

For companies which as of 1 December 2008 or before notified a price of one or more medicinal products approved for marketing in ATC group C09

Decision on future reimbursement status for medicinal products in ATC group C09 as a result of the reassessment process

16 January 2009

With this decision, the Danish Medicines Agency concludes the reassessment of the reimbursement status for medicinal products in ATC group C09 (ACE inhibitors, angiotensin II antagonists and renin inhibitors).

Case no.:
5315-9

The decision is an overall decision on the reimbursement status **as of 13 July 2009** for all medicinal products of all strengths (unless otherwise stated) in ATC group C09 and for which a price has been notified to the Danish Medicines Agency as of 1 December 2008 or before.

Presentation

The Reimbursement Committee has submitted two recommendations containing the Committee's recommendations for the future reimbursement status for medicinal products in ATC groups C02 (antihypertensives), C03 (diuretics), C07 (beta blocking agents), C08 (calcium channel blockers) and C09 (ACE inhibitors, angiotensin II antagonists and renin inhibitors). The first recommendation is dated 29 January 2008. The additional recommendation is dated 2 September 2008. The Committee's recommendations are available at www.dkma.dk > Companies > General reimbursement > Reassessment of reimbursement status for medicinal products, notifications of 14 February and 9 September 2008.

The recommendations of the Reimbursement Committee have been submitted to the affected companies, scientific societies, patient organisations etc. for consultation. In addition, we have carried out a consultation with updated prices and consumption for combination products with ATC codes C09BA01, C09BA02 and C09BB.

Please see the consultation memorandum enclosed as **Appendix 1** for the most important viewpoints stated in the consultation responses and the Danish Medicines Agency's comments thereon.

The decision made, the grounds therefore, the regulatory framework and the complaint instructions are stated below.

Decision

1. Oral combination products in ATC group C09A (ACE inhibitors) containing the individual substances
 - captopril (C09AA01)
 - enalapril (C09AA02)
 - lisinopril (C09AA03)
 - ramipril (C09AA05)
 - trandolapril (C09AA10)

maintain their current reimbursement status (general reimbursement) as of 13 July 2009.

The Danish Medicines Agency finds that these medicinal products still *meet* the criteria for being granted general reimbursement, cf. section 1(2) of the executive order on reimbursement¹.

2. Oral combination products in ATC group C09B (ACE inhibitors) containing
 - enalapril, 20 mg and hydrochlorothiazide, 12.5 mg (C09BA02)
 - lisinopril and hydrochlorothiazide (C09BA03)
 - ramipril and hydrochlorothiazide (C09BA05)

maintain their current reimbursement status (general reimbursement) as of 13 July 2009.

The Danish Medicines Agency finds that these medicinal products still *meet* the criteria for being granted general reimbursement, cf. section 1(2) of the executive order on reimbursement.

3. Oral combination products in ATC group C09B (ACE inhibitors) containing
 - captopril and hydrochlorothiazide (C09BA01)
 - enalapril, 20 mg and hydrochlorothiazide, 6 mg (C09BA02)

will as of 13 July 2009 have their reimbursement status changed and will not be granted general reimbursement.

In the opinion of the Danish Medicines Agency, these medicinal products *do not meet* the criteria for being granted general reimbursement, cf. section 1(2) of the executive order on reimbursement.

With reference to section 1(4) of the executive order on reimbursement, it is, in the opinion of the Danish Medicines Agency, not possible to identify parts of the indication ('specific diseases') which independently meet the criteria set out in the executive order on reimbursement for being granted general reimbursement (general conditional reimbursement).

¹ Danish executive order no. 180 of 17 March 2005 on reimbursement, as amended

4. Oral combination products in ATC group C09A (ACE inhibitors) containing the individual substances
- perindopril (C09AA04)
 - quinapril (C09AA06)
 - benazepril (C09AA07)
 - fosinopril (C09AA09)
- will as of 13 July 2009 have their reimbursement status changed and will not be granted general reimbursement.

