Sultanate of Oman
Ministry of Health
Directorate General of Pharmaceutical
Affairs and Drug Control
Muscat

سلطنة عُمان
وزارة الصحة
المديرية العامة للصيدلة
والرقابة الدوائية
مسقط

To:

Director General of Royal Hospital
Director General of Khoula Hospital
Director General of Medical Supplies (MOH)
Director General of Pvt. Health Est. Affairs (to kindly arrange distribution to all Pvt. Health Institutions)
Director General of Health Services in all Governorates
Director of Rational Use of Medicine (MOH)
Hospital Director (Al Nahda Hospital)
Hospital Director (Al Massara Hospital)
The Head of Medical Services in SQU Hospital
The Head of Medical Services in Royal Oman Police
The Head of Medical Services in Ministry of Defense
The Head of Medical Services in The Diwan
The Head of Medical Services in The Sultan's Special Force
The Head of Medical Services in Internal Security Services
The Head of Medical Services in Petroleum
The Head of Medical Services in LNG Oman
Director of Pharmacy of Qaboos Comprehensive Cancer Care & Research Center
Director of Pharmacy & Medical Stores in all Governorate (for distribution pls.)
Marketing Authorization Holders & Pharmaceutical Companies
ALL PRIVATE PHARMACIES & DRUG STORES

After Compliments,

Please find attached our Circular No 93 **dated** 16/5/2023 **regarding Nitrofurantoin: reminder of the risks of pulmonary and hepatic adverse drug reactions.**

Copy to:

- **Director, Office of H.E. The Undersecretary for Health Affairs**
- **Director of Pharmacovigilance & Drug Information Dept, DGPA&DC**
- **Director of Drug Control Department, DGPA&DC**
- **Director of Pharmaceutical Licensing Department, DGPA&DC**
- **Director of Central Quality Control Lab., DGPA&DC**
- **Director of Medical Device Control, DGPA&DC**
- **Section Head PV for Herbal Medicine & Health Products.**
- **Section Head PV for Human Medicine**
- **Section Head of Central Drug Information**

PADC
المديرية العامة للصيدلة والرقابة الدوائية
Directorate General of Pharmaceutical Affairs & Drug Control

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Circular No. 93 / 2023

24-10-1444 H

15-05-2023

Subject: Nitrofurantoin: reminder of the risks of pulmonary and hepatic adverse drug reactions.

The DGPA&DC would like to share a safety information issued from Medicine and Healthcare Products Regulatory Authority (MHRA) regarding the use of nitrofurantoin. Healthcare professionals prescribing nitrofurantoin should be alert to the risks of pulmonary and hepatic adverse drug reactions and advise patients to be vigilant for the signs and symptoms in need of further investigation.

Advice for healthcare professionals:

- Advise patients and caregivers to be vigilant for new or worsening respiratory symptoms while taking nitrofurantoin and promptly investigate any symptoms that may indicate a pulmonary adverse reaction
- Pulmonary reactions may occur with short- or long-term use of nitrofurantoin, and increased vigilance for acute pulmonary reactions is required in the first week of treatment
- Patients receiving long-term therapy, for example for recurrent urinary tract infections, should be closely monitored for new or worsening respiratory symptoms, especially if elderly
- immediately discontinue nitrofurantoin if new or worsening symptoms of pulmonary damage occur.
- Be vigilant for symptoms and signs of liver dysfunction in patients taking nitrofurantoin for any duration, but particularly with long-term use, and monitor patients periodically for signs of hepatitis and for changes in biochemical tests that would indicate hepatitis or liver injury.
- Use caution when prescribing nitrofurantoin in patients with pulmonary disease or hepatic dysfunction, which may mask the signs and symptoms of adverse reactions.
- Advise patients to read carefully the advice in the Patient Information Leaflet about symptoms of possible pulmonary and hepatic reactions and to seek medical advice if they experience these symptoms.

