PACKAGE INSERT

1. NAME OF MEDICINE:
RUBIDOKS 10 mg [Concentrate for solution for Infusion]
RUBIDOKS 20 mg [Concentrate for solution for Infusion]
RUBIDOKS 50 mg [Concentrate for solution for Infusion]
R**UBIDOKS 100 mg** [Concentrate for solution for Infusion]
RUBIDOKS 200 mg [Concentrate for solution for Infusion]

2. QUALITATIVE AND QUANTITAVIE COMPOSITION:
RUBIDOKS 10 mg [Concentrate for solution for Infusion]: contains 10 mg doxorubicin hydrochloride as a concentration of 2 mg/ml in an isotonic solution
RUBIDOKS 20 mg [Concentrate for solution for Infusion]: contains 20 mg doxorubicin hydrochloride as a concentration of 2 mg/ml in an isotonic solution
RUBIDOKS 50 mg [Concentrate for solution for Infusion]: contains 50 mg doxorubicin hydrochloride as a concentration of 2 mg/ml in an isotonic solution
RUBIDOKS 100 mg [Concentrate for solution for Infusion]: contains 100 mg doxorubicin hydrochloride as a concentration of 2 mg/ml in an isotonic solution
RUBIDOKS 200 mg [Concentrate for solution for Infusion]: contains 200 mg doxorubicin hydrochloride as a concentration of 2 mg/ml in an isotonic solution
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM
Concentrate for solution for Infusion.

4. CLINICAL PARTICULARS
4.1 Therapeutic Indications
RUBIDOKS is indicated, with or without other cytotoxic medicine (s) or appropriate therapeutic intervention (s), for treatment of the following neoplastic conditions:
- Acute leukaemias (acute lymphoblastic leukaemia [ALL] and acute myelogenous leukaemia [AML]), lymphomas and a number of solid tumours.
- Metastatic adenocarcinoma of the breast, carcinoma of the bladder, bronchogenic carcinoma and neuroblastoma.
- Metastatic thyroid carcinoma, carcinoma of the endometrium, testes, prostate, cervix, head and neck, and plasma cell myeloma.
- Carcinoma of the ovary against which it is active when administered with cisplatin and cyclophosphamide.
- Carcinoma of the breast and small (oat) cell carcinoma of the lung when administered concurrently with other cytotoxic medicines.
- A wide range of sarcomas including osteogenic, Ewing's and soft tissue sarcoma.
- Hodgkin's disease where it is effective in the ABVD (doxorubicin/ bleomycin / vinblastin / dacarbazine) combination.
- Non-Hodgkin's lymphomas if administered concurrently in the BACOP combination.

4.2 Posology and method of administration
Posology:
Treatment of solid tumours:
When **RUBIDOKS** is administered as a single medicine, the recommended dose per cycle is 60 – 90 mg/m2 of body surface area every 3 – 4 weeks.
Administration of **RUBIDOKS** in a weekly regimen of 10 – 20 mg/m2 has also been shown to be effective.
RUBIDOKS is generally given as a single dose per cycle; however, it is possible to give the medicine dosage per cycle in divided administrations:
0,6 mg/kg/day for 3 days (25 mg/m2/day for 3 days) or
0,8 mg/kg/day for 2 days (30 mg/m2/day for 2 days) or
1,6 mg/kg/day for 1 day (60 mg/m2/day for 1 day)
If **RUBIDOKS** is used in combination with other antitumour medicines, the recommended dose per cycle is in the 30 – 60 mg/m2 range, repeated every 21 days.
As **RUBIDOKS** is a myelosuppressive medicine, the interval between cycles may need to be increased, or the medicine dosage reduced, in patients whose WBC counts (particularly neutrophils) are below the range of normal values before any treatment cycle. Dosage may also need to be reduced in children, in the elderly, obese patients and in pre-treated patients in whom the marrow reserve may be low.

Treatment of acute leukaemias:
In acute leukaemia the dosage schedule is based on the patient's response.
0,4 – 0,5 mg/kg/day for 3 days is the recommended starting dose.
According to the anti-leukaemia and myelosuppressive effect obtained, this course can be repeated a second or even a third time with an interval between courses of not less than 7 – 10 days.

