may cause side effects such as abnormal heart rhythm and breathing problems.
- Other medicines used for HIV infection: amprenavir, indinavir, lopinavir/ritonavir combination tablet, ritonavir, or atazanavir/ritonavir combination tablet or saquinavir.
- Medicines used to treat fungal infections (antifungals): itraconazole and ketoconazole since no dosage recommendations are available when used in combination with TRIBUSS.
- Voriconazole (used to treat fungal infections).

Please inform your doctor if you take any of the following medicines, since this may require changes in medication, dose changes or careful monitoring of blood medicine levels:

- Medicines such as cidofovir, acyclovir, valacyclovir, ganciclovir and valganciclovir. These compete for excretion by the kidney.
- Selective serotonin reuptake inhibitors (SSRIs) for the treatment of depression.
- Medicines used to lower blood fats (also called statins): atorvastatin, pravastatin, simvastatin. TRIBUSS can reduce the amount of statins in your blood.
- Medicines used to treat convulsions (seizures) (anticonvulsants): carbamazepine, phenytoin, phenobarbitone. TRIBUSS can reduce the amount of the anticonvulsant medicine in your blood. Carbamazepine can reduce the amount of efavirenz, one of the components of TRIBUSS, in your blood.
- Medicines used to treat bacterial infections, including tuberculosis and AIDS-related infections: clarithromycin, rifabutin and rifampicin.
- Immunosuppressants (used in kidney or liver transplant patients) such as tacrolimus.
- Indinavir, another antiretroviral.
- Hormonal contraceptives (e.g. the pill or contraceptive implant). Because the potential for efavirenz, a component of TRIBUSS, to interact with hormonal contraceptives has not been fully studied, a reliable method of barrier contraception (e.g. a condom) should always be used in addition to the hormonal contraceptive (see Pregnancy and breastfeeding).
- Methadone, a medicine used to treat opiate addiction.
- Sertraline, a medicine used to treat depression.
- Diltiazem or similar medicines (called calcium channel blockers).
- Ritonavir: medicine used to treat HIV (a viral infection).
- Cimetidine: medicine used to treat stomach ulcers and indigestion.

These are not all the medicines that may cause problems if you take TRIBUSS. Be sure to tell your healthcare provider about all medicines that you take.

Keep a complete list at all times of all the medicines that you take.

HOW TO TAKE TRIBUSS

Always take TRIBUSS tablets exactly as your doctor has instructed you. You should check with your doctor or pharmacist if you are unsure.

Do not share medicines prescribed for you with any other person.

The usual dose of TRIBUSS is one tablet once a day.

- You should take TRIBUSS on an empty stomach.
- Swallow the TRIBUSS tablet whole with water.
- Taking TRIBUSS at bedtime may make some side effects less bothersome such as dizziness or headaches.
- Tell your healthcare provider if you start any new medicine or change how you take old ones. Your doses may need adjustment.

If you have the impression that the effect of TRIBUSS is too strong or too weak, tell your healthcare provider.

If you take more TRIBUSS tablets than you should

In the event of an overdose, consult your healthcare provider, immediately. If neither is available, seek help at the nearest hospital or poison control centre.

If you forget to take or missed a dose of TRIBUSS

It is important that you do not miss any doses. If you miss a dose of TRIBUSS, take it as soon as possible that day and then take your next scheduled dose at its regular time.

If it is almost time for your next dose, skip the missed dose and go back to your normal dosing schedule. **Do not** take 2 doses at the same time. Contact your healthcare provider if you are not sure what to do. Do not take more than one dose of TRIBUSS in a day.

Effects when treatment with TRIBUSS is stopped

You should not stop treatment unless your healthcare provider instructs you to. When your TRIBUSS supply starts to run low, get more from your healthcare provider or pharmacy. This is very important because the amount of virus in your blood may increase if the medicine is stopped for even a short time. The virus may develop resistance to TRIBUSS and become harder to treat.

POSSIBLE SIDE EFFECTS

TRIBUSS can have side effects.

Not all side effects reported for TRIBUSS are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking TRIBUSS, please consult your healthcare provider for advice.

If any of the following happens, stop taking TRIBUSS and tell your healthcare provider immediately or go to the casualty department at your nearest hospital:

- Swelling of the hands, feet, ankles, face, lips, mouth or throat, which may cause difficulty in swallowing or breathing;
- rash or itching;
- blistering of the skin, mouth, eyes and genitals as these may be due to a serious allergic reaction known as Stevens-Johnson Syndrome (SJS).