In the opinion of the Danish Medicines Agency, these medicinal products *do not meet* the criteria for being granted general reimbursement, cf. section 1(2) of the executive order on reimbursement.

With reference to section 1(4) of the executive order on reimbursement, it is, in the opinion of the Danish Medicines Agency, not possible to identify parts of the indication ('specific diseases') which independently meet the criteria set out in the executive order on reimbursement for being granted general reimbursement (general conditional reimbursement).

5. Oral combination products in ATC group C09B (ACE inhibitors) containing
- perindopril and indapamide (C09BA04)
 - perindopril and amlodipine (C09BB)
- will as of 13 July 2008 have their reimbursement status changed and will not be granted general reimbursement.

In the opinion of the Danish Medicines Agency, these medicinal products *do not meet* the criteria for being granted general reimbursement, cf. section 1(2) of the executive order on reimbursement.

With reference to section 1(4) of the executive order on reimbursement, it is, in the opinion of the Danish Medicines Agency, not possible to identify parts of the indication ('specific diseases') which independently meet the criteria set out in the executive order on reimbursement for being granted general reimbursement (general conditional reimbursement).

6. Oral medicinal products in ATC group C09C (angiotensin II antagonists) and C09X (renin inhibitors) containing the individual substances
- losartan (C09CA01)
 - eprosartan (C09CA02)
 - valsartan (C09CA03)
 - irbesartan (C09CA04)
 - candesartan (C09CA06)
 - telmisartan (C09CA07)
 - olmesartan (C09CA08)

- aliskiren (C09XA02) will as of 13 July 2009 have their reimbursement status changed and will be granted general conditional reimbursement with the condition:

“Patients with hypertension or any other type of cardiovascular disease requiring treatment, where treatment with medicinal products acting on the renin-angiotensin system that are eligible for general unconditional reimbursement

- has proven inadequate or 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.”

With reference to section 1(2), item 2 of the executive order on reimbursement, in relation to the question of general reimbursement, the Danish Medicines Agency finds that the relationship between the price of the medicinal products and their therapeutic value is not reasonable when comparing the individual substances in question with the individual ACE inhibitor substances captopril, enalapril, lisinopril, ramipril and trandolapril. With reference to section 1(3), item 5 of the executive order on reimbursement, the Danish Medicines Agency also finds that there is a risk that the medicinal products in question will be used as first-line treatment, even though this should not be the case in the opinion of the Danish Medicines Agency.

With reference to section 1(4) of the executive order on reimbursement, the Danish Medicines Agency finds that these medicinal products within the above condition *meet* the criteria for being granted general reimbursement, cf. section 1(2), item 2, of the executive order on reimbursement.

7. Oral combination products in ATC group C09D (angiotensin II antagonists) containing

- losartan and hydrochlorothiazide (C09DA01)
- eprosartan and hydrochlorothiazide (C09DA02)
- valsartan and hydrochlorothiazide (C09DA03)
- irbesartan and hydrochlorothiazide (C09DA04)
- candesartan and hydrochlorothiazide (C09DA06)
- telmisartan and hydrochlorothiazide (C09DA07)
- olmesartan and hydrochlorothiazide (C09DA08)
- valsartan and amlodipine (C09DB01)

will as of 13 July 2009 have their reimbursement status changed and will be granted general conditional reimbursement with the condition:

“Patients with hypertension or any other type of cardiovascular disease requiring treatment, where treatment with medicinal products acting on the renin-angiotensin system that are eligible for general unconditional reimbursement

- has proven inadequate or 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.”

With reference to section 1(2), item 2 of the executive order on reimbursement, in relation to the question of general reimbursement, the Danish Medicines Agency finds that the relationship between the price of the medicinal products and their therapeutic value is not reasonable when comparing the combination products in question with combination products containing enalapril, lisinopril and ramipril, possibly supplemented with the individual ACE inhibitor substances captopril, enalapril, lisinopril, ramipril and trandolapril. With reference to section 1(3), item 5 of the executive order on reimbursement, the Danish Medicines Agency also finds that there is a risk that the medicinal products in question will be used as first-line treatment, even though this should not be the case in the opinion of the Danish Medicines Agency.