Special populations:
Hepatic dysfunction:
In the presence of impaired hepatic function, it is suggested that RUBIDOKS dosage be reduced as follows:

Serum Bilirubin	Dose Reduction
1,2 – 3,0 mg/100 ml	50 % (i.e. 50 % of normal dose to be given)
> 3 mg /100 ml	75 % (i.e. 25 % of normal dose to be given)

RUBIDOKS should not be administered to patients with severe hepatic impairment (See "section 4.3")

Paediatric population
Method of administration
RUBIDOKS should not be given orally and should not be injected intramuscularly or subcutaneously. It is administered by intravenous injection.
Intravenous administration:
Intravenous administration of **RUBIDOKS** should be performed with caution. It is recommended that **RUBIDOKS** be administered into the tubing of a freely flowing intravenous infusion (isotonic sodium chloride or 5 % glucose solution) over a period of 3 to 5 minutes. This technique is intended to minimize the risk of thrombosis or perivenous extravasation.
Any unused portion must be discarded as this preparation is intended for single dose administration.

Incompatibilities:
RUBIDOKS should not be mixed with other medicines. Contact with alkaline solutions should be avoided since this can lead to hydrolysis of **RUBIDOKS**.
RUBIDOKS should not be mixed with heparin due to chemical incompatibility that may lead to precipitation.
Instructions for use/handling:

Intravenous administration
RUBIDOKS should be administered into the tubing of a freely flowing intravenous infusion (0,9 % sodium chloride or 5 % glucose solution) for not less than 3 – 10 minutes to minimise the risk of thrombosis or perivenous extravasation.
A direct push injection is not recommended due to the risk of extravasation, which may occur even in the presence of adequate blood return upon needle aspiration (See "Section 4.4").

Protective measures
The following protective recommendations are given due to the toxic nature of the substance:
- Personnel should be trained in good technique for reconstitution and handling.
- Pregnant staff should be excluded from working with RUBIDOKS.
- Personnel handling RUBIDOKS should wear protective clothing: goggles, gowns and disposable gloves and masks.
- Spillage or leakage should be treated with dilute sodium hypochlorite (1 % available
- chlorine) solution, preferably by soaking, and then water.
- All cleaning materials should be disposed of as indicated previously.
- In case of skin contact, thoroughly wash the affected area with soap and water or sodium bicarbonate solution. However, do not abrade the skin by using a scrub brush.
- In case of contact with the eye(s), hold back the eyelid(s) and flush the affected eye(s) with copious amounts of water for at least 15 minutes. Then seek medical evaluation by a medical practitioner.
- Always wash hands after removing gloves.

4.3 Contraindications
- Hypersensitivity to doxorubicin or any other component of the product, other anthracyclines or anthracenediones.

Patients with the following conditions:
- Persistent myelosuppression
- Hepatic impairment
- Myocardial insufficiency
- Recent myocardial infarction
- Severe dysrythmias
- Previous treatment with maximum cumulative doses of **RUBIDOKS**, daunorubicin, epirubicin, idarubicin, and/or other anthracyclines and anthracenediones (See "section 4.4")
- Pregnancy and lactation

4.4 Special warnings and precautions for use
RUBIDOKS should be administered only under the supervision of a doctor experienced in cancer chemotherapy.
Patients should be advised not to conceive and the use of contraceptives is advised.
Patients should recover from acute toxicities of prior cytotoxic treatment (such as stomatitis, neutropenia, thrombocytopenia and generalised infections) before beginning treatment with **RUBIDOKS**.
RUBIDOKS is incompatible with heparin and should also not be mixed with other medicines.
RUBIDOKS should be given with great care, in reduced doses, to elderly patients and to those with hepatic impairment.
The systemic clearance of **RUBIDOKS** is reduced in obese patients (i.e. > 130 % ideal body weight; See "section 4").
Initial treatment calls for a careful baseline monitoring of various laboratory parameters and cardiac function. Blood counts and measurement of haemoglobin concentration should be carried out routinely.

Secondary leukaemia
Secondary leukaemia, with or without a preleukaemic phase, has been reported in patients treated with **RUBIDOKS**. Secondary leukaemia is more common when such medicines are given in combination with DNA-damaging antineoplastic agents, when patients have been heavily pre-treated with cytotoxic medicines or when doses of the **RUBIDOKS** have been escalated. These leukaemias can have a 1 to 3-year latency period.

