Module 1.3.2: PATIENT INFORMATION LEAFLET

Information for the Patient about

CIPLA NEVIRAPINE

SCHEDULING STATUS:

S4

PROPRIETARY NAME, STRENGTH AND PHARMACEUTICAL FORM:

CIPLA NEVIRAPINE containing 200 mg **nevirapine** (Tablets)

Read all of this leaflet carefully before you start taking CIPLA NEVIRAPINE:

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

The active ingredient in **CIPLA NEVIRAPINE** is nevirapine.

CIPLA NEVIRAPINE (Tablets): Each uncoated tablet contains 200 mg nevirapine.

Inactive ingredients are lactose monohydrate, magnesium stearate, corn starch, microcrystalline cellulose and sodium starch glycollate.

CIPLA NEVIRAPINE (Tablets) contains sugar: Each tablet contains 164,00 mg lactose monohydrate.

WARNING:

THE FIRST 18 WEEKS OF THERAPY WITH CIPLA NEVIRAPINE IS A CRITICAL PERIOD AND YOUR DOCTOR WILL MONITOR YOU INTENSIVELY TO IDENTIFY THE POTENTIAL APPEARANCE OF SEVERE AND LIFE-THREATENING SKIN REACTIONS (INCLUDING CASES OF BLISTER-FORMING SKIN RASHES THAT MAY RESULT IN DEATH) OR SERIOUS INFLAMMATION OF THE LIVER (HEPATITIS) OR LIVER FAILURE.

The greatest risk of liver events and skin reactions occurs in the first 6 weeks of therapy, however, the risk continues past this period and monitoring should continue at frequent intervals. Women and people with higher CD4+ counts at the start of CIPLA NEVIRAPINE treatment are at increased risk.

In some cases, liver injury has progressed despite stopping treatment. If you develop signs or symptoms of hepatitis, severe skin reaction or allergic reactions, you must stop taking CIPLA NEVIRAPINE and seek medical evaluation immediately. You should not take CIPLA NEVIRAPINE following severe liver, skin or allergic reactions.

Do not alter your dosage; especially not in the 14-days lead-in period (see "HOW TO TAKE CIPLA NEVIRAPINE").

CIPLA NEVIRAPINE SHOULD ALWAYS BE TAKEN WITH AT LEAST TWO ADDITIONAL ANTIRETROVIRAL AGENTS TO PREVENT THE VIRUS FROM DEVELOPING RESISTANCE (BECOMING LESS SUSCEPTIBLE) TO IT.

WHAT CIPLA NEVIRAPINE IS USED FOR:

CIPLA NEVIRAPINE belongs to a group of medicines called antiretrovirals, used in the treatment of Human Immunodeficiency Virus (HIV) infection in both adults and children.

CIPLA NEVIRAPINE is used in combination with other additional antiretroviral medicines (HIV medicines) for the treatment of HIV-1 infection.

CIPLA NEVIRAPINE is also used to reduce the risk of transmission of HIV-1 infection from mother to child in HIV-infected pregnant women who are not taking antiretroviral therapy at the time of labour, and their new-born babies.

BEFORE YOU TAKE CIPLA NEVIRAPINE:

Do NOT take CIPLA NEVIRAPINE:

- If you or your child are allergic (hypersensitive) to nevirapine or to any of the inactive ingredients of **CIPLA NEVIRAPINE**.
- If you or your child have been diagnosed with liver function impairment or kidney failure.
- If you or your child previously experienced hepatitis, severe skin rash, allergic reaction or liver injury while on **CIPLA NEVIRAPINE** treatment.
- If you have permanent liver disease or changes in liver function.
- If you are currently taking herbal products containing St John's Wort (*Hypericum perforatum*) as it may reduce the effectiveness of **CIPLA NEVIRAPINE**.
- The safety of **CIPLA NEVIRAPINE** in pregnant or breastfeeding women has not been established. Women should make use of barrier contraceptive

methods while taking **CIPLA NEVIRAPINE** (see also **Pregnancy and breast feeding**).

Take special care with CIPLA NEVIRAPINE:

The first 18 weeks of treatment with CIPLA NEVIRAPINE is an important period and you may have to undergo intensive monitoring to identify the potential appearance of severe and life-threatening skin reactions or serious hepatitis (inflammation of the liver) or liver failure.

The greatest risk of liver events and skin reactions occurs in the first 6 weeks of therapy.

You should inform your doctor if you, or your child have previously been treated with single-dose **CIPLA NEVIRAPINE** for prevention of mother to child transmission of HIV-1, since **CIPLA NEVIRAPINE** may be less effective if you or your child have to take it thereafter as part of your treatment.

