PATIENT INFORMATION LEAFLET

SCHEDULING STATUS:

S4

PROPRIETARY NAME, STRENGTH AND PHARMACEUTICAL FORM

ERIGE 600 mg TABLETS (Tablet).

Efavirenz.

Read all of this leaflet carefully before you start taking ERIGE TABLETS

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or pharmacist
- **ERIGE TABLETS** 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.

1. WHAT ERIGE TABLETS CONTAINS:

- The active substance is efavirenz. Each film-coated tablet contains 600 mg efavirenz.
- The other ingredients are: Croscarmellose sodium, hydroxypropyl cellulose, lactose monohydrate, magnesium stearate, microcrystalline cellulose, opadry yellow and sodium lauryl sulfate.

2. WHAT ERIGE TABLETS IS USED FOR:

ERIGE TABLETS are indicated in combination with other antiretroviral agents for the treatment of HIV-1 infected adults, adolescents and children weighing greater than or equal to 40 kg.

3. BEFORE YOU TAKE ERIGE TABLETS:

Do not take ERIGE TABLETS:

- If you are hypersensitive to efavirenz or any ingredient of the formulation
- If you are using terfenadine astemizole, cisapride, midazolam, trizolam or ergot derivatives. This can create the potential for serious and/or life-threatening adverse events (eg. cardiac arrhythmias,

prolonged sedation or respiratory depression).

Take special care with ERIGE TABLETS:

- **ERIGE TABLETS** must not be used as a single agent to treat HIV or added on as a sole agent to a failing regimen, please consult your doctor, pharmacist or other healthcare professional for advice.
- Monitoring of cholesterol should be considered in patients treated with efavirenz.
- You may develop a condition known as lipodystrophy while taking **ERIGE TABLETS**. Inform your doctor or healthcare professional if you notice a change in the distribution of your body fat (e.g. accumulation of fat around the waist/stomach area, on the back of the neck and between the shoulders (buffalo hump), breast enlargement), wasting of the arms, legs and facial muscles, and increased blood glucose and lipid values.
- If you are taking **ERIGE TABLETS** for the first time you may develop a condition known as Immune Reconstitution Inflammatory Syndrome (IRIS), within the first few months of treatment. This condition can cause opportunistic infections that are being treated to become worse or opportunistic diseases that were asymptomatic to be unmasked. Tell your doctor or healthcare professional if your general health worsens or if you think you may have an infection. You should not stop taking **ERIGE TABLETS**. Your doctor will treat the infections appropriately.
- You may develop a condition known as osteonecrosis while taking **ERIGE TABLETS**. Seek medical advice if you experience joint aches and pain, joint stiffness or difficulty in movement.
- You may continue to develop opportunistic infections and other complications of HIV infection while taking **ERIGE TABLETS**. You should remain under close observation by healthcare professionals experienced in the treatment of patients with associated HIV disease. Regular monitoring of viral load and CD4 counts needs to be done.
- You are still at risk of transmitting HIV to others through sexual contact or blood contamination while taking current antiretroviral therapy including **ERIGE TABLETS**. Appropriate precautions should continue to be employed.

Pregnancy and Breastfeeding:

Safety of **ERIGE TABLETS** in pregnant and lactating women has not been established. Women of childbearing potential should undergo pregnancy testing prior to initiation of efavirenz. The safety in lactation

has not been established. It is recommended that HIV-infected women do not breastfeed their infants under any circumstances in order to avoid transmission of HIV.

If you are pregnant or breastfeeding your baby, please consult your doctor, pharmacist or other healthcare professional for advice before taking **ERIGE TABLETS**.

Driving and using machinery:

Do not drive or operating machinery should you feel sleepy, drowsy, or feel that your concentration is impaired.

Important information about some of the ingredients of ERIGE TABLETS:

ERIGE TABLETS contains lactose (milk sugar). If you know you are unable to digest and metabolize lactose (i.e lactose intolerance), tell your doctor before taking **ERIGE TABLETS**.

Taking other medicines with ERIGE TABLETS:

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

(This includes complementary or traditional medicines.)

ERIGE TABLETS interacts with indinavir, ritonavir, saquinavir, rifampicin, clarithromycin, oral contraceptives, methadone and St. John's Wort.

4. HOW TO TAKE ERIGE TABLETS:

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

Always take **ERIGE TABLETS** exactly as your doctor has instructed you. You should check with your doctor or pharmacist if you are unsure. If you have the impression that the effect of **ERIGE TABLETS** is too strong or too weak, talk to your doctor or pharmacist.

Adults:

The recommended dosage of efavirenz in combination with a protease inhibitor and/or nucleoside analogue reverse transcriptase inhibitors (NRTIs) is 600 mg orally, once daily.

