

Company

Consultation with stakeholders - Reassessment of reimbursement status for dihydropyridine calcium channel blockers - ATC group C08CA

14 October 2008

The Danish Medicines Agency has assessed the question of the future reimbursement status for medicinal products in ATC group C08CA on the basis of updated information about prices and consumption of these medicinal products. Please see **Appendix I**.

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5315-9

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On this basis, we expect to attach a reimbursement condition to medicinal products in ATC group C08CA containing isradipine, nifedipine, nitrendipine, lacidipine and lercanidipine, restricting it to:

“Patients with hypertension or any other type of cardiovascular disease requiring treatment where treatment with less expensive dihydropyridine calcium channel blockers

- is not tolerated or
- in exceptional cases has been deemed inappropriate by a doctor based on an overall clinical assessment of the patient’s condition.”

In the period from 28 July 2008 to 19 October 2008, the average lowest price of treatment per day for these medicinal products ranged between DKK 3.11 and DKK 8.90.

It is expected that medicinal products in ATC group C08CA containing amlodipine and felodipine will still be eligible for general unconditional reimbursement.

In the period from 28 July 2008 to 19 October 2008, the average lowest price of treatment per day for these medicinal products ranged between DKK 0.34 and DKK 0.64.

From the Reimbursement Committee’s recommendation of 29 January 2008, the following appeared among other things:

“The different calcium channel blockers can overall be considered to be equally effective for the treatment of uncomplicated hypertension and preventive symptomatic treatment of angina pectoris, with the exception of nimodipine which is only indicated for spasms in subarachnoidal haemorrhage. In addition, verapamil and diltiazem are used for the treatment of tachyarrhythmias, and nifedipine is also used for Raynaud’s phenomenon.

In the group of dihydropyridines (C08C), amlodipine, felodipine, isradipine, lacidipine, lercanidipine, nifedipine and nitrendipine, the price gap for oral treatment is large: DKK 0.90 to DKK 8.90 (for nimodipine: DKK 65.90). Differences in adverse reactions and interactions may, however, influence the choice of medicinal product, and in the opinion of the Reimbursement Committee the consumption of the more expensive calcium channel blockers is at a level which indicates that these medicinal products are primarily used when the cheaper ones cannot be used as only some 10 per cent of the users of dihydropyridines received the more expensive products in 2006. For the first ten months of 2007, the share was the same.

In summary, it is the opinion of the Reimbursement Committee that the use of the calcium channel blockers – the majority of the consumption being the cheaper substances amlodipine and felodipine – is appropriate and the Committee thus recommends that the calcium channel blockers maintain the current reimbursement status.”

The Danish Medicines Agency agrees with the Reimbursement Committee’s medical assessment of the medicinal products and their use. However, when it comes to the consumption of dihydropyridines, we believe that the number of patients in treatment with the expensive dihydropyridines is too high as many of these patients would gain the same effect from treatment with the less expensive dihydropyridines amlodipine and felodipine.

In 2007, 258,778 persons received treatment with dihydropyridines. 25,968, or 10 percent, received treatment with the expensive dihydropyridines (isradipine, nifedipine, nitrendipine, lacidipine and lercanidipine). The proportion was on the same level in the first half of 2008. In 2007, the expenses of treatment with these medicinal products accounted for 28.9 percent of the total expenses for dihydropyridine treatment. In the first half of 2008, the proportion was 25.7 percent.

The Danish Medicines Agency recognises that individual patients may require other treatment options than amlodipine or felodipine due to adverse reactions or interactions caused by these substances or - with

respect to nifedipine – for the treatment of Raynaud's phenomenon. The proposed reimbursement condition allows for this. For these patients, the doctor merely has to write “tilskud” (reimbursement) on the prescription.

We enclose as **Appendix II** a list of your company's medicinal products affected by this consultation.

We kindly request you to submit any remarks you may have to the above no later than **Tuesday 11 November 2008**.

We will include your consultation response in our assessment basis when making a decision on the medicinal products' future reimbursement status once the consultation period has expired.

Please be aware that we will post the consultation responses that we receive on our website.

Yours sincerely

A handwritten signature in black ink, appearing to read 'Karen Kolenda', written in a cursive style.

