DIPARTIMENT TAS-SAĦĦA DEPARTMENT OF HEALTH
MALTA

L-Uffiċċju tal-Uffiċjal Mediku Ewlieni *Office of the Chief Medical Officer*

DH CIRCULAR No. 431/2012
DH: 3943/2012

13th November 2012

Attention All: Consultants
Medical Officers
Pharmacists
Pharmacy Technicians
Nurses

Re: Methotrexate 2.5mg Tablets

The following information about methotrexate is being brought to you for your attention since there have been some reported prescribing and dispensing errors with this medicine. Tablets are being prescribed once daily instead of **once weekly**.

Daily instead of weekly administration in patients with psoriasis or rheumatoid arthritis may result in fatal toxicity.
The most common dose-related toxic effects of methotrexate are on the bone marrow and gastrointestinal tract. Bone-marrow depression can occur abruptly, and leucopenia, thrombocytopenia, and anaemia may all occur. Ulceration of the mouth and gastrointestinal disturbances are also early signs of toxicity: stomatitis and diarrhea during treatment indicate that it may need to be interrupted; otherwise haemorrhagic enteritis, intestinal perforation, and death may follow.
Methotrexate is associated with liver damage, both acute (notably after high doses) and, more seriously, chronic (generally after long-term use). Hepatic fibrosis and cirrhosis may develop without obvious signs of hepatotoxicity, and have led to eventual death. Other adverse effects include renal failure and tubular necrosis after high doses, pulmonary reactions including life-threatening interstitial lung disease, skin reactions (sometimes severe), alopecia, and ocular irritation.

Disease	**Dosage Regimen** (as stated in BNF 64)
Malignant Diseases	Leukaemia in children (maintenance), 15mg/m^2 weekly in combination with other drugs
Crohn's Disease	Maintenance of remission of severe Crohn's disease [unlicensed indication], adult over 18 years, 10–25mg once weekly
Psoriasis	Adult over 18 years, 2.5–10mg once weekly, increased according to response in steps of 2.5–5mg at intervals of at least 1 week; usual dose is 7.5–15mg once weekly; max. weekly dose 30mg.
Rheumatoid Arthritis	Moderate to severe active rheumatoid arthritis, adult over 18 years, 7.5mg once weekly, adjusted according to response; max. weekly dose 20mg.

"PALAZZO CASTELLANIA" 15, MERCHANTS STREET, VALLETTA, VLT 03
Tel. Nos. +00356 21224071/ 2299 2232 Fax no. +00356 2299 2663
e-mail: cmo.mhec@gov.mt

Kindly note that the above doses are **weekly** doses. To avoid error with low-dose methotrexate, it is recommended that:

- the patient is carefully advised of the dose and frequency and the reason for taking methotrexate and any other prescribed medicine (e.g. folic acid);
- only one strength of methotrexate tablet is prescribed and dispensed;
- the prescription and the dispensing label clearly show the dose and frequency of methotrexate administration;
- the patient is warned to report immediately the onset of any feature of blood disorders (e.g. sore throat, bruising, and mouth ulcers), liver toxicity (e.g. nausea, vomiting, abdominal discomfort, and dark urine), and respiratory effects (e.g. shortness of breath).

Thank you
For your attention, please

Dr. Natasha Azzopardi Muscat
Chief Medical Officer

"PALAZZO CASTELLANIA" 15, MERCHANTS STREET, VALLETTA, VLT 03
Tel. Nos. +00356 21224071/ 2299 2232 **Fax no. +00356 2299 2663**
e-mail: **cmo.mhec@gov.mt**