Efavirenz may be taken with or without food, as desired. A high fat meal may increase the absorption of

efavirenz and should be avoided.

In order to improve the tolerability of nervous system side effects, bedtime dosing is recommended during the first two to four weeks of therapy and in patients who continue to experience these symptoms (see **POSSIBLE SIDE EFFECTS**).

Concomitant Antiretroviral Therapy:

ERIGE TABLETS must be given in combination with other antiretroviral medications (see **Taking other medicines with ERIGE TABLETS**).

Adolescents and children (17 years and under):

ERIGE TABLETS may be taken with or without food, as desired. **ERIGE TABLETS** can only be used in adults and children who weigh greater than or equal to 40 kg.

If you take more ERIGE TABLETS than you should:

Some patients accidentally taking 600 mg twice daily have reported increased nervous system symptoms.

In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison control centre.

If you forget to take ERIGE TABLETS:

Do not take a double dose to make up for forgotten individual doses.

5. POSSIBLE SIDE EFFECTS:

ERIGE TABLETS can have side effects.

Efavirenz was generally well tolerated in clinical trials. Efavirenz has been studied in over 9 000 patients. In a subset of 1 008 patients who received 600 mg efavirenz daily in combination with protease inhibitors and/or NRTIs in controlled clinical studies, the most frequently reported treatment- related undesirable effects of at least moderate severity reported in at least 5 % of patients were rash (11,6 %), dizziness (8,5 %), nausea (8,0%), headache (5,7 %), and fatigue (5,5 %). Nausea was reported with a higher frequency in the control groups. The most notable undesirable effects associated with efavirenz are rash and nervous system symptoms.

Other, less frequent, clinically significant treatment-related undesirable effects reported in all clinical trials include: allergic reaction, abnormal coordination, ataxia, confusion, stupor, vertigo, vomiting, diarrhoea, hepatitis, impaired concentration, insomnia, anxiety, abnormal dreams, somnolence, depression, abnormal thinking, agitation, amnesia, delirium, emotional lability, euphoria, hallucination and psychosis.

Additional undesirable effects reported in post-marketing surveillance include neurosis and paranoid reaction, convulsions and blurred vision.

The type and frequency of undesirable effects in children was generally similar to that of adult patients with the exception that rash was reported more frequently in children and was more often of higher grade than in adults.

Rash: In clinical trials, 26 % of patients treated with 600 mg of efavirenz experienced skin rash compared with 17 % of patients treated in control groups. Skin rash was considered treatment-related in 18 % of patients treated with efavirenz. Severe rash occurred in less than 1 % of patients treated with efavirenz and 1,7 % discontinued therapy because of rash. The incidence of erythema multiforme or Stevens-Johnson Syndrome was 0.14 %.
Rash was reported in 26 of 57 children (46 %) treated with efavirenz and was severe in 3 patients (5 %). Prophylaxis with appropriate antihistamines prior to initiating therapy with efavirenz in children may be considered.
Rashes are usually mild-to-moderate maculopapular skin eruptions that occur within the first two weeks of initiating therapy with efavirenz. In most patients rash resolves with continuing therapy with efavirenz within one month. Efavirenz can be reinitiated in patients interrupting therapy because of rash. Use of appropriate antihistamines and/or corticosteroids is recommended when efavirenz is restarted. Experience with efavirenz in patients who discontinued other antiretroviral agents of the NNRTI class is limited. Nineteen patients who discontinued nevirapine because of rash have been treated with efavirenz. Nine of these patients developed mild-to-moderate rash while receiving therapy with efavirenz, and two discontinued because of rash.

Nervous System Symptoms: There have been reports (approximately 1 to 2 per thousand Efavirenz treated

patients) of delusions and inappropriate behavior, predominantly in patients with a history of mental illness or substance abuse. Severe acute depression (including suicidal ideation/attempts) has also been infrequently reported in both efavirenz-treated and control-treated patients. Patients who experience these symptoms should contact their doctor immediately because discontinuation of efavirenz may be required.
Fifty two percent of patients receiving efavirenz reported central nervous system and psychiatric symptoms. These symptoms included, but were not limited to, dizziness, impaired concentration, somnolence, abnormal dreams and insomnia. In controlled trials, these symptoms were severe in 2,0 % of patients receiving efavirenz 600 mg QD and in 1,3 % of patients receiving control regimens. In clinical trials, 2,1 % of efavirenz-treated patients discontinued therapy because of nervous system symptoms. These symptoms usually begin during the first or second day of therapy and generally resolve after the first 2 to 4 weeks. In one clinical study, the monthly prevalence of nervous system symptoms of at least moderate severity between weeks 4 and 45 ranged from 5 % to 9 % in patients treated with regimens containing efavirenz and 3 % to 5 % in patients treated with the control regimen. Patients should be informed that these symptoms are likely to improve with continued therapy. Dosing at bedtime improves the tolerability of these symptoms and is recommended during the first weeks of therapy and in patients who continue to experience these symptoms. Patients receiving **ERIGE TABLETS** should be altered to the potential for additive central nervous system effects when **ERIGE TABLETS** is used concomitantly with alcohol or psychoactive drugs.