Karen Kolenda

Medicinal products in ATC group C08CA, dihydropyridine calcium channel blockers – not including nimodipine

Treatment price per day: The listed prices per day are based on the medicinal products' reimbursement prices calculated in accordance with the Danish Medicines Agency's guidelines for evaluation and comparison of medicinal products in reassessments of reimbursement status dated 4 July 2006 (reimbursement periods starting on 28 July 2008 to 6 October 2008).

Consumption: The number of persons in treatment is based on the Danish Medicines Agency's Register of Medicinal Product Statistics, cf. www.medstat.dk.

Monotherapy for oral use

| C08CA01 | Amlodipine |
|-------------------------|---|
| Pharmaceutical forms | Tablets |
| Traded name(s) | Amlodipin "1A Farma, Amlodipin "Actavis", Amlodipin "Alternova" , Amlodipin "BMM Pharma", Amlodipin "Copyfarm", Amlodipin "GEA", Amlodipin "Hexal", Amlodipin "KRKA", Amlodipin "Orion", Amlodipin "PCD", Amlodipin "Ranbaxy", Amlodipin "ratiopharm", Amlodipin "Sandoz", Amlovis, Norvasc |
| Treatment price per day | 5-10 mg tablets: DKK 0.34 - DKK 0.43 |
| Consumption | 174,747 persons in treatment in 2006 203,181 persons in treatment in 2007 191,749 persons in treatment from January to June 2008 |

| C08CA02 | Felodipine |
|-------------------------|---|
| Pharmaceutical forms | Prolonged-release tablets |
| Traded name(s) | Felodin, Felodipin "Actavis", Felodipin "Hexal", Felodipin "ratiopharm", Felodipin "Sandoz", Felodipin Retard "1A Farma", Hydac, Plendil, Plendur |
| Treatment price per day | 5-10 mg prolonged-release tablets: DKK 0.51-0.64 |
| Consumption | 33,796 persons in treatment in 2006 33,704 persons in treatment in 2007 31,033 persons in treatment from January to June 2008 |

| C08CA03 | Isradipine |
|-------------------------|--|
| Pharmaceutical forms | Prolonged-release capsules |
| Traded name(s) | Lomir Retard |
| Treatment price per day | 5-10 mg prolonged-release capsules: DKK 4.17 - DKK 8.34 |
| Consumption | 2,181 persons in treatment in 2006 2,102 persons in treatment in 2007 1,853 persons in treatment from January to June 2008 |

| | |
|-------------------------|--|
| C08CA05 | Nifedipine |
| Pharmaceutical forms | Tablets, capsules, prolonged-release tablets |
| Traded name(s) | Adalat, Adalat Oros, Hexadilat, Nifecodan, Nifedipin "Alternova", Nifedipin "NM" |
| Treatment price per day | 30-120 mg capsules: DKK 3.11 - DKK 8.90 (prolonged-release) 30 mg: DKK 2.79 - DKK 11.16 |
| Consumption | 11,330 persons in treatment in 2006 10,930 persons in treatment in 2007 9,523 persons in treatment from January to June 2008 |

| | |
|-------------------------|--|
| C08CA08 | Nitrendipine |
| Pharmaceutical forms | Tablets |
| Traded name(s) | Baypress |
| Treatment price per day | 10-20 mg tablets: DKK 3.34 - DKK 4.86 |
| Consumption | 740 persons in treatment in 2006 682 persons in treatment in 2007 616 persons in treatment from January to June 2008 |

| | |
|-------------------------|--|
| C08CA09 | Lacidipine |
| Pharmaceutical forms | Tablets |
| Traded name(s) | Midotens, Motens |
| Treatment price per day | 2-4 mg tablets: DKK 5.31 - DKK 6.69 |
| Consumption | 1,988 persons in treatment in 2006 1,980 persons in treatment in 2007 1,831 persons in treatment from January to June 2008 |

| | |
|-------------------------|--|
| C08CA13 | Lercanidipine |
| Pharmaceutical forms | Tablets |
| Traded name(s) | Zanidip, Zanedip |
| Treatment price per day | 10-20 mg tablets: DKK 3.47 - DKK 5.03 |
| Consumption | 7,850 persons in treatment in 2006 10,374 persons in treatment in 2007 10,980 persons in treatment from January to June 2008 |