These are all very serious side effects. If you have them, you may have had a serious allergic reaction to TRIBUSS. You may need urgent medical attention or hospitalisation.

Tell your healthcare provider immediately or go to the casualty department at your nearest hospital if you notice any of the following:

- Lactic acidosis (build-up of an acid in the blood). Lactic acidosis can be a medical emergency and may need to be treated in the hospital. Call your healthcare provider right away if you get any of the following signs of lactic acidosis:
  - You feel weak and tired
  - You have unusual muscle pain
  - You have stomach pain with nausea and vomiting
  - You feel cold, especially in your arms and legs
  - You feel dizzy and lightheaded
  - You have a fast and irregular heartbeat;
- serious liver problems (hepatotoxicity), with liver enlargement (hepatomegaly) and fat in the liver (steatosis). Call your healthcare provider right away if you get any of the following signs of liver problems:
  - Yellow discolouration of your skin and the white part of your eyeballs known as jaundice
  - Darkening of your urine
  - Your bowel movements turn lighter in colour
  - You feel sick to your stomach (nausea)
  - You have stomach pain;
- “flare-ups” of hepatitis B virus (HBV) infection, in which the disease suddenly returns in a worse way than before. Your healthcare provider will monitor your condition for several months after stopping TRIBUSS if you have both HIV and HBV infection and may recommend treatment for your HBV;

- serious psychiatric problems. A small number of patients may experience severe depression, strange thoughts, thoughts of suicide or angry behaviour while taking TRIBUSS. Contact your healthcare provider right away if you think you are having these psychiatric symptoms;
- a sudden, violent, irregular movement of the body (convulsions);
- kidney problems. Should you notice blood in your urine, have difficult or painful urination and pain in the lower back, contact your healthcare provider immediately;
- you have the feeling that your heart is beating too hard or too fast, skipping a beat, or fluttering and you heart rate increases (palpitations and tachycardia);
- you have a persistent dry cough that often gets worse at night, fever, shortness of breath, fatigue or tiredness with chest pain that gets worse when you take a deep breath or cough (pneumonia); you have difficulty catching your breath or noisy breathing with very fast, shallow breaths and cold, clammy skin , difficulty breathing (dyspnoea).

These are all serious side effects. You may need urgent medical attention.

Tell your healthcare provider if you notice any of the following:

The following side effects have been reported frequently:

- Dizziness, headache;
- vomiting, diarrhoea, winds (flatulence), indigestion (dyspepsia);
- obsessive desire to lose weight by refusing to eat (anorexia); weight loss;
- you have muscle weakness and cramps (elevation of creatinine kinase) or muscle dysfunction and weakness (hypophosphatemia);
- you experience pain below the ribs and above the pelvis (abdominal pain).
- extreme tiredness (fatigue);

The following side effects have been reported less frequently:

- you have trouble sleeping (insomnia), have a need to sleep all the time or sleeping for unusually long periods (somnolence);
- drowsiness, fainting due to drop in blood pressure (syncope) or you experience problems with your balance (vertigo);
- you have trouble concentrating and/or unusual dreams during treatment with TRIBUSS;
- you are confused, having trouble remembering familiar places, memory loss (amnesia);
- you have a loss of motivation or willingness to continue with daily activities (apathy);
- you have abnormal physical weakness or lack of energy (asthenia);
- you have a feeling of panic, fear, inability to stay calm (anxiety), you find your yourself being annoyed at small things (agitation); have rapid changes in moods (emotional lability) or you have the feeling of discomfort, illness, or uneasiness (malaise);
- you have an increased feeling of excitement and happiness (euphoria), seeing things that are not real (hallucination);
- you have trouble moving different parts of your body together (abnormal coordination), the loss of full control of bodily movements (ataxia), reduced sense of touch or sensation (hypoaesthesia), abnormal sensation of the body, such as numbness, tingling, or burning (paraesthesia);
- you have pains in your joints (arthralgia), you have pain in your muscles or groups of muscles (myalgia);
- shaking of your arms, leg, hands (tremor) or you have the feeling that your muscles are weak (myopathy);
- shooting pains in your head or face (neuralgia) or your feet and hands tingle (peripheral neuropathy);
- problems speaking or pronouncing words (speech disorder);
- abnormal vision;
- noises or ringing in the ears (tinnitus);