Skin reactions:

Severe and life-threatening skin reactions, including fatal cases, have occurred in people treated with CIPLA NEVIRAPINE.

If you experience a severe rash or a rash accompanied by fever, blistering, lesions inside the mouth, eye inflammation, swelling of the face, muscle or joint aches, or generally feeling unwell, you should stop taking CIPLA NEVIRAPINE and immediately seek help from your doctor. You should also not

use CIPLA NEVIRAPINE again.

If a hypersensitivity (severe allergic) reaction occurs, characterised by rash with fever, joint pain, muscle pain and swelling of lymph glands, plus internal organ involvement, such as inflammation of the liver, abnormal white blood cell counts, and kidney dysfunction, stop taking CIPLA NEVIRAPINE and immediately seek help from your doctor.

If you should experience any rash during the lead-in period of 14 days, tell your doctor and your dose of **CIPLA NEVIRAPINE** should not be increased until the rash has disappeared (see **"HOW TO TAKE CIPLA NEVIRAPINE"**).
If your baby is receiving treatment with **CIPLA NEVIRAPINE** you should monitor your baby carefully, particularly in the first 18 weeks of treatment, for any skin reactions.

If you take more **CIPLA NEVIRAPINE** than the dose prescribed by your doctor, you may be at increased risk of serious skin reactions.

Please inform your doctor if you are experiencing any skin and/or liver reactions associated with **CIPLA NEVIRAPINE** as it may lead to breakdown of muscles that may cause kidney damage (rhabdomyolysis).

Risk factors for developing serious skin reactions include failure to follow the initial dosing instructions during the lead-in dosing period. If you experience any skin rash, you should immediately report to your doctor, as a long delay between the initial

symptoms and medical consultation may increase the risk of a more serious outcome of skin reactions.

Your doctor may perform a blood test to evaluate your liver function if he/she is of the opinion that CIPLA NEVIRAPINE is responsible for your skin rash. Depending on the results of these tests, your doctor may decide to permanently stop treatment with CIPLA NEVIRAPINE.

Liver reactions:

Severe or life-threatening liver damage (including very severe cases of liver inflammation which have resulted in death) has occurred in patients treated with CIPLA NEVIRAPINE. Serious liver inflammation and liver failure have been reported in CIPLA NEVIRAPINE-treated patients in the first 18 weeks of therapy, but some cases have occurred later. The first 18 weeks of treatment is a critical period during which you will be closely monitored. The risk of liver complications is greatest during the first 6 weeks of therapy, however, the risk continues past this period and monitoring should continue at frequent intervals throughout treatment.

If you have a severe underlying liver disorder, you should tell your doctor as you should not take **CIPLA NEVIRAPINE** (see **"Do NOT take CIPLA NEVIRAPINE"**). If you have chronic hepatitis B or C virus infection and you are receiving treatment with combination antiretroviral therapy, you are at an increased risk for severe and potentially fatal liver adverse events. Tell your doctor if you have pre-existing liver dysfunction, including chronic active hepatitis, you may have a higher risk of liver

function abnormalities during treatment with a combination of antiretroviral medicines and your doctor will monitor you for possible adverse events. Your doctor may decide to interrupt or stop treatment if there is evidence of worsening liver disease.

Liver reactions are a major toxicity of **CIPLA NEVIRAPINE** and should you develop any symptoms suggestive of hepatitis (loss of appetite, nausea, jaundice) you should contact your doctor promptly.

Liver function monitoring:

Your doctor may perform a blood test to determine your liver function before you start treatment with **CIPLA NEVIRAPINE**.

Abnormal liver function has been reported with **CIPLA NEVIRAPINE**, some in the first few weeks of therapy. You may have to undergo regular monitoring of liver function during the first 18 weeks of treatment. Your doctor will decide whether to proceed with, or stop treatment. Less frequent monitoring is needed thereafter. You should be vigilant for early signs or findings of hepatitis (inflammation of the liver), such as loss of appetite, nausea, jaundice, increased bile pigment in the urine (dark urine), pale or clay-coloured stools, enlargement of the liver or liver tenderness. You should immediately report to your doctor should any of these symptoms occur.

If you suffer from mild to moderate impairment of liver function, your doctor will monitor you carefully during treatment with **CIPLA NEVIRAPINE**. You should not receive treatment with **CIPLA NEVIRAPINE** if you suffer from severe impairment of liver function (see **"Do NOT take CIPLA NEVIRAPINE"**).

If you are taking **CIPLA NEVIRAPINE** with zidovudine (an anti-HIV medicine) you may experience side effects such as decreased white blood cell counts (granulocytopenia), which may be monitored by your doctor with blood tests.

