Patient Information Leaflet:

Information for the Patient about

CIPLA-DOXORUBICIN 10

CIPLA-DOXORUBICIN 50

Read this entire leaflet carefully before you receive CIPLA-DOXORUBICIN.

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

SCHEDULING STATUS:

S4

PROPRIETARY NAME (AND DOSAGE FORM):

CIPLA-DOXORUBICIN 10 (Powder for solution for injection)

CIPLA-DOXORUBICIN 50 (Powder for solution for injection)

WHAT CIPLA-DOXORUBICIN CONTAINS:

CIPLA-DOXORUBIN 10: Each vial contains doxorubicin hydrochloride 10 mg. Inactive ingredients include lactose monohydrate.

CIPLA-DOXORUBICIN 50: Each vial contains doxorubicin hydrochloride 50 mg. Inactive ingredients include lactose monohydrate.

Doxorubicin belongs to a class of medicines known as cytostatic agents, in other words medicines for the treatment of cancer.

WHAT CIPLA-DOXORUBICIN IS USED FOR:

CIPLA-DOXORUBICIN is indicated for the treatment of a variety of cancers, including the following:

- Acute leukaemias (blood cancer), lymphomas (cancer of lymph glands or spleen) and a number of solid tumours.
- Cancer of the breast that has spread to other organs, bladder cancer, cancer of the airways and cancers of nerve or brain tissue.
- Thyroid cancer that has spread to other organs, cancer of the lining of the womb, cancers of the testes, prostate, cervix (neck of womb), and head and neck cancers, and certain types of white blood cell cancers.
- Cancer of the ovary if given in combination with other chemotherapeutic (anticancer) medicines (cisplatin and cyclophosphamide).
- Cancer of the breast and small (oat) cell cancer of the lung when given concurrently with other chemotherapeutic medicines.
- Cancers arising in connective tissue (called sarcomas) that may involve bone tissue or other soft tissues.
- Hodgkin's disease, a cancer of lymph tissue (lymphoma), if given with other chemotherapeutic agents.
- Non-Hodgkin's lymphomas if administered concurrently with other chemotherapeutic medicines.

Your doctor will decide whether or not you qualify for treatment with **CIPLA-DOXORUBICIN**.

BEFORE YOU RECEIVE CIPLA-DOXORUBICIN:

Do not receive **CIPLA-DOXORUBICIN** if you:

- Are known to be hypersensitive (allergic) to **CIPLA-DOXORUBICIN**, other medicines belonging to the same class (anthracyclines) or to any components of the formulation.
- Have low white blood cell or red blood cell counts or low platelet counts.
- Have impairment of liver function.
- Have heart failure or any other heart disease.
- Recently suffered a heart attack (myocardial infarction).
- Suffer from abnormal heart rhythm.
- Have already received treatment with maximum cumulative doses of doxorubicin or other similar compounds. Your doctor will be able to tell you if this is the case.
- Are pregnant or breast feeding.

Take special care with CIPLA-DOXORUBICIN:

CIPLA-DOXORUBICIN should be given only under supervision of a doctor experienced in cancer chemotherapy.

Females are advised to use reliable contraception if they are of child-bearing age, since treatment with **CIPLA-DOXORUBICIN** may harm their unborn babies.

If you developed complications from treatment with other anticancer medicines, such as mouth ulcers, low blood cell or platelet counts, or generalised infections, you should first recover from these before you begin treatment with **CIPLA-DOXORUBICIN**.

If you are elderly, have liver impairment or if you are obese, your doctor may decide to alter your **CIPLA-DOXORUBICIN** dosage.

Treatment with **CIPLA-DOXORUBICIN** may damage your heart and this may present as early or late events. Early events usually involve abnormal heart rhythm or ECG abnormalities, such as rapid heart rate or a slow heart rate. These early events do not usually predict subsequent development of delayed damage to the heart (cardiotoxicity), are rarely of clinical importance (and therefore rarely requires treatment or intervention) and are generally not a consideration for stopping treatment with **CIPLA-DOXORUBICIN**.
Late cardiotoxicity usually develops late in the course of therapy with **CIPLA-DOXORUBICIN** or within two to three months after treatment was stopped, but later events, several months to years after completion of treatment, have also been reported. Late toxicity usually present with signs and symptoms of heart failure, such as swelling of the feet or ankles or even stomach or face, shortness of breath, inability to lie down due to shortness of breath, coughing of pink sputum and generally feeling tired and unwell. Life-threatening heart failure is the most severe form of heart damage caused by **CIPLA-DOXORUBICIN**.

Your doctor will monitor the function of your heart before treatment with **CIPLA-DOXORUBICIN** is initiated as well as regularly during treatment. Your doctor may have to perform several special investigations to monitor your heart function and these may include electrocardiograms (ECG), echocardiography (ECHO) or multi-gated radionuclide angiography (MUGA). Your doctor will be able to provide you with more information regarding these tests.

