

## DIVIZJONI TAS-SAHHA

Palazzo Castellania, 15, Triq il-Merkanti,  
Il-Belt, CMR 02  
Malta



## HEALTH DIVISION

Palazzo Castellania, 15 Merchants Street,  
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**DH Circular No 234/2006**

**19<sup>th</sup> July 2006**

**Attention all Medical Practitioners  
Pharmacists  
Nurses**

### **Re: Fluvastatin 80mg and Simvastatin 20mg Interchange Update**

(Update of Circular 214/2006 of the 22<sup>nd</sup> June 2006)

A statin is the recommended drug of choice in many people with hypercholesterolaemia. The Government Pharmaceutical Services are now procuring simvastatin 20mg (Zocor<sup>®</sup>) instead of fluvastatin 80mg XL (Lescol<sup>®</sup> XL). Simvastatin 20mg is therapeutically equivalent to fluvastatin 80mg, and thus the two drugs are therapeutically interchangeable.

The statins which will now be available on the formulary of the Government Health Services are:

- A. fluvastatin – 20mg (Lescol<sup>®</sup>) and 40mg (Lescol<sup>®</sup>)
- B. simvastatin – 10mg (Simvacor<sup>®</sup>) and 20mg (Zocor<sup>®</sup>)
- C. atorvastatin – 20mg (Lipitor<sup>®</sup>)

All new patients requiring a statin equivalent to fluvastatin 80mg XL are to be started on simvastatin 20mg. Patients currently taking fluvastatin 80mg XL tablets shall be changed over to simvastatin 20mg tablets. A valid prescription for simvastatin 20mg is to be issued by the respective doctor.

Doctors are asked to change over the patients requiring high dose statin to simvastatin 20mg. Prescriptions need to be made accordingly. Should the interchange be impossible for any particular patient, a prescription for fluvastatin 80mg daily, is to be made by the respective doctor and 2 tablets of fluvastatin 40mg daily will be dispensed to the patient.

Please refer to the attached guidelines for prescribing of statins to patients eligible through the Government Health Services.

For your attention please,

Dr J.M.Cachia  
a / Director General (Health)

## PRESCRIBING OF STATINS

The following statins are available through the Government Health Services:

- A. fluvastatin– 20 mg (Lescol<sup>®</sup>) and 40 mg (Lescol<sup>®</sup>) as per protocol attached
- B. simvastatin – 10 mg (Simvacor<sup>®</sup>) and 20 mg (Zocor<sup>®</sup>) as per protocol attached
- C. atorvastatin – 20 mg (Lipitor<sup>®</sup>) available only in special circumstances

While ‘Summary of Product Characteristics’ for these products are available on the Medicines Authority web-site (<http://www.medicinesauthority.gov.mt/products/search.htm>) the following information is being forwarded to you for your attention.

All statins can be associated with a number of side effects (including myotoxicity, hepatotoxicity). Factors that may increase the risk for myotoxicity are higher doses, drug interactions and renal failure. The metabolic pathways for the various statins differ: fluvastatin is metabolized through cytochrome P 450 isoenzyme CYP2C9, while simvastatin and atorvastatin are metabolized through CYP3A4. This may result in different drug interactions involving statins combined with drugs having the same metabolic pathway. For example when potent CYP 3A4 inhibitors are combined with CYP 3A4 metabolised statins (simvastatin, atorvastatin), the blood level of the involved statin can increase, and may further add to the risk of side effects, particularly of myotoxicity.

Interactions with statins include but are not limited to the following:

### **Amiodarone**

Concomitant use with high doses of simvastatin, exceeding 20 mg daily, may increase risk of myotoxicity: higher doses are not recommended

### **Antifungal Agents**

Concurrent used with azole antifungals (imidazole, triazole, itraconazole, ketoconazole) may be associated with increased risk of myotoxicity and should be avoided.

### **Calcium channel blockers**

Verapamil and diltiazem increase the risk of myotoxicity with higher levels of simvastatin; it is recommended not to use doses of simvastatin higher than 20 mg when used concomitantly with verapamil and 40 mg with diltiazem.

### **Cyclosporin.**

Dose of simvastatin should not exceed 10 mg daiy; higher doses may be associated with increased risk of myotoxicity. Fluvastatin, having a different metabolic pathway, is not associated with increased risk of myotoxicity in these circumstances.

### **Grapefruit Juice**

Grapefruit juice inhibits CYP 3A4 and its use with simvastatin increases plasma levels of simvastatin: concomitant use should be avoided.

### **HIV protease inhibitors**

Concurrent use of simvastatin with these drugs (including lopinavir with ritonavir, nelfinavir, ritonavir, saquinavir and indinavir) is contraindicated because of an increased risk of myotoxicity.

### **Macrolide Antibiotics.**

Concomitant use of with these drugs (e.g. clarithromycin, erythromycin, telithromycin) is contraindicated because of the increased risk of myotoxicity.