If you suffer from kidney failure and require haemodialysis, you may require dosage adjustments.

Therapy with **CIPLA NEVIRAPINE** may cause changes in body shape due to changes in fat distribution (lipodystrophy). These may include loss of fat from the legs, arms and face, increased fat in the abdomen (belly) and other internal organs, breast enlargement and fatty lumps on the back of the neck ('buffalo hump'). In addition, other metabolic abnormalities, such as increases in blood lipid (fat) and cholesterol levels, resistance to insulin, high blood glucose (sugar) levels and high blood levels of lactate, have also been reported.

Immune reconstitution syndrome, which is an inflammatory immune response to previously acquired opportunistic infections, and which may cause deterioration in your physical well-being, has been reported during the initial phase of therapy with a combination of antiretroviral medicines, including **CIPLA NEVIRAPINE**. This happened in patients with HIV infection with severe impairment of immune function. Please discuss this with your treating doctor.

Osteonecrosis (death of bone tissue caused by loss of blood supply to the bone) has also been reported in patients with advanced HIV disease or in patients who have been exposed to treatment with combination antiretroviral agents for an extended

period of time. 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.

CIPLA NEVIRAPINE is not a cure for HIV infection. You may continue to develop opportunistic infections and other complications of HIV infection. Treatment with **CIPLA NEVIRAPINE** has not been shown to reduce the incidence or frequency of such illnesses. You should therefore remain under close supervision of your doctor.

CIPLA NEVIRAPINE has not been proven to prevent the risk of transmitting HIV to others through sexual contact or blood contamination. You need to continue to take appropriate precautions against transmitting the virus to other people (such as the use of condoms during sexual intercourse).

Oral contraceptives (the pill) and other hormonal methods of birth control (e.g. the injection) should not be used as the sole method of contraception in women taking **CIPLA NEVIRAPINE**, since it may lower plasma levels of these medicines (see **"Taking other medicines with CIPLA NEVIRAPINE"**). For this reason, and to reduce the risk of HIV transmission, the use of barrier contraception (e.g. condoms) is recommended.

Taking CIPLA NEVIRAPINE with food and drink:

CIPLA NEVIRAPINE can be taken with or without food (see **"HOW TO TAKE CIPLA NEVIRAPINE"**).

Pregnancy and breastfeeding:

The safety of **CIPLA NEVIRAPINE** in pregnant or breastfeeding women, except when used as a single dose during labour, has not been established.

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

You should not breastfeed your baby while taking **CIPLA NEVIRAPINE**. Breastfeeding is associated with a significantly higher rate of HIV-1 transmission than that seen in babies not receiving breast milk. Please ask your doctor or other healthcare professional for advice regarding alternative forms of feeding.

Women should make use of adequate contraception (birth control) when taking **CIPLA NEVIRAPINE**. Please discuss this with your doctor, pharmacist or other healthcare professional.

Please inform your doctor or pharmacist if you are taking oral contraceptives (i.e. the pill), since co-administration with **CIPLA NEVIRAPINE** may make the pill less effective (please see **"Take special care with CIPLA NEVIRAPINE"**).

Driving and using machinery:

There is evidence that **CIPLA NEVIRAPINE** can cause sleepiness. Therefore, care should be taken if you are driving or operating machinery. If you feel sleepy then you should stop driving or operating machinery.

Important information about some of the ingredients of CIPLA NEVIRAPINE:

Lactose:

CIPLA NEVIRAPINE contains sugar (lactose) 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/fructose or galactose intolerance should not take **CIPLA NEVIRAPINE**.

Taking other medicines with CIPLA NEVIRAPINE:

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

In particular, please inform your doctor or pharmacist if you are taking any of the following medicines:

- Other antiretroviral medicines, especially zidovudine, tenofovir (in combination with emtricitabine), efavirenz, delavirdine, etravirine, rilpivirine, atazanavir (in combination with ritonavir), fosamprenavir, lopinavir (in combination with ritonavir), saquinavir, indinavir, and elvitegravir (in combination with cobicistat).
- Ketoconazole, itraconazole and fluconazole for the treatment of fungal infections.
- Warfarin, a blood thinner, since combination with **CIPLA NEVIRAPINE** may require more frequent blood tests to monitor the efficacy of warfarin.
- Clarithromycin, an antibiotic for the treatment of bacterial infections.
- Rifampicin and rifabutin, antibiotics for the treatment of tuberculosis, as

combination with **CIPLA NEVIRAPINE** may require dosage adjustments.