Cardiac function
Cardiotoxicity is a risk of **RUBIDOKS** treatment that may be manifested by early (i.e. acute) or late (i.e. delayed) events.
Early events: This consists mainly of sinus tachycardia and/or ECG abnormalities such as nonspecific
ST-T wave changes. Tachydysrythmias, including premature ventricular contractions and ventricular tachycardia, bradycardia as well as atrioventricular and bundle-branch block have also been reported. These events do not usually predict subsequent development of delayed cardiotoxicity, are rarely of clinical importance, and are generally not a consideration for discontinuation of **RUBIDOKS** treatment.
Late events: Delayed cardiotoxicity usually develops late in the course of therapy with **RUBIDOKS** or within 2 to 3 months after treatment termination, but later events, several months to years after completion of treatment, have also been reported. Delayed cardiomyopathy is manifested by reduced left ventricular ejection fraction (LVEF) and/or signs and symptoms of congestive heart failure (CHF) such as dyspnoea, pulmonary oedema, dependent oedema, cardiomegaly and hepatomegaly, oliguria, ascites, pleural effusion and gallop rhythm. Subacute effects such as pericarditis/myocarditis have also been reported. Life-threatening CHF is the most severe form of **RUBIDOKS**-induced cardiomyopathy and represents the cumulative dose-limiting toxicity of the medicine.
Cardiac function should be assessed before patients undergo treatment with **RUBIDOKS** and must be monitored throughout therapy to minimise the risk of incurring severe cardiac impairment. The risk may be decreased through regular monitoring of LVEF during the course of treatment with prompt discontinuation of **RUBIDOKS** at the first sign of impaired function. The appropriate quantitative method for repeated assessment of cardiac function (evaluations of LVEF) includes multi-gated radionuclide angiography or echocardiography (ECHO). A baseline cardiac evaluation with an ECG and either a multi-gated radionuclide angiography scan or an ECHO is recommended, especially in patients with risk factors for increased cardiotoxicity. Repeated multi-gated radionuclide angiography or ECHO determinations of LVEF should be performed, particularly with higher, cumulative anthracycline doses.
Haematologic toxicity
RUBIDOKS may produce myelosuppression. Haematologic profiles should be assessed before and during each cycle of therapy with **RUBIDOKS**, including differential white blood cell (WBC) counts. A dose-dependent, reversible leukaemia and/or granulocytopenia (neutropenia) is the predominant manifestation of **RUBIDOKS** haematologic toxicity and is the most common acute dose-limiting toxicity of this medicine. Leukopenia and neutropenia generally reach the nadir between days 10– 14 after medicine administration; the WBC/neutrophil counts return to normal values in most cases by day 21. Thrombocytopenia and anaemia may also occur. Clinical consequences of severe myelosuppression include fever, infections, sepsis/septicaemia, septic shock, haemorrhage, tissue hypoxia or death.

Fertility impairment
In women, **RUBIDOKS** may cause infertility during the time of medicine administration. **RUBIDOKS** may cause amenorrhoea. Ovulation and menstruation appear to return after termination of therapy, although premature menopause can occur.
RUBIDOKS is mutagenic and can induce chromosomal damage in human spermatozoa.
Oligospermia or azoospermia may be permanent. Men undergoing **RUBIDOKS** treatment should use effective contraceptive methods.

Gastrointestinal
RUBIDOKS is emetogenic. Mucositis/stomatitis generally appear early after medicine administration and, if severe, may progress over a few days to mucosal ulcerations. Most patients recover from this adverse event by the third week of therapy.

Liver function
The major route of elimination of **RUBIDOKS** is the hepatobiliary system. Serum total bilirubin should be monitored before and during treatment with RUBIDOKS.
Patients with elevated bilirubin may experience slower clearance of the medicine with an increase in overall toxicity. Lower doses are recommended in these patients (See "Section 4.2"). Patients with severe hepatic impairment should not receive **RUBIDOKS** (See "Section 4.3").

Effects at site of injection
Phlebosclerosis may result from an injection into a small vessel or from repeated injections into the same vein. Following the recommended administration procedures may minimise the risk of phlebitis/ thrombophlebitis at the injection site (See "**Section 4.2 – method of administration**").