Treatment with **CIPLA-DOXORUBICIN** may depress the function of your bone marrow. Bone marrow is responsible for the production of white and red blood cells as well as platelets. White blood cells are necessary to maintain a healthy immune system and to fight infections. Red blood cells carry oxygen and platelets are necessary for blood clotting. You will have to undergo blood tests before and during each cycle of **CIPLA-DOXORUBICIN** therapy to evaluate your blood cell counts.

Some patients who received **CIPLA-DOXORUBICIN** subsequently developed blood cancer (leukaemia). Leukaemia may appear within 1 to 3 years following treatment with **CIPLA-DOXORUBICIN**. Your doctor will monitor you for this complication.

Leukaemia, which is reversible, and low white cell counts are the most common reason for reducing the dose of **CIPLA-DOXORUBICIN** or for stopping treatment. White cell counts are at their lowest between 10 to 14 days after administration of **CIPLA-DOXORUBICIN** and return to normal values in most cases by day 21. Consequences of bone marrow suppression include fever, infections, sepsis, septic shock, bleeding, too little oxygen

delivered to your organs and death. If you develop a fever or think you may be suffering from an infection, please inform your doctor immediately.

CIPLA-DOXORUBICIN may cause infertility in women during the time of medicine administration. It may also cause absence of menstruation, but ovulation and menstruation appear to return after treatment is stopped. However, some patients may develop premature menopause (menopause at an earlier age than normally expected).
Treatment with **CIPLA-DOXORUBICIN** may damage chromosomes in sperm. Low sperm counts and absence of sperm may be permanent. Men who are receiving treatment with **CIPLA-DOXORUBICIN** should use effective contraceptive measures.

CIPLA-DOXORUBIN may cause severe nausea and vomiting. In addition it may also cause inflammation with sores in the mouth or on the lips. This may progress to ulcers. Most patients recover from this adverse event by the third week of therapy.

You will undergo blood tests before and periodically during treatment with **CIPLA-DOXORUBICIN** to monitor your liver function. Depending on the results of these tests, your doctor may decide to change the dosage of your medicine.

If **CIPLA-DOXORUBICIN** is injected into a small vein or repeatedly into the same vein, hardening of the vessel walls (phlebosclerosis) may occur. You

may also develop pain around the injection area or red streaks along the vein. If **CIPLA-DOXORUBICIN** leaks into the tissues surrounding the vein, it may cause severe tissue lesions with blister formation and inflammation as well as skin death. If you experience pain, swelling and redness or other changes surrounding the injection area, please inform your treating doctor.

Some patients developed secondary leukaemia when **CIPLA-DOXORUBICIN** was given in association with other DNA-damaging chemotherapeutic medicines. It may take between 1 and 3 years for this complication to develop. Your doctor will monitor you for this adverse event.

Use in pregnancy and breast feeding:

The safety of **CIPLA-DOXORUBICIN** in pregnancy and breast feeding has not been established. Thus use in pregnancy and breast feeding is contra-indicated. Adequate contraception to avoid pregnancy is indicated.

If you are pregnant or breast feeding your baby while receiving CIPLA-DOXORUBICIN, please consult your doctor, pharmacist or other healthcare professional for advice.

Important information about some of the ingredients in CIPLA-DOXORUBICIN:

CIPLA-DOXORUBICIN contains lactose monohydrate. If you suffer from a condition known as hereditary galactose intolerance, you should not receive

this medicine. You should also not receive **CIPLA-DOXORUBICIN** if you suffer from the rare Lapp lactose deficiency. Please discuss this with your treating doctor if you are unsure.

Taking other medicines with CIPLA-DOXORUBICIN?

If you are taking other medicines on a regular basis, including complementary or traditional medicines, the use of CIPLA-DOXORUBICIN with these medicines may cause undesirable interactions. Please consult your doctor, pharmacist or other healthcare professional for advice.

CIPLA-DOXORUBICIN is mainly used in combination with other anticancer medicines. You will be monitored for additive toxicity in terms of bone marrow function/blood cell counts and side-effects involving the stomach and intestines.

If you are receiving other medicines that may reduce heart function or that influence heart function (such as calcium channel blockers for hypertension or abnormal heart rhythms), your doctor will monitor you for possible complications.

If you receive any medicine that results in changes in liver function, it may have an impact on how your body reacts to **CIPLA-DOXORUBICIN**.

HOW TO RECEIVE CIPLA-DOXORUBICIN:

CIPLA-DOXORUBICIN is administered intravenously (into a vein) over a period of 3 to 5 minutes. Your doctor will decide the appropriate dosage and times of administration. He/she may decide to alter your dose should you develop any side-effects, such as low white cell counts or liver or heart function abnormalities. Your doctor will also tell you how long treatment with **CIPLA-DOXORUBICIN** will last.