With reference to section 1(4) of the executive order on reimbursement, the Danish Medicines Agency finds that these medicinal products within the above condition *meet* the criteria for being granted general reimbursement, cf. section 1(2), item 2 of the executive order on reimbursement.

Grounds

With reference to the fact that the medicinal products in ATC group C09 are recommended equally for all indications and class effect within each of the medicinal product groups ACE inhibitors and angiotensin II antagonists, the Reimbursement Committee found, in its recommendation of 29 January 2008, that the relationship between the price of the ACE inhibitors perindopril, quinapril, benazepril, fosinopril and trandolapril and their therapeutic value was not reasonable when compared to the price of medicinal products containing the other ACE inhibitors captopril, enalapril, lisinopril and ramipril. Against this background, the Reimbursement Committee recommended that the general reimbursement for the ACE inhibitors perindopril, quinapril, benazepril, fosinopril and trandolapril be discontinued.

For the angiotensin II antagonists and the renin inhibitor aliskiren in ATC groups C09C, C09D and C09X, the Reimbursement Committee found that the therapeutic value of the medicinal products did not measure up to the price paid in respect of the large number of patients who can be treated

with one of the cheaper ACE inhibitors containing captopril, enalapril, lisinopril and ramipril eligible for general reimbursement.

The Reimbursement Committee's additional recommendation of 2 September 2008 was based on the assumption that the Danish Medicines Agency will include any changes in price and consumption occurring after the Committee submitted its first recommendation on 29 January 2008 in its assessment basis.

Appendix II/C09 contains an updated price and consumption list for individual substances in ATC group C09 specifying the average lowest prices of treatment per day, the consumption at active substance level as well as the names and pharmaceutical forms of all medicinal products comprised by this decision. The prices of treatment per day are calculated over six price periods for the period 22 September 2008 to 14 December 2008. For these medicinal products, the dose used is established on the basis of the indication of hypertension.

Appendix III/C09 contains an updated price and consumption list specifying the average lowest unit prices calculated over the same period for combination products in ATC group C09 and for the individual substances of similar strength and in relevant comparable pharmaceutical form.

The prices of treatment on which the decision is based are calculated in accordance with the Danish Medicines Agency's guidelines of 4 July 2006 for evaluation and comparison of medicinal products in reassessments of reimbursement status, cf. below under Regulatory framework.

Changes in price and consumption which have occurred after 1 December 2008 do not give rise to a changed assessment, cf., however, below.

Re 1, 4 and 6 – Individual substances for oral treatment

The Danish Medicines Agency emphasises the Reimbursement Committee's reference to the fact that the medicinal products in ATC group C09 are recommended equally for all indications and class effect within each of the medicinal product groups ACE inhibitors and angiotensin II antagonists.

Re 1 and 4 – ACE inhibitors – Individual substances

Appendix II/C09 shows that the average lowest price of treatment per day for oral treatment with the individual substances captopril, enalapril, lisinopril, ramipril and trandolapril is between DKK 0.36 and DKK 1.37.

By comparison, the average lowest price of treatment per day for oral treatment with the individual substances perindopril, quinapril, benazepril and fosinopril is between DKK 3.80 and DKK 22.76.

Against this background, the Danish Medicines Agency finds that the relationship between the price of medicinal products containing the individual substances perindopril, quinapril, benazepril and fosinopril and their therapeutic value is not reasonable.

With reference to the fact that the medicinal products in ATC group C09 are recommended equally for all indications and class effect within the ACE inhibitors, it is, in the opinion of the Danish Medicines Agency, not possible to identify parts of the indication ('specific diseases') for these medicinal products which independently meet the criteria set out in the executive order on reimbursement for being granted general reimbursement (general conditional reimbursement).

With reference to the prices in Appendix II/C09, the Danish Medicines Agency finds that the relationship between the price of medicinal products containing the individual substances captopril, enalapril, lisinopril, ramipril and trandolapril and their therapeutic value is reasonable .