Extravasation
Extravasation of **RUBIDOKS** during intravenous injection may produce local pain, severe tissue lesions (vesication, severe cellulitis) and necrosis. Should signs or symptoms of extravasation occur during intravenous administration of **RUBIDOKS**, the medicine infusion should be stopped immediately.

Other
RUBIDOKS may potentiate the toxicity of other anticancer therapies. Exacerbation of cyclophosphamide-induced haemorrhagic cystitis and enhanced hepatotoxicity of 6-mercaptopurine have been reported. Radiation-induced toxicities (myocardium, mucosae, skin and liver) have also been reported.
As with other cytotoxic agents, thrombophlebitis and thromboembolic phenomena including pulmonary embolism (in some cases fatal) have been coincidentally reported with the use of **RUBIDOKS**.

Tumour-lysis syndrome
RUBIDOKS may induce hyperuricaemia as a consequence of the extensive purine catabolism that accompanies drug induced rapid lysis of neoplastic cells (tumour-lysis syndrome). Blood uric acid levels, potassium, calcium phosphate and creatinine should be evaluated after initial treatment. Hydration, urine alkalinisation, and prophylaxis with allopurinol to prevent hyperuricaemia may minimize potential complications of tumour lysis syndrome.

Vaccinations
Administration of live or live-attenuated vaccines in patients immuno-compromised by chemotherapeutic agents including **RUBIDOKS**, may result in serious or fatal infections. Vaccination with a live vaccine should be avoided in patients receiving **RUBIDOKS**. Killed or inactivated vaccines may be administered; however, the response to such vaccines may be diminished.

4.5 Interaction with other medicines and other forms of interaction
RUBIDOKS is a major substrate of cytochrome P450 CYP3A4 and CYP2D6, and P-glycoprotein (P-gp). Clinically significant interactions have been reported with inhibitors of CYP3A4, CYP2D6, and/or P-gp (e.g., verapamil), resulting in increased concentration and clinical effect of **RUBIDOKS**. Inducers of CYP3A4 (e.g, phenobarbital, phenytoin, St. John's Wort) and P-gp inducers may decrease the concentration of **RUBIDOKS**.
The addition of ciclosporin to **RUBIDOKS** may result in increases in area under the concentration-time curve (AUC) for both **RUBIDOKS** and doxorubicinol possibly due to a decrease in clearance of the parent drug and a decrease in metabolism of doxorubicinol. Literature reports suggest that adding ciclosporin to **RUBIDOKS** results in more profound and prolonged haematologic toxicity than that observed with **RUBIDOKS** alone. Coma and seizures have also been described with concomitant administration of ciclosporin and **RUBIDOKS**.
High dose ciclosporin increases the serum levels and myelotoxicity of **RUBIDOKS**.
RUBIDOKS is mainly used in combination with other cytotoxic medicines. Additive toxicity may occur especially with regard to bone marrow/haematologic and gastrointestinal effects (See "section 4.4"). The use of **RUBIDOKS** in combination chemotherapy with other potentially cardiotoxic medicine, as well as the concomitant use of other cardioactive compounds (e.g. calcium channel blockers), requires monitoring of cardiac function throughout treatment. Changes in hepatic function induced by concomitant therapies may affect **RUBIDOKS** metabolism, pharmacokinetics, therapeutic efficacy and/or toxicity.
Paclitaxel can cause increased plasma-concentrations of **RUBIDOKS** and/or its metabolites when given prior to **RUBIDOKS**. A smaller increase is observed when paclitaxel is administered after **RUBIDOKS**.

4.6 Fertility, pregnancy and lactation
Women of childbearing potential/Contraception in males and females:
Patients should be advised not to conceive and the use of contraceptives is advised. (See "Section 4.4"). **RUBIDOKS** may cause amenorrhoea.
Ovulation and menstruation appear to return after termination of therapy, although premature menopause can occur. (See "Section 4.4").

