PHARMACY BULLETIN

EDITION 16 ISSUE 9 PPUKM 2015

Updates on Safety of Metoclopramide by PRP Asnirah & Ms Izyan

Malaysian Adverse Drug Reactions Advisory Committee (MADRAC) has tighten the indication of metoclopramide and has instructed companies to update the product inserts of all metoclopramide-containing products following studies conducted by the National Pharmaceutical Control Bureau (NPCB). Currently there are **31 products** containing metoclopramide registered with NPCB; 17 tablet preparations, 4 syrups, 9 parenteral products and 1 suppository. From 2000 to 2014, NPCB has received a total of **558 reports** with **972 adverse events** for products containing metoclopramide. Around **426 (76.3%)** of the ADRs were related to neurological side effects involving oculogyric crisis symptoms and extrapyramidal symptoms, while another **132 (23.7%)** reports were non-neurological such as **rash, itching, increased sweating and shortness** of **breath**. Further analysis showed that more than half **(220/426 or 51.6%)** of the ADRs occurred in pediatric patients, especially use of suppository among pediatrics less than 1 year old.

Table 1: Reported Neurological Adverse Drug Reactions Among Pediatric Patients According to Age Category

Dosage form of metoclopramide	**Patient's age (years old)**				
	< 1	1-6	7-12	13-18	Total
Injection	2 (2.5%)	4 (4.9%)	5 (6.2%)	70 (86.4%)	**81 (36.8%)**
Oral (tablets/syrups)	5 (4.2%)	10 (8.5%)	63 (53.4%)	40 (33.9%)	**118 (53.6%)**
Suppository	5 (71.4%)	2 (28.6%)	0	0	**7 (3.2%)**
Unreported	0	0	9 (64.3%)	5 (35.7%)	**14 (6.4%)**
Total	**12**	**16**	**77**	**115**	**220**

On 8th January 2015, Drug Control Authority (DCA) issued a directive **[Bil. (24) dlm.BPFK/PPP/07/25]**, summarized as follow:

- Restrict the **indication** as **second-line option**, especially for pediatric patients (1-18 years old)
- All metoclopramide products are **contraindicated** for patients **<1 year old**
- Restrict the **dose and duration** of use
- Change the dose **frequency** to reduce serious neurological adverse effects

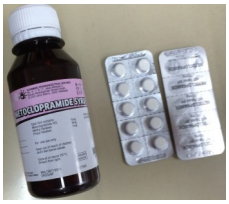
Table 2: Summary of the **UPDATED INDICATION** according to the new recommendation :

	Adult	**Pediatrics (1-18years)**
Injection	• Prevention of post-op nausea & vomiting, symptomatic treatment of nausea & vomiting, including nausea & vomiting induced by migraine attacks. • Prevention of radiotherapy –induced nausea and vomiting (RINV)	• Prevention of delayed chemotherapy-induced nausea and vomiting (CINV) as a **second-line option.** • Prevention of post-operative nausea and vomiting (PONV) as **second line option**.
Oral	• Prevention of delayed CINV & RINV • Symptomatic treatment of nausea & vomiting (including acute migraine induced nausea & vomiting)	• Prevention of delayed CINV as a **second-line option.**
Rectal	• Prevention of delayed CINV & RINV	**Not indicated**

Table 3: Summary of the **UPDATED RECOMMENDED DOSE** according to the new recommendation

	Adult	Pediatrics (1-18years) *according to weight
Injection	Can be administered IV/IM IV must be administered as slow bolus (≥3min)	
	• 10mg 1 to 3 times daily • Max daily dose 30mg or 0.5mg/kg • Shortest possible duration and switch to oral/rectal route and should be instituted as quickly as possible	• 0.1-0.15mg/kg, OD-TDS by IV • Max daily dose 0.5mg/kg [Please refer the dosing table for pediatrics below (Table 4)]
Oral	• 10mg, up to 3 times daily • Max daily dose 30 mg or 0.5mg/kg body weight • Max duration 5 days	• Dose 0.1-0.15mg/kg body weight, repeated up to 3 times daily • Max dose in 24 hour is 0.5mg/kg body weight • For the prevention of delayed CINV, maximum treatment duration is 5 days • For the prevention of delayed PONV, maximum duration is 48 hours • Tablets are **NOT** suitable for use in children **<30kg**
Rectal	• Minimum interval of **6 hours** between 2 administrations is to be respected , even if vomiting or rejection of the dose occurs	**Not indicated**

Table 4: Metoclopramide Dose Among Pediatrics According to Body Weight

Age (years old)	Body Weight (kg)	Dose	Frequency
1-3	10-14	1mg	Up to 3 times a day 
3-5	15-19	2mg	
5-9	20-29	2.5mg	
9-18	30-60	5mg	
15-18	Above 60kg	10mg	

In PPUKM, metoclopramide is available in 3 forms; the 10mg tablet, injection 10mg/2mL and also the 5mg/5mL syrup preparation. Healthcare professionals are reminded to comply to the new recommendations on metoclopramide and report all adverse drug reactions suspected to NPCB via online reporting [**http://portal.bpfk.gov.my/reporting-healthcare-professional]** or call **03-78835400 (ext 8460/8462/8470).**

Discontinuation of Penicillamine 250mg (ARTAMIN) by Sandoz Company

Please be informed that Cap Penicillamine 250mg (ARTAMIN) is no longer available due to production constraints at Sandoz's manufacturing site. Doctors are encouraged to use alternative. Penicillamine is used in many conditions such as overdose of heavy metals (copper or mercury), rheumatoid arthritis and cystinuria.

For alternatives, kindly call Drug Information Centre at 03-91455401 or 03-91455415.