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Tarikh : 04 DEC 2019

SEMUA PEMEGANG PENDAFTARAN

SEMUA PERSATUAN BERKENAAN
(SEPERTI DI SENARAI EDARAN)

Tuan/ Puan,

PERATURAN-PERATURAN KAWALAN DADAH DAN KOSMETIK 1984
ARAHAN PENGARAH KANAN PERKHIDMATAN FARMASI BILANGAN 19 TAHUN 2019: DIREKTIF UNTUK SEMUA PRODUK YANG MENGANDUNGI CARBIMAZOLE ATAU METHIMAZOLE (THIAMAZOLE): PENGEMASKINIAN SISIP BUNGKUSAN DAN RISALAH MAKLUMAT UBAT UNTUK PENGGUNA (RiMUP) DENGAN MAKLUMAT KESELAMATAN BERKAITAN RISIKO PANKREATITIS AKUT (*ACUTE PANCREATITIS*) DAN PENGUKUHAN MAKLUMAT KESELAMATAN BERKAITAN RISIKO KECACATAN KONGENITAL (*CONGENITAL MALFORMATION*)

Adalah saya merujuk kepada Arahan Bilangan 19 Tahun 2019 oleh Pengarah Kanan Perkhidmatan Farmasi.

2. Dimaklumkan bahawa Pengarah Kanan Perkhidmatan Farmasi, Kementerian Kesihatan Malaysia dalam Arahan Bilangan 19 Tahun 2019 telah bersetuju untuk memasukkan maklumat keselamatan berkaitan risiko pankreatitis akut *(acute pancreatitis)* dan pengukuhan maklumat keselamatan berkaitan risiko kecacatan kongenital *(congenital malformation)* bagi produk yang mengandungi carbimazole atau methimazole (thiamazole) seperti pada surat arahan Bil.(19) BPFK/PPP/07/25 Jld.3.

3. Pihak pemegang pendaftaran adalah diarahkan untuk mematuhi keperluan tersebut.

Sekian, terima kasih.

"**BERKHIDMAT UNTUK NEGARA**"

Saya yang menjalankan amanah,

(DATIN DR. FARIDAH ARYANI BINTI MD. YUSOF) **RPh 1197**
Pengarah
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ARAHAN DI BAWAH PERATURAN 29 PERATURAN – PERATURAN KAWALAN DADAH DAN KOSMETIK 1984

BILANGAN 19 TAHUN 2019

DIREKTIF UNTUK SEMUA PRODUK YANG MENGANDUNGI CARBIMAZOLE ATAU METHIMAZOLE (THIAMAZOLE): PENGEMASKINIAN SISIP BUNGKUSAN DAN RISALAH MAKLUMAT UBAT UNTUK PENGGUNA (RiMUP) DENGAN MAKLUMAT KESELAMATAN BERKAITAN RISIKO PANKREATITIS AKUT (*ACUTE PANCREATITIS*) DAN PENGUKUHAN MAKLUMAT KESELAMATAN BERKAITAN RISIKO KECACATAN KONGENITAL (*CONGENITAL MALFORMATION*)

TUJUAN

1.1 Arahan ini dikeluarkan oleh Pengarah Kanan Perkhidmatan Farmasi di bawah Peraturan 29 (1) Peraturan-peraturan Kawalan Dadah dan Kosmetik 1984.

1.2 Arahan ini ditujukan kepada semua pemegang pendaftaran produk yang mengandungi carbimazole atau methimazole (thiamazole) bagi mengemaskini sisip bungkusan dan risalah maklumat ubat untuk pengguna (RiMUP) dengan maklumat keselamatan berkaitan risiko pankreatitis akut *(acute pancreatitis)* dan pengukuhan maklumat keselamatan berkaitan risiko kecacatan kongenital *(congenital malformation)*.

LATAR BELAKANG

2.1 Pihak Berkuasa Kawalan Dadah (PBKD) dalam mesyuarat kali ke **340** pada **13 November 2019** telah membuat keputusan bagi semua produk yang mengandungi carbimazole atau methimazole (thiamazole) bagi mengemaskini sisip bungkusan dan risalah maklumat ubat untuk pengguna (RiMUP) dengan maklumat keselamatan berkaitan risiko pankreatitis akut (*acute pancreatitis)* dan pengukuhan maklumat keselamatan berkaitan risiko kecacatan kongenital (*congenital malformation*).

PELAKSANAAN

3.1 Oleh itu arahan – arahan berikut perlu dipatuhi untuk semua produk yang mengandungi carbimazole atau methimazole (thiamazole) seperti berikut:-

3.1.1 Sisip bungkusan

Pada bahagian *Contraindications*:

Patients with a history of acute pancreatitis after administration of carbimazole or active metabolite, methimazole (thiamazole).

Pada bahagian *Warnings and Precautions:*

There have been post-marketing reports of acute pancreatitis in patients receiving carbimazole or its active metabolite, methimazole (thiamazole). In case of acute pancreatitis, carbimazole or methimazole (thiamazole) should be discontinued immediately. Carbimazole or methimazole (thiamazole) must not be given to patients with a history of acute pancreatitis after administration of carbimazole or its active metabolite methimazole (thiamazole). Re-exposure may result in recurrence of acute pancreatitis, with decreased time to onset.

Women of childbearing potential and pregnancy
Women of childbearing potential have to use effective contraceptive measures during treatment.

