Pharmacy Bulletin

Pharmacy Department, HCTM, PPUKM

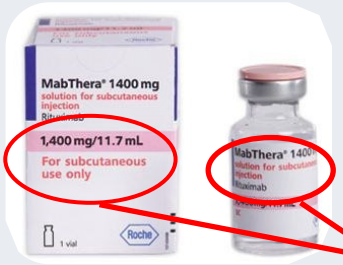
Edition 17, Issue 8

Updates on MabThera® (Rituximab) Risk Minimization Measures

Recently Roche (M) issued a letter to all Healthcare Professional on 2 different formulation of Rituximab (Mabthera) available in Malaysia. It is a proactive step taken by the company to minimize risk due to administration error that may arise from confusion of the 2 different formulations. The 2 formulations are **SUBCUTANEOUS** and **INTRAVENOUS** and their differences are as

new

Select the CORRECT MabThera® FORMULATION

SUBCUTANEOUS Inj [SC] *Not available in PPUKM*	**INTRAVENOUS** Infusion [IV] *available in PPUKM*
For use in non-Hodgkin's lymphoma only	**For use in ALL MabThera®-approved indications**
1) Non-Hodgkin's Lymphoma A. Treatment of relapsed or chemo resistant low grade or follicular, CD20-positive B-cell non-Hodgkin's Lymphoma. B. Previously untreated patients with stage III-IV follicular lymphoma in combination with chemotherapy. C. Patients with follicular lymphoma as maintenance treatment after response to induction therapy. D. Patients with CD20-positive diffuse large B-cell non-Hodgkin's lymphoma in combination with CHOP (cyclophosphamide, doxorubicin, vincristine and prednisone) chemotherapy.	1) Non-Hodgkin's Lymphoma (as stated on the left) 2) Chronic Lymphocytic Leukemia (CLL) 3) Rheumatoid Arthritis 4) Granulomatosis with polyangiitis (Wegener's) (GPA) and Microscopic polyngiitis (MPA)
	
ALERT!! Check for specific MabThera® SC packaging characteristics before use: ♦ Red Labelling: **'For subcutaneous use only', 'solution for subcutaneous injection'** and **'SC'.**	
MabThera® 1,400 mg solution for subcutaneous injection	**MabThera® 500 mg** and **MabThera® 100 mg** concentrate for solution for infusion
Withdraw directly from vial and administer by **subcutaneous Injection**	Dilute with 0.9% NaCl or 5% Glucose and administer by **Intravenous Infusion**

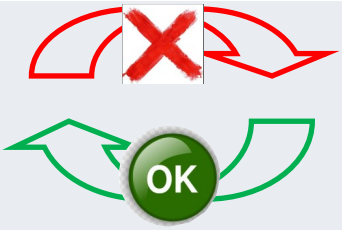
new

The NEWLY APPROVED SC formulation has added recombinant human hyaluronidase (rHuPH20) into the rituximab formulation. rHuPH20:

- functions as an excipient (permeation enhancer) in the formulation of Rituximab
- allows larger SC-injectable administration volume to be administered comfortably than the acceptable volume (~2mL).
- The availability of SC formulation of MabThera® also reduces the potential for administration route errors and off label use

Potential Harm due to Administration Route Error

SC



IV

Accidental SC administration of the IV formulations :

- Unlikely to cause significant harm as the IV formulation has a lower concentration of rituximab than the SC formulation.
- The patient would receive an ineffective dose of rituximab if the error was not detected.

Accidental IV administration of the SC formulations or incorrect injection technique could potentially result in:

1) **Systemic exposure to hyaluronidase (rHuPH20)**
   - Increased risk of **embryofetal toxicity**.
   - Concern of embryofetal toxicity following systemic exposure is based on conservative interpretation of pharmacokinetic and toxicology data derived from animal studies.
2) **Faster rate of rituximab infusion**
   - Increased risk of infusion-related reactions: hypotension, fever, urticaria, bronchospasm, angioedema , dyspnea.
3) **Overdose**
   - This is due to the high concentration of rituximab in the SC formulation
   - Increased risk of infections as patients are B cell depleted. Requires regular blood cell count monitoring.

Use in Special Population

PREGNANCY

IV and SC Formulation

- Should not be administered to pregnant women unless possible benefit outweighs the potential risk.
- Transient B-cell depletion and lymphocytopenia have been reported in some infants born to mothers exposed to rituximab during pregnancy.

NURSING MOTHERS

- Rituximab **should not** be administered to nursing mothers.

PAEDIATRIC USE

- Hypogammaglobulinaemia has been observed in paediatric patients requiring long-term immunoglobulin substitution therapy.
- The consequences of long term B cell in paediatric patients are unknown.

Important Reminder

ADMINISTRATION OF MabThera® 1,400 MG SOLUTION FOR SC INJECTION

- All patients must receive their first dose of MabThera® by **IV infusion** (using MabThera® concentrate for solution for infusion).
- MabThera® SC should only be given at the second or subsequent cycle of treatment.
- Premedication consisting of an anti-pyretic and anti-histaminic should always be given before each administration of MabThera® .
- Glucocorticoids should be considered if MabThera® is not given in combination with glucocorticoid containing chemotherapy for the treatment of NHL.
- MabThera® SC should be administered in an environment where full resuscitation facilities are immediately available.

Announcement From Pharmacy Department

Dear Healthcare Professionals,

Kindly note that these are the new operating hours for these units in Pharmacy :

Unit	Old Opening Time	NEW OPENING TIME
Emergency Pharmacy	Open 24 hours	Everyday : 7.30 am—**12 am** . Closed from 12 am-8 am (Starting **18.9.2017**)
In-patient Pharmacy	Everyday : 7.30 am—10 pm	Mon—Fri : 8 am— **8 pm** ; Sat, Sun & Public Holiday : 8 am –**3pm** (starting **1.10.2017**)

We appreciate if doctors can prescribe the patients' drugs earlier to ensure patients received it on time, including discharge patients. Wards are advised to collect all drugs from Inpatient Pharmacy before it closes. Any requests for drug supply after this time will only be entertained for **CRITICAL/LIFE SAVING drugs** only.

Article contribution by PRP Hazirah

EDITORS :

IZYAN DIYANA IBRAHIM
izyandi@ppukm.ukm.edu.my
03-91455415

MICHELLE TAN HWEE PHENG
hptan@ppukkm.ukm.edu.my
03-91455401

PDF version available in
http://www.ppukm.ukm.my/farmasi/

PPUKM APPS
NOW AVAILABLE ON:

GET IT ON Google Play — Drug Formulary, DIY– Formularies

Available on the App Store — PPUKM Formulary