20th February 2012

Circular No. P04/2012

Dear Healthcare Professional,

Re: European Medicines Agency reviews dose recommendations for anti-tuberculosis medicines used in children

The Medicines Authority would like to inform you of the European Medicines Agency (EMA) review of dosing recommendations from the World Health Organization (WHO) for first-line anti-tuberculosis medicines in children. While most cases of tuberculosis are limited to developing countries, tuberculosis disease is still prevalent in some European Member States. Malta has one of the lowest reported incidence rates of tuberculosis in Western Europe. [1]

The review of anti-tuberculosis medication was triggered in 2011 by the French medicines agency, following the publication of pharmacokinetic data on use of anti-tuberculosis medicines in children, which showed that weight-based dosing regimens based on corresponding adult weight might lead to sub-optimal exposure in children. The issue was recognised by the WHO in 2008, which subsequently recommended changes to dosing. The review did not address multi-resistant tuberculosis. This review also aimed at optimising the therapeutic management of the disease in the European Union and harmonising dosing in order to encourage the development of fixed dose combinations (FDC) by pharmaceutical companies. FDCs are important as they can improve how successful the patient is in

[1] Farrugia B, Gauci C, Fiorini A, Cacciottolo J: Tuberculosis in Malta: comparisons between the young and elderly in a low incidence country. Malta Medical Journal, 2010: 1; 21

following medical advice in terms of taking medicine at the right time and taking the correct number and combination of tablets. This can be especially challenging with children.

While the EMA's Committee for Human Medicinal Products (CHMP) acknowledged that the dosing regimen of first-line anti-tuberculosis therapies is difficult to define in children due to the limited data available and several other influencing factors, it agreed with the WHO dosing recommendations for ethambutol, isoniazid, pyrazinamide and rifampicin for children above three months as follows:

Ethambutol:	20 (15-25) mg/kg
Isoniazid:	10 (10-15) mg/kg
Pyrazinamide:	35 (30-40) mg/kg
Rifampicin:	15 (10-20) mg/kg

The availability of these medicines in Malta is given in Table1.

The Committee acknowledged the WHO conclusion that no dosing recommendation can be made in children less than three months due to the lack of specific data. The Medicines Authority is in agreement with the full **press release** issued by the EMA.

Table 1: Active ingredients and pharmaceutical form of antimycobacterial medicinal products authorised in Malta.

Active Ingredients	Pharmaceutical Form
Ethambutol Hydrochloride BP 100mg	COATED TABLET
Ethambutol Hydrochloride BP 400mg	COATED TABLET
Isoniazid BP 100mg	TABLET
Isoniazid 50mg/2ml	I.M INJECTION
Pyrazinamide 500mg	FILM-COATED TABLET
Rifampicin 150mg, Isoniazid 100mg	TABLET, SUGAR COATED
Rifampicin 20mg/mll	ORAL SUSPENSION
Rifampicin 300mg	CAPSULE, HARD
Rifampicin 150mg, Isoniazid 100mg	COATED TABLET
Rifampicin 300mg, Isoniazid 150mg	COATED TABLET
Rifampicin 600mg	POWDER AND SOLVENT FOR SOLUTION FOR INFUSION
Rifampicin 600mg/vial (as sodium)	POWDER FOR SOLUTION FOR INFUSION

*** Information obtained from Malta Medicines List and Government Hospital Formulary List

Healthcare professionals are encouraged to regularly check the Medicines Authority website for product safety updates as these are issued on an ongoing basis.