Pregnancy
The use of **RUBIDOKS** is contraindicated during pregnancy (see "sections 4.3 and 4.5").
Breast feeding
The use of **RUBIDOKS** is contraindicated during lactation (see "sections 4.3 and 4.5").
Fertility
In women, **RUBIDOKS** may cause infertility during the time of medicine administration. **RUBIDOKS** is mutagenic and can induce chromosomal damage in human spermatozoa.
Oligospermia or azoospermia may be permanent. Men undergoing **RUBIDOKS** treatment should use effective contraceptive methods. (See "section 4.4")

4.7 Effects on ability to drive and use machines
The effect of **RUBIDOKS** on the ability to drive or use machinery has not been systematically evaluated.

4.8 Undesirable effects
Infections and infestations:
Frequent: Infection, sepsis/septicaemia.
Neoplasms benign, malignant and unspecified (including cysts and polyps):
Frequency not known: Acute lymphocytic leukaemia, acute myeloid leukaemia.
Blood and lymphatic system disorders:
Frequent: Leukopenia (see "section 4.4"), anaemia, thrombocytopenia, haemorrhage, and neutropenia.
Less frequent: Acute lymphocytic leukaemia, acute myelogenous leukaemia (see " section 4.4").
Immune system disorders:
Less frequent: Anaphylaxis, allergic reaction.
Metabolism and nutrition disorders:
Frequent: Decreased appetite
Less frequent: Hyperuricaemia or uric acid nephropathy. This occurs most frequently during initial treatment of patients with leukaemia or lymphoma as a result of rapid cell breakdown that leads to elevated serum uric acid concentrations.
Eye disorders:
Less frequent: Conjunctivitis/keratitis, lacrimation.
Cardiac disorders:
Frequent: ECG abnormalities, sinus tachycardia, tachydysrhythmias, atrioventricular and bundle branch block, asymptomatic reductions in left ventricular ejection fraction, and congestive heart failure (see " section 4.4")
Vascular:
Less frequent: Phlebitis, thrombophlebitis, thromboembolism, hot flushes, embolism.
Gastrointestinal:
Frequent: Oesophagitis, stomatitis, nausea and vomiting (may be severe), diarrhoea, mucositis, abdominal pain, anorexia, and dehydration.
Less frequent: Gastric erosions, gastrointestinal bleeding, hyperpigmentation of the oral mucosa, colitis, and gastrointestinal ulceration.
Hepatobiliary disorders:
Less frequent: Changes in transaminase levels.
Skin and subcutaneous tissue disorders:
Frequent: Alopecia, rash/itch, skin changes.
Less frequent: Skin and nail hyperpigmentation, hypersensitivity reactions in irradiated skin (radiation recall reactions), photosensitivity urticaria, and acral erythema.
Renal and urinary disorders:
Frequent: Red colouration of urine for 1 to 2 days after administration.
Reproductive system and breast disorders:
Frequent: Amenorrhoea, oligospermia, azoospermia.
General disorders and administrative site conditions:
Frequent: Malaise/asthenia, fever, chills, shock, local toxicity.
Less frequent: Extravasation, cellulitis or tissue necrosis at injection site, phlebosclerosis.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicines. Healthcare providers are asked to report any suspected adverse reactions to SAHPRA via the **"6.04 Adverse Reactions Reporting Form"**, found online under SAHPRA's publications:
https://www.sahpra.org.za/Publications/Index/8

5. PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties
The medicine class is: Cytostatic agent, A 26
Mechanism of action:
Doxorubicin is an anthracycline antibiotic with anti-neoplastic activity against a range of tumours. Its exact mechanism of antineoplastic activity is unknown but is thought involve binding to DNA by intercalation between base pairs and inhibition of DNA and RNA synthesis by template disordering and steric obstruction. Other possible mechanisms of antineoplastic activity include binding to cell membrane lipids, thus altering a variety of cellular functions and interacting with topoisomerase II to form DNA-cleavable complexes.

5.2 Pharmacokinetic properties
Distribution:
Doxorubicin is quickly and widely distributed into the extravascular compartments, as indicated by a rapid (5 to 10 min) distribution half-life and by a steady state distribution volume in excess of 20 to 30 litres/kg. However, doxorubicin does not cross the blood-brain barrier in
detectable amounts but may cross the placenta and is distributed into breast milk. Binding of doxorubicin to plasma protein is extensive.