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Advice for healthcare professionals to give to patients and caregivers:

- Nitrofurantoin is an effective antibiotic used to prevent and treat infections of the bladder, kidney, and other parts of the urinary tract, but it has been linked to side effects affecting the lungs and liver.
- If you are taking nitrofurantoin, seek medical advice if you experience trouble breathing, shortness of breath, a lingering cough, coughing up blood or mucus, or pain or discomfort when breathing. These may be symptoms of a side effect affecting the lungs.
- Talk to your doctor or another healthcare professional promptly if you develop yellowing of the skin or eyes, upper right abdominal pain, dark urine and pale or grey-colored stools, itching or joint pain and swelling. These may be symptoms of a side effect affecting the liver.

Pulmonary damage and nitrofurantoin:

Nitrofurantoin is a broad-spectrum antibacterial agent, which has been available since the 1950s. It is indicated in adults, children and infants over 3 months old for:

- Treatment and prophylaxis of acute or recurrent uncomplicated urinary tract infections (UTIs).
- Treatment and prophylaxis of acute or recurrent uncomplicated pyelitis.

The NICE guidelines on antimicrobial prescribing for UTIs recommend nitrofurantoin as one of the first choices, particularly if there is a high risk of trimethoprim resistance. Treatment courses for infections are indicated to last between 3 and 7 days. However, some patients may be given a daily dose as prophylaxis for recurrent UTIs.

The potential for acute pulmonary damage with nitrofurantoin is well-documented in the product information for nitrofurantoin. The Summary of Product Characteristics (SmPC) states that acute, subacute and chronic pulmonary adverse reactions have been observed in patients treated with nitrofurantoin. Symptoms of acute pulmonary reactions usually include fever, chills, cough, chest pain, dyspnea, pulmonary infiltration with consolidation or pleural effusion on chest X-ray, and eosinophilia. For subacute pulmonary reactions, fever and eosinophilia occur less often than in the acute form.

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Information from published studies on the frequency or severity of pulmonary adverse drug reactions in association with acute use of nitrofurantoin is limited. A precise estimate of frequency of these pulmonary adverse drug reactions and the frequency of fatal outcomes cannot be made, but evidence from observational studies suggests that the pulmonary adverse drug reactions in association with acute use of nitrofurantoin are infrequent.

If symptoms of pulmonary damage occur, nitrofurantoin should be discontinued immediately. The Patient Information Leaflet (PIL) advises patients that lung adverse reactions may occur and that patients should consult a doctor immediately if they notice symptoms of a lung reaction. Close monitoring of pulmonary conditions is advised for patients receiving long-term therapy (especially elderly people). Patients and careers should be reminded about the symptoms of pulmonary damage and the need to seek prompt medical advice if they experience these symptoms.

Reminder of the risk of hepatic reactions:

Nitrofurantoin can rarely cause hepatic reactions, including cholesteric jaundice, chronic active hepatitis, autoimmune hepatitis, and hepatic necrosis. Events with a fatal outcome have been reported. Nitrofurantoin should be discontinued immediately if hepatitis occurs.

The onset of hepatitis may be gradual and may not have obvious symptoms at first. It is important to monitor patients periodically for changes in biochemical tests that could indicate hepatic dysfunction and for clinical signs or symptoms of liver abnormality, especially in patients taking long-term nitrofurantoin.

When scheduling periodic monitoring, take into account relevant local guidance, as well as any pre-existing conditions that might mask the symptoms of a hepatic reaction and the patient's ability to recognize symptoms and seek advice in the event of a hepatic reaction. This periodic monitoring may be an opportunity to remind patients about the possible symptoms of hepatic reactions and to remind them to seek medical advice if they experience these symptoms.

Call to report:

Nitrofurantoin is registered in Oman, healthcare professionals, patients, and caregivers are requested to submit adverse drug reactions reports to the pharmacovigilance department in the DGPA&DC.

Dr. Mohammed Hamdan Al Rubaie

Director General