Re 6 – Angiotensin II antagonists and renin inhibitors – Individual substances

Appendix II/C09 shows that the average lowest price of treatment per day for oral treatment with the individual substances losartan, eprosartan, valsartan, irbesartan, candesartan, telmisartan, olmesartan and aliskiren is between DKK 5.29 and DKK 11.22.

By comparison, the average lowest price of treatment per day for oral treatment with the individual ACE inhibitor substances captopril, enalapril, lisinopril, ramipril and trandolapril is between DKK 0.36 and DKK 1.37.

As for the large number of patients who can be treated with one of these cheaper ACE inhibitors eligible for general reimbursement, in relation to the question of general reimbursement and with reference to section 1(2), item 2 of the executive order on reimbursement, the Danish Medicines Agency finds that the relationship between the price of the angiotensin II antagonists and the renin inhibitor aliskiren and their therapeutic value is not reasonable when comparing the medicinal products in question with the individual substances containing captopril, enalapril, lisinopril, ramipril and trandolapril.

With reference to section 1(3), item 5 of the executive order on reimbursement, the Danish Medicines Agency also finds, cf. below, that there is a risk that the medicinal products in question will be used as first-line treatment, even though this should not be the case in the opinion of the Danish Medicines Agency.

Figures from the Danish Medicines Agency's Register of Medicinal Product Statistics show that in 2007 a total of 525,096 persons were being treated with ACE inhibitors and/or angiotensin II antagonists. Of these, 222,438, corresponding to 42 per cent, were being treated with an angiotensin II antagonist. In the first six months of 2008, the percentage was the same as in 2007: 42 per cent. Figures for 2006 and the first ten months of 2007, on which the Reimbursement Committee's recommendation was based, showed that 43 per cent were being treated with an angiotensin II antagonist. This situation has thus not changed.

The Reimbursement Committee also referred to a survey conducted by the Danish Medicines Agency² which showed that for 46 per cent of the patients who in 2006 started a treatment with an angiotensin II antagonist, no prior treatment had been attempted with an ACE inhibitor. Updated figures for 2007 show that this situation only changed marginally in 2007 whereas figures from the second and third quarters of 2008 show a downward trend, 42 and 37 per cent, respectively. In the opinion of the Danish Medicines Agency, this is still not rational.

The Danish Medicines Agency emphasises that that the Reimbursement Committee refers to the fact that 5-20 per cent of patients treated with ACE inhibitors have adverse reactions in the form of cough. The consumption of angiotensin II antagonists is thus still not overall rational. In addition to this, cf. above, the figures show that many new patients start a treatment with angiotensin II antagonists without no prior treatment having been attempted with an ACE inhibitor.

For patients who do not tolerate or who cannot be treated adequately with captopril, enalapril, lisinopril, ramipril and trandolapril, the Danish Medicines Agency finds that the relationship between the price of angiotensin II antagonists and the renin inhibitor aliskiren and their therapeutic value is reasonable. In the very special cases where the doctor, based on an overall clinical assessment of the patient's condition, does not find treatment with captopril, enalapril, lisinopril, ramipril and trandolapril appropriate, we also find that the relationship between the price of treatment for angiotensin II antagonists and the renin inhibitor aliskiren and their therapeutic value is reasonable. These cases are comprised by the condition, cf. above under item 6.

Re 2, 3, 5 and 7 – Combination products for oral treatment

The Danish Medicines Agency emphasises the Reimbursement Committee's reference to the fact that the medicinal products in ATC group C09 are recommended equally for all indications and there is class

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<http://www.laegemiddelstyrelsen.dk/publikationer/netpub/forbrugsanalyser/angiotensin/html/chapter05.htm> (in Danish)

effect within each of the medicinal product groups ACE inhibitors and angiotensin II antagonists.

As the basis of our assessment of the future reimbursement status for combination products in ATC group C09, we have, taking the actual marketed strengths and pharmaceutical forms of the combination products in question as our point of departure, calculated the average lowest unit price for the combination product and the individual substances, respectively, of similar strength and in relevant comparable pharmaceutical form. Please see **Appendix III/C09**.

