Biro Pengawalan Farmaseutikal Kebangsaan
National Pharmaceutical Control Bureau
KEMENTERIAN KESIHATAN MALAYSIA
MINISTRY OF HEALTH MALAYSIA

Ruj. Kami : (18) dlm. BPFK/PPP/01/03 Jld. 3
Tarikh : 06 AUG 2014

SEMUA PEMEGANG PENDAFTARAN

SEMUA PERSATUAN BERKENAAN
(SEPERTI DI SENARAI EDARAN)

Tuan/ Puan,

PEKELILING UNTUK MENGEMASKINI SISIP BUNGKUSAN SEMUA PRODUK YANG MENGANDUNGI SIMVASTATIN DENGAN MEMUATKAN KONTRAINDIKASI DAN HAD DOS YANG BARU

Saya dengan segala hormatnya merujuk kepada perkara di atas.

1. Pihak Berkuasa Kawalan Dadah (PBKD) dalam mesyuarat kali ke **277** pada **7 Julai 2014** telah bersetuju untuk mengehadkan penggunaan produk yang mengandungi simvastatin dengan memuatkan kontraindikasi baru dan had dos baru apabila digunakan bersama ubat tertentu bagi mengurangkan risiko kecederaan otot.

2. Oleh itu arahan – arahan berikut perlu dipatuhi untuk semua produk yang mengandungi simvastatin dengan pengemaskinian pada sisip bungkusan seperti berikut:-

2.1 Pada bahagian ***Dosage and Administration***

The 80mg dose is only recommended in patients at high risk for cardiovascular complications who have not achieved treatment goals on lower doses and when the benefits are expected to outweigh the potential risks.

Concomitant Therapy
In patients taking fibrates (other than gemfibrozil and fenofibrate) concomitantly with [Product Name], the dose of [Product Name] should not exceed 10mg/day.

In patients taking amiodarone, verapamil or diltiazem concomitantly with [Product Name], the dose of [Product Name] should not exceed 20mg/day.

Jalan Universiti. P. O. Box 319, 46730 Petaling Jaya, Selangor, Malaysia
Tel. : + 603 7883 5400 Fax : + 603 7956 2924 / 7958 1312
http : //www.bpfk.gov.my

In patients taking amlodipine or lipid-lowering dose of niacin (≥1g/day) concomitantly with [Product Name], the dose of [Product Name] should not exceed 40mg/day.

2.2 Pada bahagian ***Contraindications***

- *Concomitant administration of potent CYP3A4 inhibitors (e.g. itraconazole, ketoconazole, posaconazole, voriconazole, HIV protease inhibitors, boceprevir, telaprevir, erythromycin, clarithromycin, telithromycin and nefazodone).*
- *Concomitant administration of gemfibrozil, cyclosporine, or danazol.*

2.3 Pada bahagian **Interactions**

Contraindicated Drugs
Potent inhibitors of CYP3A4: Concomitant use with medicines labeled as having a potent inhibitory effect on CYP3A4 at therapeutic doses (e.g.: itraconazole, ketoconazole, posaconazole, voriconazole, erythromycin, clarithromycin, telithromycin, HIV protease inhibitors, boceprevir, telaprevir or nefazodone) is contraindicated. If treatment with potent CYP3A4 inhibitors is unavoidable, therapy with simvastatin should be suspended during the course of treatment.

Gemfibrozil, cyclosporine or danazol: Concomitant use of these drugs with simvastatin is contraindicated.

Other Drugs
- *Other fibrates: The dose of simvastatin should not exceed 10 mg daily in patients receiving concomitant medication with fibrates other than gemfibrozil or fenofibrate. When simvastatin and fenofibrate are given concomitantly, there is no evidence that the risk of myopathy exceeds the sum of the individual risks of each agent. Caution should be used when prescribing fenofibrate with simvastatin, as either agent can cause myopathy when given alone. Addition of fibrates to simvastatin typically provides little additional reduction in LDL-C, but further reductions of TG and further increases in HDL-C may be obtained. Combinations of fibrates with simvastatin have been used without myopathy in small short-term clinical studies with careful monitoring.*

- *Amiodarone: In a clinical trial, myopathy was reported in 6% of patients receiving simvastatin 80 mg and amiodarone. The dose of simvastatin*

should not exceed 20 mg daily in patients receiving concomitant medication with amiodarone.

- *Calcium channel blockers:*
  - *Verapamil or diltiazem: In a clinical trial, patients on diltiazem treated concomitantly with simvastatin 80 mg had an increased risk of myopathy. The dose of simvastatin should not exceed 20 mg daily in patients receiving concomitant medication with verapamil or diltiazem.*

  - *Amlodipine: In a clinical trial, patients on amlodipine treated concomitantly with simvastatin 80 mg had a slightly increased risk of myopathy. The dose of simvastatin should not exceed 40 mg daily in patients receiving concomitant medication with amlodipine.*

  - *Niacin (≥1g/day): The dose of simvastatin should not exceed 40mg daily in patients receiving concomitant medication with niacin (nicotinic acid) ≥ 1g/day. Cases of myopathy/rhabdomyolysis have been observed with simvastatin co-administered with lipid-modifying doses (≥ 1 g/day) of niacin.*

3. Tarikh pelaksanaan keperluan mengemaskini maklumat berkenaan pada sisip bungkusan semua produk yang mengandungi simvastatin bagi:

(a) Permohonan baru dan produk yang sedang dalam proses penilaian : **01 Ogos 2014**

(b) Produk berdaftar : **dalam tempoh Enam bulan mulai 01 Ogos 2014**

4. Permohonan pindaan pada sisip bungkusan perlu dikemukakan sebagai permohonan variasi.

5. Tarikh kuat kuasa arahan ini ialah mulai **01 Ogos 2014.**

Sekian, terima kasih.

"BERKHIDMAT UNTUK NEGARA"

Saya yang menurut perintah,

TAN ANN LING
Pengarah Regulatori Farmasi
Biro Pengawalan Farmaseutikal Kebangsaan
Kementerian Kesihatan Malaysia

ra/nb/ppp/bpfk/090714

s.k. 1. Pengarah Kanan Perkhidmatan Farmasi
Bahagian Perkhidmatan Farmasi
Kementerian Kesihatan Malaysia.

2. Pengarah Penguatkuasa Farmasi
Bahagian Perkhidmatan Farmasi
Kementerian Kesihatan Malaysia.

3. Pengarah Amalan dan Perkembangan Farmasi
Bahagian Perkhidmatan Farmasi
Kementerian Kesihatan Malaysia.