Metabolism:
Doxorubicin is metabolised to a significant extent by the liver. The major active metabolite is 13-OH-doxorubicinol.

Elimination:
The elimination half-life of doxorubicin and 13-OH-doxorubicinol is 20 to 48 hours.
Forty to fifty percent of the administered dose is recovered in the bile or in the faeces in seven days, of which about half is as unchanged medicine. Renal excretion is modest, accounting for only 5 – 10 percent of the administered dose in 5 days.

5.3. Pre-Clinical safety data
No additional information is available.

6. PHARMACEUTICAL PARTICULARS
6.1 List of excipients
The excipients are: Sodium Chloride, hydrochloric acid, water for injections.

6.2 Incompatibilities
RUBIDOKS should not be mixed with other medicines. Contact with alkaline solutions should be avoided since this can lead to hydrolysis of **RUBIDOKS**.
RUBIDOKS should not be mixed with heparin due to chemical incompatibility that may lead to precipitation. (see section 4.2)

6.3 Shelf life
18 months

6.4 Special Precautions for storage
Store in a refrigerator between 2 – 8 °C and protect from light.

6.5 Nature and contents of container
RUBIDOKS is a red solution packed in clear colourless Type I borosilicate glass vials with 20 mm Teflon lined chlorobutyl Type 1 rubber stoppers and 20 mm aluminium flip-off seals with plastic caps.
RUBIDOKS 10 mg is packed in a 6 ml vial. Each vial is packed in a single carton pack
RUBIDOKS 20 mg is packed in a 10 ml vial. Each vial is packed in a single carton pack
RUBIDOKS 50 mg is packed in a 25 ml vial. Each vial is packed in a single carton pack
RUBIDOKS 100 mg is packed in a 50 ml vial. Each vial is packed in a single carton pack
RUBIDOKS 200 mg is packed in a 100 ml vial. Each vial is packed in a single carton pack.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling
Any unused product or waste material should be disposed of in accordance with local requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION
Innovata Pharmaceuticals (Pty) LTD
Crownwood Office Park
100 Northern Parkway
Ormonde
Johannesburg
2091

8. MANUFACTURED BY:
Sichuan Huiyu Pharmaceuticals Co.,Ltd.
Building 3, No.333, Hanyang Road,
Shizhong District, Neijiang,
Sichuan CN-641000, China

9. REGISTRATION NUMBERS
Namibia: NS2
Zimbabwe: PP
Zambia: POM
Botswana: S2

10. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

11. DATE OF REVISION OF THETEXT
14/08/2023

520 mm

250 mm
Front Side

Type: Pack Insert
Size: 400 x 520 mm

GRAPHIC DESIGNER	REGULATORY AFFAIRS		REVIEWED BY MEDICAL	Manufacturers Approval
	Prepared by	Reviewed by		
Sign:	Sign:	Sign:	YES ☐ NO ☐	YES ☐ NO ☐
Date:	Date:	Date:	Date:	Date:

PATIENT INFORMATION LEAFLET

PRODUCT NAME, STRENGTH AND PHARMACEUTICAL FORM
RUBIDOKS 10 mg [Concentrate for solution for Infusion]
RUBIDOKS 20 mg [Concentrate for solution for Infusion]
RUBIDOKS 50 mg [Concentrate for solution for Infusion]
RUBIDOKS 100 mg [Concentrate for solution for Infusion]
RUBIDOKS 200 mg [Concentrate for solution for Infusion]

Read all of this leaflet carefully before you start taking RUBIDOKS
- Keep this leaflet. You may need to read it again
- If you have further questions, please ask your doctor, pharmacist, nurse or other health care provider

What is in this leaflet
1. WHAT RUBIDOKS IS AND WHAT IT IS USED FOR:
The active substance is doxorubicin hydrochloride.
- **RUBIDOKS** belongs to a group of medicines called cytotoxics used for treatment of cancers.
- **RUBIDOKS** slows or stops the growth of cancer cells and increases their likelihood to die
- **RUBIDOKS** is used to treat a variety of cancers, either alone or in combination with other medicines. The way in which it is used depends upon the type of cancer that is being treated. **RUBIDOKS** can be used in both adults and children.
- **RUBIDOKS** is used in the treatment of cancers of the breast, the bladder, ovary, bones, thyroid and lung. In addition, **RUBIDOKS** is used to treat cancers of the blood forming tissues such as malignant lymphomas, leukaemia and multiple myeloma.