### **Phenytoin**

Small changes in pharmacokinetics with concomitant administration of fluvastatin is possible. Routine monitoring of phenytoin levels is warranted

**Rifampicin**

Appropriate adjustment of fluvastatin dosage may be warranted to ensure satisfactory reduction of lipid levels.

**Warfarin**

Warfarin goes through several different CYP3A4 pathways, any of which might serve as a source of interaction with statins. Simvastatin and atorvastatin have the potential of raising INR in patients taking warfarin. Fluvastatin, metabolized through the CYP2C9 pathway can also interfere with warfarin metabolism and raise INR. It is prudent to monitor INR carefully in patients on warfarin who are also taking a statin.

**All patients receiving treatment with statins should be advised to report any unexplained muscle pain, tenderness or weakness regardless of statin used or concomitant drugs. Patients experiencing any of these symptoms should be advised to discontinue their lipid therapy immediately and obtain a CPK level as soon as possible.**

# **HMG CoA Reductase Inhibitors (Statins)**

**Prescriber Criteria:** Consultant

**Clinical Indications:** Hypercholesterolaemia

**Conditions qualifying patients for drug:**

Treatment with statins is provided to patients up to 75 years of age, when any of the following three criteria are met with:

1. LDL cholesterol  $\geq 4.1$ mmol/L with either:
  - i. documented ischaemic heart disease OR
  - ii. diabetes mellitus
  
2. LDL cholesterol  $\geq 4.1$ mmol/L, without ischaemic heart disease but with 2 or more of the following risk factors:
  - i hypertension (blood pressure persistently above 160/95mmHg)
  - ii family history for IHD (first degree relatives aged  $\leq 50$ )
  - iii cerebral/peripheral vascular disease
  - iv obesity (BMI  $> 35\%$ )
  
3. Patients with familial (type 2) hypercholesterolaemia

**Investigations prior to starting treatment:** Fasting lipid profile

Liver function tests  
Creatine kinase estimation  
Thyroid function tests  
Fasting blood glucose

**Objective indicators of efficacy:** Blood cholesterol levels.

**Patient Consent form:** No need for patient consent form or other declaration. However, all patients have to be informed of potential side-effects by the responsible physician.

**Specific request form available (carbonized in triplicate).**

**Duration of approval:** 3 years

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19<sup>th</sup> July 2006

Dear Patient,

Please note that the medication Fluvastatin 80mg (Lescol<sup>®</sup> XL) is being replaced by simvastatin 20mg (Zocor<sup>®</sup>) on the formulary of the Government Health Services. Fluvastatin and simvastatin are both used for the treatment of high cholesterol levels.

The following points should be considered:

- Lescol<sup>®</sup> XL (fluvastatin 80mg) will no longer be available from the government hospitals and health centres, but fluvastatin 20mg and 40mg continue to be available.
- In terms of efficacy 80mg of fluvastatin (Lescol<sup>®</sup>) is equivalent to 20mg of simvastatin (Zocor<sup>®</sup> and Simvacor<sup>®</sup>).
- Both fluvastatin (Lescol<sup>®</sup>) and simvastatin (Zocor<sup>®</sup> or Simvacor<sup>®</sup>) reduce cholesterol levels and are equivalent.
- Patients must inform doctors of all medicines they are taking.
- Patients should consult their doctor in case of difficulty.

Sincerely,

Dr. J.M. Cachia  
a / Director General (Health)

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19 ta' Lulju 2006

Għażiż pazjent,

Nixtieq ninfurmak li l-mediċina Fluvastatin 80mg (Lescol<sup>®</sup> XL) mhix se tibqa' fuq il-Formularju tas-Servizzi tas-Saħħa tal-Gvern u minflok se jkun hemm Simvastatin 20mg (Zocor<sup>®</sup>). Fluvastatin u simvastatin huma t-tnejn mediċini li jiġu użati għat-trattament ta' livelli għoljin ta' kolesterol fid-demem.

Dawn il-punti li ġejjin għandhom jiġu meqjusa:

- Lescol<sup>®</sup> XL (fluvastatin 80mg) mhux se jinstab aktar fl-ispizeriji ta' l-isptar u ċ-ċentri tas-Saħħa, iżda fluvastatin 20mg u 40mg se jibqgħu jiġu provduti..
- Fir-rigward ta' effettività, 80mg ta' fluvastatin (Lescol<sup>®</sup>) huwa ekwivalenti għal simvastatin 20mg (Zocor<sup>®</sup> u Simvacor<sup>®</sup>).
- Iż-żewġ mediċini jahdmu bl-istess mod biex ibaxxu l-livell tal-kolesterol.
- Pazjenti għandhom jinfurmaw lit-tobba bil-mediċini kollha li jkunu qed jieħdu.
- F'każ ta' xi diffikulta', il-pazjenti għandhom jieħdu parir mingħand it-tabib tagħhom.

Dejjem tieghek,

Dr J.M. Cachia  
a / Director General (Health)