Patients should be informed that **ERIGE TABLETS** may cause dizziness, impaired concentration, and/or drowsiness. Patients should be instructed that if they experience these symptoms they should avoid potentially hazardous tasks such as driving or operating machinery. Adverse clinical experiences of moderate to severe intensity observed in less than 2 % of patients receiving efavirenz in all Phase II/III studies and considered at least possibly related or of unknown relationship to treatment and of at least moderate severity are listed below by body system:

General disorders and administrative site conditions:
Alcohol intolerance, allergic reaction, asthenia, hot flushes, influenza-like symptoms, malaise, pain and syncope.

Gastrointestinal disorders:

Gastritis, gastroenteritis and gastroesophageal reflux, taste perversion.

Ear and labyrinth disorders:

Tinnitus.

Cardiac disorders:

Blushing, palpitations and tachycardia.

Hepato-biliary disorders:

Hepatitis.

Metabolism and nutrition disorders:

Weight gain and weight loss.

Musculoskeletal, connective tissue and bone disorders:

Arthralgia and myalgia.

Nervous system disorders:

Aggravated depression, agitation, amnesia, anxiety, apathy, appetite increased, ataxia, confusion, emotional lability, euphoria hallucination, impaired coordination, impotence, libido decreased, libido increased, migraine headaches, neuralgia, paraesthesia peripheral neuropathy, speech disorder, tremor and vertigo.

Respiratory, thoracic and mediastinal disorders:

Asthma, sinusitis and upper respiratory tract infections.

Skin and subcutaneous tissue disorders:

Acne, alopecia, eczema, folliculitis, seborrhea, skin exfoliation and urticaria.

Eye disorders:

Abnormal vision.

Investigations:

Raised liver enzyme values have occurred, particularly in patients with viral hepatitis. Raised serum-cholesterol and triglyceride concentrations have been reported.

Liver enzymes: Elevations of AST and ALT to greater than five times the upper limit of the normal range were seen in 3 % of 1 008 patients treated with 600 mg of efavirenz. Similar elevations were seen in patients treated with control regimens. In 156 patients treated with 600 mg of efavirenz who were seropositive for Hepatitis B and/or C, 7 % developed AST levels and 8 % developed ALT levels greater than five times the upper limit of the normal range. In 91 patients seropositive for Hepatitis B and/or C, treated with control regimens, 5 % developed AST elevations and 4 % developed ALT elevations to these levels. Elevations of GOT to greater than five times the upper limit of the normal range were observed in 4 % of all patients treated with 600 mg of efavirenz and in 10 % of patients seropositive for Hepatitis B or C. In patients treated with control regimens. The incidence of GOT elevations to this level was 1.5 to 2 % irrespective of Hepatitis B or C serology. Isolated elevations of GOT in patients receiving efavirenz may reflect enzyme induction not associated with liver toxicity.

Lipids: Increases in total cholesterol of 10 to 20 % have been observed in some uninfected volunteers receiving efavirenz. Increases in non-fasting total cholesterol and HDL of approximately 20 % and 25 %., respectively were observed in patients treated with efavirenz+SDV+STC and of approximately 40 % and 35 **%,** in patients treated with efavirenz+IDV. The effects of efavirenz on triglycerides and LDL were not well-characterised. The clinical significance of these findings is unknown.

Not all side effects reported for **ERIGE TABLETS** are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking **ERIGE TABLETS**, please consult your doctor, pharmacist or other healthcare professional for advice.

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

6. STORING AND DISPOSING OF ERIGE TABLETS:

Store at or below 30 °C

STORE ALL MEDICINES OUT OF REACH OF CHILDREN.

Return all unused medicine to your pharmacist.

Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

7. **PRESENTATION OF ERIGE TABLETS:**

Tablets are packed in milky white round 80 ml HDPE containers with screw type polypropylene closure with induction sealing wad.

Pack size: 30 tablets per HDPE container.

8. IDENTIFICATION OF ERIGE TABLETS:

Yellow coloured oval biconvex film-coated tablets debossed with 'D' on one side and '37' on the other side.

9. REGISTRATION NUMBER/REFERENCE NUMBER:

A40/20.2.8/0513

12. NAME AND ADDRESS OF REGISTRATION HOLDER:

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