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

POSSIBLE SIDE-EFFECTS:

CIPLA-DOXORUBICIN may have unintended or undesirable effects.

One of the most serious, and potential life-threatening, side-effects associated with **CIPLA-DOXORUBICIN** therapy is low white blood cell counts. White blood cells are necessary to maintain a healthy immune system and to fight infections. You should immediately report to your doctor if you develop fever or chills, cough or hoarseness, lower back or flank pain, painful or difficult urination or a sore throat.

Other serious side-effects, which you should report to your doctor as a matter of urgency, include:

- Allergic reactions, presenting with swelling of the face, lips, or throat, skin rash or hives, and difficulty breathing. Severe allergic reactions may result in death if not treated promptly.

- Swelling of the feet or legs, or shortness of breath accompanied by an inability to lie down or coughing of pink-coloured sputum, as these symptoms may be indicative of heart failure.
- Palpitations, as this may indicate heart damage.
- Ulcers in the mouth.
- Any bleeding complications, including vomiting of blood or blood per rectum.
- Severe foul-smelling diarrhoea accompanied by stomach cramps and fever as this may indicate infection or inflammation of the large bowel.
- Fever and/or chills.

Other side-effects with **CIPLA-DOXORUBICIN** that you should report to your doctor as soon as possible include:

- Secondary infections.
- Low red blood cell counts (presenting with tiredness or shortness of breath) and low platelet counts (presenting with easy bruising, pinpoint red spots on the skin, or bleeding from the gums).
- High blood uric acid levels causing attacks of gout, which usually presents with severe pain, swelling and redness of a joint, such as those of the big toe or knee. This occurs most commonly during initial treatment of patients with leukaemia or lymphoma as a result of rapid cell breakdown that leads to elevated blood uric acid concentrations.
- Painful red eyes with formation of pus (yellow discharge) or any reduction in vision.
- Pain, swelling or red streaks at the injection site.

- Nausea and vomiting (which may be severe).
- Heartburn or regurgitation or pain with eating, as this may indicate inflammation of the lining of the oesophagus or stomach or a stomach ulcer.
- Diarrhoea.
- Suppression of testicular or ovarian function. This may interfere with the production of sperm in men and the menstrual cycle in women.

Other side-effects with **CIPLA-DOXORUBICIN** that you should report to your doctor if they continue or become bothersome include:

- Tearing of the eyes.
- Hot flushes.
- Stomach pain.
- Loss of appetite.
- Redness with inflammation and pain of skin previously exposed to radiation therapy (radiation recall reactions).
- Hives (urticaria) occurring on sun-exposed skin.
- Skin rash or darkening of the nails, palms or soles.
- Reddening of the skin covering fingers, toes, ears and other peripheral parts.
- Generally feeling unwell and tiredness.

Other side-effects with **CIPLA-DOXORUBICIN** include:

- Dehydration.
- Darkening of the membrane inside the mouth.

- Changes in liver enzyme levels.
- Hair loss.
- Red discolouration of urine for 1 to 2 days after administration.
- Severe drop in blood pressure.

Not all side-effects reported for this medicine are included in this leaflet. Should your general health worsen while taking CIPLA-DOXORUBICIN, 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.

STORAGE AND DISPOSING OF CIPLA-DOXORUBICIN:

Freeze-dried powder:

Store at or below 25 ºC. Protect from light.

Vials should not be frozen. Keep vial in the outer carton until required for use.

KEEP OUT OF REACH OF CHILDREN.

Reconstituted solution:

The reconstituted solution is stable for 24 hours at room temperature below 25 ºC or for 48 hours in a refrigerator between 2 – 8 ºC. Protect from light.

KEEP OUT OF REACH OF CHILDREN.

PRESENTATION OF CIPLA-DOXORUBICIN:

CIPLA-DOXORUBICIN 10: Carton containing a 15 ml clear, transparent glass vial closed by a grey slotted rubber stopper and 20 mm blue flip-off-tear-off seal.

CIPLA-DOXORUBICIN 50: Carton containing a 50 ml clear, transparent glass vial closed by a grey slotted rubber stopper and 20 mm red flip-off-tear-off seal.

IDENTIFICATION OF CIPLA-DOXORUBICIN:

Freeze-dried powder:

CIPLA-DOXORUBICIN 10: Orange/red-coloured powder or cake.

CIPLA-DOXORUBICIN 50: Orange/red-coloured powder or cake.

Reconstituted solution:

CIPLA-DOXORUBICIN 10: A clear red-coloured solution free from visible particles.

CIPLA-DOXORUBICIN 50: A clear red-coloured solution free from visible particles.

REGISTRATION NUMBERS:

CIPLA DOXORUBICIN 10: 41/26/0034

CIPLA DOXORUBICIN 50: 41/26/0035

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

CIPLA MEDPRO (PTY) LTD

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