Re 2 – Combination products containing enalapril³, lisinopril and ramipril

With reference to the prices in Appendix III/C09, the Danish Medicines Agency finds that the relationship between the price of combination products containing the individual substances enalapril, lisinopril and ramipril in combination with hydrochlorothiazide and their therapeutic value is reasonable.

In relation to the combination product containing 10 mg of lisinopril and 12.5 mg of hydrochlorothiazide, we emphasise that the lowest average unit price is decreasing in price periods starting after 1 December 2008.

Re 3 – Combination products containing captopril

For combination products containing captopril and hydrochlorothiazide, the Danish Medicines Agency finds that the relationship between the lowest average unit price of DKK 5.76 and the therapeutic value is not reasonable as captopril alone costs DKK 0.44. With reference to the Reimbursement Committee's viewpoints concerning class effect within the group of ACE inhibitors, which is expressed in the Committee's recommendations of 29 January 2008 and 2 September 2008, it is finally emphasised that the average lowest unit prices of combination products containing hydrochlorothiazide and the equieffective doses of ACE inhibitors enalapril, lisinopril and ramipril are cheaper, cf. Appendix III/C09.

It is, in the opinion of the Danish Medicines Agency, not possible to identify parts of the indication ('specific diseases') for the combination product which independently meets the criteria set out in the executive order on reimbursement for being granted general reimbursement (general conditional reimbursement).

Re 3 – Combination products containing 20 mg of enalapril and 6 mg of hydrochlorothiazide

³ Cf., however, below under Re 3 on combination products containing 20 mg of enalapril and 6 mg of hydrochlorothiazide

Appendix III/C09 shows that the average lowest unit price of the combination product, tablets containing 20 mg of enalapril and 6 mg of hydrochlorothiazide, is DKK 5.93.

The average lowest unit price of combination products containing 20 mg of enalapril and 12.5 mg of hydrochlorothiazide is DKK 0.32. The average lowest unit price of the individual substance enalapril, 20 mg tablets, is DKK 0.36. Hydrochlorothiazide is not marketed as an individual substance. The Danish Medicines Agency agrees with the Reimbursement Committee that combination products may support good compliance in the use of medicinal products. The Danish Medicines Agency does not, however, find that the high price of the combination of enalapril 20 mg and hydrochlorothiazide 6 mg can be justified. The Danish Medicines Agency does thus not find that the therapeutic value measures up to the price. We do not find that there are any other special circumstances related to the medicinal product that can justify the high price of the medicinal product.

It is, in the opinion of the Danish Medicines Agency, not possible to identify parts of the indication ('specific diseases') for the combination product which independently meets the criteria set out in the executive order on reimbursement for being granted general reimbursement (general conditional reimbursement).

Re 5 – Combination products containing perindopril and amlodipine

Appendix III/C09 shows that the average lowest unit price of combination products containing 5 mg of perindopril in combination with 5 mg and 10 mg of amlodipine, respectively, is DKK 5.42 and DKK 7.17 for 10 mg of perindopril in combination with 5 mg and 10 mg of amlodipine, respectively.

The same appendix shows that the average lowest unit price of individual substances containing the ACE inhibitors enalapril, lisinopril and ramipril in equieffective doses corresponding to perindopril 5 mg and 10 mg is between DKK 0.31 and DKK 1.37. The average lowest unit price per day for amlodipine 5 and 10 mg in the same period is DKK 0.26 to DKK 0.32, cf. Appendix III/C09.

This information shows that the price of the combination product is significantly higher than the sum of the prices of the less expensive ACE inhibitors and amlodipine in separate formulations.

The Danish Medicines Agency agrees with the Reimbursement Committee that combination products may support good compliance in the use of medicinal products, but the Danish Medicines Agency does not, however, find that this circumstance in itself can justify a price that significantly exceeds the price of a combination of a less expensive ACE inhibitor and amlodipine separately. The Danish Medicines Agency does not find that

there are any other special circumstances related to the combination product that can justify the price difference.