- changes in your ability to taste for example the taste difference between sweet and salty (taste perversion);
- a sudden feeling of heat (hot flushes);
- tests may show that you have an increase of fatty deposits in your blood vessels (high cholesterol) or you have an increased level of natural fats and oil build up (raised triglyceride concentrations);
- you are coughing at night or wheezing with a tight chest (asthma);
- you have skin or mouth lesions that have a pink-red centre surrounded by a pale ring border and an outer pink-red ring (erythema multiforme); you have sores on your skin that are itchy, raised, red or skin-coloured (urticaria) or flaking/peeling of skin (skin exfoliation);
- partial or complete absence of hair from areas of the body where it normally grows; baldness (alopecia);
- you have abdominal pain that may radiate to the back, nausea and vomiting, worsening pain after eating, tenderness to touch of the abdomen, fever and chills, weakness and lethargy (pancreatitis).

It is possible that these symptoms may be more severe if TRIBUSS is used with alcohol or mood altering (street) medicines.

The following side effects have been reported but the frequency is unknown:

- Changes in body fat. Changes in body fat develop in some patients taking TRIBUSS. These changes may include an increased amount of fat in the upper back and neck (“buffalo hump”), in the breasts and around the trunk. Loss of fat from the legs, arms and face may also happen. The cause and long-term health effects of these fat changes or weight gain are not known;

- changes in bone mineral density (thinning bones). It is not known whether long-term use of TRIBUSS will cause damage to your bones. If you have had bone problems in the past, your healthcare provider may need to do tests to check your bone mineral density or may prescribe medicines to help your bone mineral density (osteomalacia);
- you have the need to eat more than usual (increased appetite);
- you have a loss of appetite, upper stomach pain, nausea and vomiting, continuous upset stomach (gastritis); you have diarrhoea, cramps, nausea, vomiting and fever (gastroenteritis) or difficulty passing stool (constipation) or you have burning pain in the chest that usually occurs after eating and worsens when lying down (gastro-oesophageal reflux);
- your nose is blocked, you have trouble breathing through your nose, headaches, sore throat (sinusitis),
- discolouration (dark streaks, white streaks, or changes in nail colour), change in nail shape (nail disorders);
- you have small, white-headed pimples which appear around the hair follicles. They may itch or be painful (folliculosis); you have acne; you have rashes, dryness, flakiness, peeling, or redness of the skin (seborrhoea); you have swelling, difficulty breathing, a burning sensation, a red itchy rash sometimes resembling small blisters, and peeling of the skin (photoallergic dermatitis); you have a rash/ patchy dry skin that appears on the arms and behind the knees (eczema); or you develop small spots or freckles on your skin (skin discolouration);
- inability in a man to achieve an erection or orgasm (impotence); increased or decreased in sexual desire (libido);
- decrease of white blood cells within your blood (neutropenia) ,decrease of red blood cells within your blood (anaemia);
- sweating; fever;

- you have an itchy or runny nose with sneezing, and a blocked nose (rhinitis); or you have a sore throat, phlegm on your chest, wheezing, coughing, tight chest (upper respiratory tract infections) influenza-like symptoms;
- enlargement of a man's breasts (gynaecomastia);
- you do not pass urine as often as usual or excess loss of glucose, bicarbonate, phosphates (phosphorus salts), uric acid, potassium, and certain amino acids in your urine (Fanconi syndrome);
- you are extremely thirsty as well as pass urine more often than usual (nephrogenic diabetes insipidus)(polyuria);
- you have back pain or any type of pain;
- change in colour of your palms and or soles (hyperpigmentation).

Contact your healthcare provider before stopping TRIBUSS because of side effects or for any other reason.

If you notice any side effects not mentioned in this leaflet, please inform your healthcare provider.

STORING AND DISPOSING OF TRIBUSS

- Store at or below 30 °C.
- Keep the container tightly closed.
- Keep in original packaging until required for use.
- Do not store in a bathroom.
- Do not use after the expiry date stated on the label.
- Return all unused medicine to your pharmacist.
- Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

STORE ALL MEDICINES OUT OF REACH OF CHILDREN.

PRESENTATION OF TRIBUSS

28 or 30 or 84 tablets are packed in a white opaque wide mouth high density polyethylene container and sealed with a white opaque polypropylene cap together with a desiccant. The container is packed into an outer cardboard carton together with a leaflet.

Not all packs and pack sizes are necessarily marketed.

IDENTIFICATION OF TRIBUSS

A pink coloured, capsule-shaped film-coated tablet debossed with “D100” on one side and plain on the other side.

REGISTRATION NUMBER

44/20.2.8/0980

NAME, BUSINESS ADDRESS AND TELEPHONE NUMBER OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION

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