The use of carbimazole or methimazole (thiamazole) in pregnant women must be based on the individual benefit/risk assessment. If carbimazole or methimazole (thiamazole) is used during pregnancy, the lowest effective dose without additional administration of thyroid hormones should be administered. Close maternal, foetal and neonatal monitoring is warranted.

Pada bahagian *Fertility, Pregnancy and Lactation:*

Women of childbearing potential and pregnancy
Women of childbearing potential have to use effective contraceptive measures during treatment (see Section Warnings and Precautions).

Pregnancy
Carbimazole or methimazole (thiamazole) crosses the placenta but, provided the mother's dose is within the standard range and her thyroid status is monitored; there is no evidence of neonatal thyroid abnormalities.

Studies have shown that the incidence of congenital malformations is greater in the children of mothers whose hyperthyroidism has remained untreated than in those who have been treated with carbimazole or methimazole (thiamazole).

However, cases of congenital malformations have been observed following the use of carbimazole or its active metabolite, methimazole (thiamazole) during pregnancy.

A causal relationship of these malformations, especially choanal atresia and aplasia cutis congenita (congenital scalp defects), to transplacental exposure to carbimazole and methimazole (thiamazole) cannot be excluded.

Therefore the use of carbimazole or methimazole (thiamazole) in non-pregnant women of childbearing potential should be based on individual risk/benefit assessment (see section Warnings and Precautions).

Cases of renal, skull, cardiovascular congenital defects, exomphalos, gastrointestinal malformation, umbilical malformation and duodenal atresia have also been reported. Therefore, carbimazole or methimazole (thiamazole) should be used in pregnancy only when propylthiouracil is not suitable.

If carbimazole or methimazole (thiamazole) is used in pregnancy, the dose must be regulated by the patient's clinical condition. The lowest dose possible should be used, and this can often be discontinued three or four weeks before term, in order to reduce the risk of neonatal complications.

The blocking-replacement regimen should not be used during pregnancy since very little thyroxine crosses the placenta in the last trimester.

Hyperthyroidism in pregnant women should be adequately treated to prevent serious maternal and foetal complications.

Carbimazole or methimazole (thiamazole) is able to cross the human placenta.

Based on human experience from epidemiological studies and spontaneous reporting, carbimazole or methimazole (thiamazole) is suspected to cause congenital malformations when administered during pregnancy, particularly in the first trimester of pregnancy and at high doses.

Reported malformations include aplasia cutis congenita, craniofacial malformations (choanal atresia; facial dysmorphism), exomphalos, oesophageal atresia, omphalo-mesenteric duct anomaly, and ventricular septal defect.

Carbimazole or methimazole (thiamazole) must only be administered during pregnancy after a strict individual benefit/risk assessment and only at the lowest effective dose without additional administration of thyroid hormones. If carbimazole or methimazole (thiamazole) is used during pregnancy, close maternal, foetal and neonatal monitoring is recommended (see section Warnings and Precautions).

Pada bahagian *Undesirable Effects/ Side Effects*:

SOC Gastrointestinal disorders

Frequency "Not Known": Acute pancreatitis

3.1.2 Risalah Maklumat Ubat Untuk Pengguna (RiMUP)

Pada bahagian *Before you use [Product Name]:*

When you must not use it:

- *Do not use <Product name> if you had inflammation of the pancreas (acute pancreatitis) after administration of carbimazole or thiamazole in the past.*

- *Before you start to use it:*
  <Product name> can cause harm to an unborn baby. If you can get pregnant, use reliable contraception from the time you start treatment and during treatment.

- *If you are pregnant, think you may be pregnant or are planning to have a baby, tell your doctor straight away. Your treatment with <product name> may need to be continued during pregnancy if the potential benefit outweighs the potential risk to you and your unborn baby.*

Pada bahagian *While you are using [Product Name]:*

Things to be careful of:
- Tell your doctor straight away if you develop fever or abdominal pain, which may be signs of inflammation of the pancreas (acute pancreatitis). <Product name> may need to be discontinued.

Pada bahagian Side Effects:

- Inflammation of the pancreas (acute pancreatitis)

4. Tarikh pelaksanaan keperluan mengemaskini maklumat berkenaan pada semua produk yang mengandungi carbimazole atau methimazole (thiamazole) bagi:

(a) Permohonan baru dan produk yang sedang dalam proses penilaian : **15 Disember 2019**

(b) Produk berdaftar : **15 Jun 2020.**

5. Permohonan pindaan pada sisip bungkusan dan RiMUP bagi produk berdaftar perlu dikemukakan sebagai permohonan variasi.

6. Tarikh kuat kuasa arahan ini ialah mulai **15 Disember 2019.**

"BERKHIDMAT UNTUK NEGARA"

(DR. RAMLI BIN ZAINAL) RPh. 1045
Pengarah Kanan Perkhidmatan Farmasi
Kementerian Kesihatan Malaysia
AAG/nb/ppp/NPRA/141119

s.k. 1. Pengarah
Bahagian Regulatori Farmasi Negara
Kementerian Kesihatan Malaysia

2. Pengarah
Bahagian Amalan dan Perkembangan Farmasi
Kementerian Kesihatan Malaysia

3. Pengarah
Bahagian Penguatkuasaan Farmasi
Kementerian Kesihatan Malaysia