- Boceprevir and telaprevir for the treatment of chronic hepatitis B and C.
- St. John's Wort for the treatment of mild depression or mood disorders (see **"Do NOT take CIPLA NEVIRAPINE"**), since it may reduce the efficacy of **CIPLA NEVIRAPINE** and afford the virus with the opportunity to develop resistance.
- Oral contraceptives (the pill) containing ethinyl oestradiol and norethindrone may be affected by **CIPLA NEVIRAPINE** and should not be used as the sole method of contraception (see **"Take special care with CIPLA NEVIRAPINE"**). You should use an additional method of birth control such as barrier contraception (e.g. condoms) if you are taking **CIPLA NEVIRAPINE**.
- Postmenopausal hormone therapy containing ethinyl oestradiol, as **CIPLA NEVIRAPINE** may decrease the levels of oestrogen.
- Methadone as co-administration with **CIPLA NEVIRAPINE** may decrease blood levels of methadone.
- Erythromycin, an antibiotic for the treatment of bacterial infections, since this may interfere with the breakdown of **CIPLA NEVIRAPINE**.

HOW TO TAKE CIPLA NEVIRAPINE:

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

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

Treatment of HIV-1 Infection:

Adults:

The usual dose, in combination with at least two additional antiretroviral medicines, is as follows:

- 200 mg (1 **CIPLA NEVIRAPINE** tablet once daily for the first 14 days **(this lead-in period should be used because it has been found to lessen the frequency of rash)**,
- followed by 200 mg (1 **CIPLA NEVIRAPINE** tablet) twice daily.

Your doctor will decide which other medicines you should take in combination with **CIPLA NEVIRAPINE**.

Children:

If your child needs to take **CIPLA NEVIRAPINE**, your doctor will calculate the most appropriate dosage based on your child's body surface area or body weight.

For adults and children (who weigh more than 46,88 kg or with a BSA ≥ 1,25+), who are able to swallow tablets easily, **CIPLA NEVIRAPINE** 200 mg tablets can be taken instead of nevirapine oral suspension.

Take **CIPLA NEVIRAPINE** every day as prescribed. Do not alter the dose without consulting your doctor.

Your doctor will perform blood tests before you start treatment with **CIPLA NEVIRAPINE** and at regular intervals during treatment. Your doctor will decide how long treatment should last, and may decide to change your dosage or to stop therapy with **CIPLA NEVIRAPINE** if you develop adverse reactions or if your liver function is adversely affected.

If you stopped taking **CIPLA NEVIRAPINE** for more than 7 days, your doctor will instruct you to start the 14 day "lead-in" period once again before returning to the twice daily dose.

You should continue to take **CIPLA NEVIRAPINE** for as long as instructed by your doctor.

To reduce the risk of transmission of HIV-1 infection from mother to child in HIV-infected pregnant women who are not taking antiretroviral therapy at the time of labour:

The dosage for HIV positive women in labour who have received appropriate counselling is:

- a single oral dose of 200 mg (1 tablet **CIPLA NEVIRAPINE** preferably more than 2 hours before delivery.

If you have the impression that **CIPLA NEVIRAPINE** is too strong or too weak, please discuss this with your doctor.

If you take more CIPLA NEVIRAPINE than you should:

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 CIPLA NEVIRAPINE:

Always take **CIPLA NEVIRAPINE** as prescribed. It is important that you continue to

take your treatment. If you miss a dose, take it as soon as you remember. If you do not remember the missed dose until the next dose is due, skip the missed dose and go back to your regular dosing schedule. Do not take a double dose to compensate for the forgotten individual dose. It is important to take **CIPLA NEVIRAPINE** regularly, because irregular intake may increase the risk of the virus developing resistance to your medication.

Effects when treatment with CIPLA NEVIRAPINE is stopped:

If you had to stop treatment with **CIPLA NEVIRAPINE** for any reason, but particularly because of side-effects, such as skin rash or liver complications, it is important that you obtain your doctor's opinion before restarting. If **CIPLA NEVIRAPINE** was stopped due to an allergic or hypersensitivity reaction, skin rash, or because of liver damage or potential liver damage due to nevirapine, you should never take **CIPLA NEVIRAPINE** or any other medicine containing nevirapine again.

POSSIBLE SIDE-EFFECTS:

CIPLA NEVIRAPINE can have side-effects.

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

The most serious side-effects due to **CIPLA NEVIRAPINE** include serious skin reactions (such as Stevens-Johnson syndrome and toxic epidermal necrolysis), liver damage, including liver failure, and a hypersensitivity syndrome characterised by

rash, fever, joint pain, muscle pain and swelling of lymph glands as well as inflammation of the liver, abnormal blood cell counts and kidney dysfunction. The first 18 weeks of treatment is a critical period, which requires close monitoring (see **"Take special care with CIPLA NEVIRAPINE"**).