2. WHAT YOU NEED TO KNOW BEFORE YOU TAKE RUBIDOKS
Do not take RUBIDOKS:
- If you are allergic to doxorubicin or any of the other ingredients of **RUBIDOKS**.
- If you have low blood cell counts, as it can lower them further.
- If you have previously been treated with doxorubicin or similar chemotherapy medicines like pharmorubicin, idarubicin, epirubicin or daunorubicin as previous treatment with these similar medicines can increase the risk of side effects with this medicine.
- If you have suffered with severe heart trouble in the past or are presently receiving treatment for this.
- If you have liver problems
- If you have a urine infection or inflammation of the bladder.
- If you are pregnant or breastfeeding.

Warnings and precautions
Take Special Care with **RUBIDOKS**:
- If you have or have ever had heart disease, either before or during radiotherapy
- If you have had or are due to have live or live-attenuated vaccinations.
- If you have a bone marrow disease
- If you have decreased bone marrow function
- If you have had prior treatment with anthracycline
- If you have had mediastinal irradiation (radiotherapy in the region between the lungs, where the heart and major blood vessels are located)
- If you have hepatic impairment (liver damage) or blocked bile flow
- If you have severe renal impairment (kidney damage)

Other medicines and RUBIDOKS:
Always tell your health care provider if you are taking any other medicine. (This includes all complementary or traditional medicines).
Problems are more likely if you have been given other anticancer medicines, especially at high doses, just before or at the same time as **RUBIDOKS**. If you have recently been treated with another anticancer medicine, you will be given time to recover from effects of the anticancer medicine before you begin treatment with this medicine. Your doctor will want to monitor you carefully during and after treatment
Please tell your doctor or pharmacist if you have recently taken any other medicines, even those not prescribed, particularly any of the following:
- Ciclosporin: Which can make the effects of **RUBIDOKS** stronger
- Calcium channel blocker: medicines for your heart.
- Sorafenib used to treat inoperable liver cancer and advanced kidney cancer.

Pregnancy and breastfeeding and fertility
If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other health care provider for advice before taking this medicine.
- Avoid becoming pregnant while you or your partner is being treated with this medicine. If you are sexually active, you are advised to use effective birth control to prevent pregnancy during treatment, whether you are male or female. It may cause birth defects, so it is important to tell your doctor if you think you are pregnant.
- You should stop breast-feeding before starting treatment with this medicine as some of the drug may get into your breast milk and possibly harm your child.
- Ask your doctor or pharmacist for advice before taking any medicine while breast-feeding.
- **RUBIDOKS** can affect fertility I in women during the time of treatment with **RUBIDOKS**
- **RUBIDOKS** may cause amenorrhoea (the absence of menstruation).

Driving and using machines
You may feel dizzy, confused or lightheaded after being given **RUBIDOKS**. If this happens, do not drive or use any tool or machines. Ask your doctor if you are not sure.
It is not always possible to predict to what extent **RUBIDOKS** may interfere with the daily activities of a patient. Patients should ensure that they do not engage in the above activities until they are aware of the measure to which **RUBIDOKS** affects them.

RUBIDOKS contains:
The excipients for **RUBIDOKS** are: Sodium Chloride, hydrochloric acid, water for injections.

3. HOW TO USE RUBIDOKS
If you are prescribed **RUBIDOKS** it will only be given to you by doctors or nurses experienced in giving chemotherapy.
RUBIDOKS will normally be given to you by a doctor or nurse through a drip (infusion) into a vein.
Your doctor will decide what dose of **RUBIDOKS** to give and the number of days treatment you will receive depending on your condition. You will be monitored regularly both during and after your treatment.
The dose is decided by taking into account the condition you have, your height and weight. From your height and weight, the doctor will calculate your body surface area; and it is this that your dose is calculated from.
While one course of treatment may sometimes be enough, more often your doctor will advise further courses that **RUBIDOKS** is not affecting the way it functions in a harmful way.

