PATIENT INFORMATION LEAFLET

SCHEDULING STATUS

S4

PROPRIETATY NAME, STRENGTH AND PHARMACEUTICAL FORM

ERIGE 50 mg CAPSULES, efavirenz, 50 mg (capsule).

ERIGE 100 mg CAPSULES, efavirenz, 100 mg (capsule).

ERIGE 200 mg CAPSULES, efavirenz, 200 mg (capsule).

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

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

- The active substance is Efavirenz.

- **ERIGE 50 mg CAPSULES**:

  Each capsule contains 50 mg Efavirenz.

- **ERIGE 100 mg CAPSULES**:

  Each capsule contains 100 mg Efavirenz.

- **ERIGE 200 mg CAPSULES**:

  Each capsule contains 200 mg Efavirenz.

- The other ingredients are: lactose monohydrate, magnesium stearate, sodium starch glycolate and sodium lauryl sulfate.

- Contains sugar (lactose monohydrate).

2. WHAT ERIGE CAPSULES IS USED FOR

ERIGE CAPSULES 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 CAPSULES

Do not take ERIGE CAPSULES:

- if you are hypersensitive (allergic) to efavirenz or any of the other ingredients of **ERIGE CAPSULES**
- if you are using terfenadine astemizole, cisapride, midazolam, triazolam or ergot derivatives. This can create the potential for serious and/or life-threatening adverse events [e.g. cardiac arrhythmias, prolonged sedation or respiratory depression].

Take special care with ERIGE CAPSULES:

ERIGE CAPSULES 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 health care professional for advice.
monitoring of cholesterol should be considered in patients treated with efavirenz.

Pregnancy and Breastfeeding:

Safety of **ERIGE CAPSULES** 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 breast-feed their infants under any circumstances in order to avoid transmission of HIV.

If you are pregnant or breast feeding your baby please consult your doctor, pharmacist or other healthcare

professional for advice before taking **ERIGE CAPSULES**.

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 CAPSULES:

ERIGE CAPSULES contains lactose and should not be administered to patients with rare hereditary problems, or a history of lactose intolerance, Lapp lactose deficiency or glucose-galactose malabsorption.

Taking other medicines with ERIGE CAPSULES

Always tell your healthcare professional if you are taking any other medicines (this includes complementary or traditional medicines).

ERIGE CAPSULES interacts with indinavir, ritonavir, saquinavir, rifampicin, clarithromycin, oral contraceptives, methadone and St. Johns wort.

4. HOW TO TAKE ERIGE CAPSULES

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

Always take **ERIGE CAPSULES** exactly as your doctor has instructed you. You should check with your doctor or pharmacist if you are unsure.

Your doctor will tell you how long your treatment with **ERIGE CAPSULES** will last.

If you have the impression that the effect of **ERIGE CAPSULES** is too strong or too weak, tell 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 CAPSULES must be given in combination with other antiretroviral medications (see Taking other medicines with **ERIGE CAPSULES**).

Adolescents and children (17 years and under):

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

If you take more ERIGE CAPSULES 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 / missed a dose of ERIGE CAPSULES:

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

5. POSSIBLE SIDE EFECTS

ERIGE CAPSULES can have side effects.

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

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 (80 %), 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 600mg 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 behaviour, 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 CAPSULES** should be altered to the potential for additive central nervous system affects when **ERIGE CAPSULES** is used concomitantly with alcohol or psychoactive drugs.

Patients should be informed that **ERIGE CAPSULES** 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 Il/Ill 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:

Body as a Whole:

Alcohol intolerance, allergic reaction, asthenia, hot flushes, influenza-like symptoms, malaise, pain and syncope.

Gastrointestinal:

Gastritis, gastroenteritis and gastroesophageal reflux.

Hearing and Vestibular:

Tinnitus.

Cardiovascular:

Blushing, palpitations and tachycardia.

Liver and Biliary System:

Hepatitis.

Metabolic and Nutritional:

Weight gain and weight loss.

Musculoskeletal:

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:

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

Special Senses:

Abnormal vision and taste perversion.

Laboratory Abnormalities:

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 HOL of approximately 20 % and 25 %, respectively were observed in patients treated with efavirenz+SDV÷3TC 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.

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

6. STORING AND DISPOSING OF ERIGE CAPSULES

Store at or below 30 °C. Protect from light. Keep the container tightly closed.

STORE ALL MEDICNES 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 CAPSULES

ERIGE 50 mg CAPSULES:

Capsules are packed in white, round 40 ml heavy weight HDPE container with 33 mm PP closure with induction sealing wad.

No desiccant is included in the container.

Pack size: 30’s: One HDPE container of 30 capsules.

ERIGE 100 mg CAPSULES:

Capsules are packed in white, round 40 ml heavy weight HDPE container with 33 mm PP closure with induction sealing wad.

No desiccant is included in the container.

Pack size: 30’s: One HDPE container of 30 capsules.

ERIGE 200 mg CAPSULES:

1. Capsules are packed in white, round 70 ml heavy weight HDPE container with 43 mm PP closure with induction sealing wad.

No desiccant is included in the container.

Pack size: 30’s: One HDPE container of 30 capsules.

2. Capsules are packed in white, round 200 ml heavy weight HDPE container with 45 mm PP closure with induction sealing wad.

No desiccant is included in the container.

Pack size: 90's: One HDPE container of 90 capsules.

8. IDENTIFICATION OF ERIGE CAPSULES

ERIGE 50 mg CAPSULES:

Yellow/white size '4' hard gelatin capsules imprinted with 'D' on yellow cap and '72' on white body with black edible ink filled with white to off-white coloured powder.

ERIGE 100 mg CAPSULES:

White/white size '2' hard gelatin capsules imprinted with 'D' on white cap and '71' on white body with black edible ink filled with white to off-white coloured powder.

ERIGE 200 mg CAPSULES:

Yellow/yellow size 'OEL' hard gelatin capsules imprinted with 'D' on yellow cap and '36' on yellow body with black edible ink filled with white to off-white coloured powder.

9. REGISTRATION NUMBER

ERIGE 50 mg CAPSULES: 41/20.2.8/0541

ERIGE 100 mg CAPSULES: 41/20.2.8/0542

ERIGE 200 mg CAPSULES: 41/20.2.8/0543

10. NAME AND ADDRESS OF REGISTRATION HOLDER

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