Please see the boxed **"Warning" at the beginning of this leaflet**. You should report any skin rash to your doctor as a matter of urgency.

Rashes are usually mild to moderate, with or without itching, located on the body, face and extremities. Allergic reactions have been reported. The majority of skin rashes of any severity occur within the first 6 weeks of treatment and some patients have required hospitalisation.

CIPLA NEVIRAPINE must be stopped immediately if you develop a severe rash with/without the above symptoms.

If any of the following happens, stop taking **CIPLA NEVIRAPINE** and tell your doctor immediately or go to the casualty department at your nearest hospital:

- Those that occur frequently:
    - Allergic reactions, or hypersensitivity syndrome, which may include a skin rash, fever, difficult breathing, wheezing, hives, itching, or swelling of the face, lips, or tongue (which may be life-threatening), or severe rash with abnormal blood cell counts and joint pain, muscle pain, swelling of lymph glands as well as inflammation of the liver and kidney dysfunction.

- Your doctor will test your liver function and may find that you have an abnormal liver function test with increases in liver enzyme levels indicating possible liver damage.

- Those that occur less frequently:
  - Any skin rash with blister formation, inflamed spots on your skin, ulcers in the mouth or at the corners of the lips and hives with itching (Stevens-Johnson syndrome, toxic epidermal necrolysis, which may be life-threatening).

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

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

- Those that occur frequently:
  - Loss of appetite, nausea, vomiting, pain over the liver area with or without jaundice (yellow discolouration of the whites of the eyes or skin) as this may indicate inflammation of the liver or liver failure. If you experience loss of appetite, nausea, unusual tiredness or weakness and vomiting, pale stools and dark urine, please report to your doctor immediately as this may indicate that you are at risk of developing liver damage (which may be fatal).
  - Fever, chills, coughing, sneezing, sore throat, skin ulcers and other signs of infection, as this may be due to low white cell counts

(granulocytopenia). Granulocytopenia may occur more frequently in children than in adults.

- Skin rash.

- Those that occur less frequently:
  - Pallor accompanied by tiredness, shortness of breath, and chest pain, as this may indicate low red blood cell counts (anaemia). Anaemia may occur more frequently in children than in adults.

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

Tell your doctor if you notice any of the following:

- Those that occur frequently:
  - Headache.
  - Nausea, vomiting, stomach pain, diarrhoea / loose stools.
  - Your doctor will conduct a blood test and may find that you have decreased blood phosphorus levels.
  - Increased blood pressure.
- Those that occur less frequently:
  - Muscle pain, joint pain.
  - Fatigue, fever.

The following events have also been reported when **CIPLA NEVIRAPINE** has been used in combination with other antiretroviral medicines: anaemia, pancreatitis (severe abdominal pain, loss of appetite, vomiting, fever and generally feeling unwell), lipodystrophy (changes in body fat distribution which may include loss of fat from the legs, arms and face, increased fat in the belly and other internal organs,

breast enlargement and fatty lumps on the back of the neck, called a 'buffalo hump'), damage to the nerves in your hands or feet (presenting with pins and needles, abnormal sensation following normal stimulation, or pain) and low platelet counts (presenting with pinpoint red spots on the skin, easy bruising or bleeding from the gums or into the urine). Liver and kidney failure syndromes have been reported less frequently.

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

STORING AND DISPOSING OF CIPLA NEVIRAPINE:

Store at or below 25 °C. Protect from light.

CIPLA NEVIRAPINE (Tablets): Keep the blisters in the outer carton until required for use or store the tablets in the original plastic container until required for use.

KEEP OUT OF REACH OF CHILDREN.

Do not use after the expiry date stated on the packaging material.

Return all unused medicine to your pharmacist.

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

PRESENTATION OF CIPLA NEVIRAPINE:

CIPLA NEVIRAPINE (Tablets): PVC film and aluminium blister strips of 10 tablets each, packed in 60’s in a carton, or sixty (60) tablets packed in a white-coloured, high density polyethylene (HDPE) bottle containing a silica gel bag and closed with a milky-coloured screw cap, packed in a carton.

IDENTIFICATION OF CIPLA NEVIRAPINE:

CIPLA NEVIRAPINE: White, oval shaped, biconvex tablet with central break line on one side and 'N' debossed on the other side.

REGISTRATION NUMBERS:

CIPLA NEVIRAPINE: 36/20.2.8/0423

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATES OF REGISTRATION:

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