If you receive more RUBIDOKS than you should
Since a health care provider will administer **RUBIDOKS**, he / she will control the dosage. However, in the event of overdosage your doctor will manage the overdosage

If you forget to use RUBIDOKS
Since a health care provider will administer **RUBIDOKS** it is unlikely that the dose will be missed.

If you stop taking RUBIDOKS
Do not stop treatment early. Treatment is continued as long as possible. If the condition gets worse or the side effects are unacceptable, the treatment will be stopped. The healthcare practitioner will take the necessary decisions when treatment is stopped.

4. POSSIBLE SIDE EFFECTS
RUBIDOKS can have side effects.
Not all side-effects reported for RUBIDOKS are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking RUBIDOKS, please consult your healthcare provider for advice.

If any of the following happens, tell your doctor immediately:
- White blood cell counts (which fight infection) can drop, increasing the chance of infections and a raised temperature or fever. You may develop chills, cough or hoarseness, lower back or flank pain, painful or difficult urination or a sore throat
- Feeling dizzy, feverish, short of breath with a tight chest or sore throat or have an itchy rash. This type of allergic reaction can be very serious.
- 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.

These are all very serious side effects. If you have them, you may have had a serious reaction to RUBIDOKS. 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:
- Secondary infections (an infection that occurs during or after treatment).
- 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.

These are all serious side effects. You may need urgent medical attention.
Tell your doctor if you notice any of the following:
Frequent:
- Loss of appetite.
- Generally feeling unwell and tiredness.
- Dehydration
- Hair loss

Less Frequent:
- Stomach pain.
- 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.

Frequency Unknown:
- Tearing of the eyes.
- Hot flushes.
- Darkening of the membrane inside the mouth
- Changes in liver enzyme levels.
- Red discolouration of urine for 1 to 2 days after administration.
- Severe drop in blood pressure.

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.
Reporting of side effects
If you get side effects, talk to your doctor or pharmacist or nurse. You can also report side effects to SAHPRA via the "**6.04 Adverse drug Reaction reporting Form**", found online under SAHPRA's publications:
https://www.sahpra.org.za/Publications/Index/8.
By reporting side effects, you can help provide more information on the safety of **RUBIDOKS**.

5. HOW TO STORE RUBIDOKS
Store in a refrigerator between 2 – 8 °C and protect from light
Any unused medicine or waste material should be returned to the pharmacy for destruction. Do not dispose of unused medicine in drains or sewerage systems (e.g toilets).
STORE ALL MEDICINES OUT OF REACH OF CHILDREN

6. CONTENTS OF THE PACK AND OTHER INFORMATION
What RUBIDOKS contains:
The active substance is doxorubicin hydrochloride
The other ingredients of **RUBIDOKS** are sodium chloride, hydrochloric acid, water for injections.

What RUBIDOKS looks like and contents of the pack.
RUBIDOKS is a red solution packed in clear colourless Type I borosilicate glass vials with 20 mm Teflon lined chlorobutyl Type 1 rubber stoppers and 20 mm aluminium flip-off seals with plastic caps
RUBIDOKS 10 mg is packed in a 6 ml vial. Each vial is packed in a single carton pack
RUBIDOKS 20 mg is packed in a 10 ml vial. Each vial is packed in a single carton pack
RUBIDOKS 50 mg is packed in a 25 ml vial. Each vial is packed in a single carton pack
RUBIDOKS 100 mg is packed in a 50 ml vial. Each vial is packed in a single carton pack
RUBIDOKS 200 mg is packed in a 100 ml vial. Each vial is packed in a single carton pack.
Not all pack sizes may be marketed.

Holder of Certificate of Registration
Innovata Pharmaceuticals (Pty) LTD
Crownwood Office Park
100 Northern Parkway
Block D
Ormonde
Johannesburg
2091
SOUTH AFRICA

Manufactured By:
Sichuan Huiyu Pharmaceuticals Co.,Ltd.
Building 3, No.333, Hanyang Road,
Shizhong District, Neijiang,
Sichuan CN-641000, China

This leaflet was revised in
14/08/2023

Registration number
Namibia: NS2
Zimbabwe: PP
Zambia: POM
Botswana: S2

Access to the corresponding Professional information.
A copy of the professional Information is contained in the packaging of **RUBIDOKS**.

Ver.00

520 mm

250 mm
Back Side