With reference to the fact that the medicinal products in ATC group C09 are recommended equally for all indications and class effect within the ACE inhibitors, as well as the above-mentioned views on the additional cost in relation to potentially better compliance, it is, in the opinion of the Danish Medicines Agency, not possible to identify parts of the indication ('specific diseases') for these medicinal products which independently meet the criteria set out in the executive order on reimbursement for being granted general reimbursement (general conditional reimbursement).

Re 5 – Combination products containing perindopril and indapamide
Appendix III/C09 shows that the average lowest unit price of combination products containing 5 mg of perindopril in combination with 1.25 mg of indapamide is DKK 8.60. At the time of the Danish Medicines Agency's first recommendation of 29 January 2008, the price was DKK 8.74. This price has thus only changed marginally.

Appendix III/C09 shows that the average lowest unit price of medicinal products containing the ACE inhibitors enalapril, lisinopril and ramipril in equieffective doses corresponding to perindopril 5 mg and 10 mg is between DKK 0.31 and DKK 1.37. The average lowest unit price per day for indapamide 1.5 mg in the same period is DKK 1.85, cf. Appendix III/C09.

This information shows that the price of the combination product is significantly higher than the sum of the prices of the less expensive ACE inhibitors and indapamide in separate formulations.

The Danish Medicines Agency agrees with the Reimbursement Committee that combination products may support good compliance in the use of medicinal products, but the Danish Medicines Agency does not, however, find that this circumstance in itself can justify a price that significantly exceeds the price of a combination of a less expensive ACE inhibitor and indapamide separately. The Danish Medicines Agency does not find that there are any other special circumstances related to the combination product that can justify the price difference.

With reference to the fact that the medicinal products in ATC group C09 are recommended equally for all indications and class effect within the ACE inhibitors, as well as the above-mentioned views on the additional cost in relation to potentially better compliance, it is, in the opinion of the Danish Medicines Agency, not possible to identify parts of the indication ('specific diseases') for these medicinal products which independently meet the criteria set out in the executive order on reimbursement for being granted general reimbursement (general conditional reimbursement).

Re 7 – Combination products containing losartan, eprosartan, valsartan, irbesartan, candesartan, telmisartan, olmesartan and hydrochlorothiazide as well as combination products containing valsartan and amlodipine

Appendix II/C09 shows that the average lowest unit prices between DKK 5.29 and DKK 16.07 for oral treatment with combination products containing losartan, eprosartan, valsartan, irbesartan, candesartan, telmisartan, olmesartan and hydrochlorothiazide as well as containing valsartan and amlodipine are at the same level as the average lowest unit price for oral treatment with the individual substances losartan, eprosartan, valsartan, irbesartan, candesartan, telmisartan and olmesartan.

Against this it may be pointed out that the average lowest unit price for oral treatment with combination products containing enalapril, lisinopril and ramipril is significantly lower. In the cases where it is necessary to supplement with individual substances to obtain the desired dose, these medicinal products are also so cheap that the total expenses for treatment are still significantly lower than the expenses for treatment with combination products containing angiotensin II antagonists.

We refer to the reasons above concerning the individual substances containing the active substances in question: *Re 6 – Angiotensin II antagonists and renin inhibitors – Individual substances*

As mentioned above, there will be cases where no combination product will be available containing enalapril, lisinopril and ramipril in equieffective doses which can replace the combination products in question containing angiotensin II antagonists and where the patient as a result of this will have to take two or, in very few instances, more tablets.

The Danish Medicines Agency agrees with the Reimbursement Committee that combination products may support good compliance in the use of medicinal products, but the Danish Medicines Agency does not, however, find that this circumstance in itself can justify a price that significantly exceeds the price of the combination products and individual substances which can replace the combination products in question containing angiotensin II antagonists.

Regulatory framework

The legal basis for reassessment and withdrawal of reimbursement granted is sections 3 and 4 of Danish executive order no. 180 of 17 March 2005 on reimbursement and in accordance with the principles laid down in the Danish Medicines Agency's guidelines of 8 June 2005 on the procedure for reassessment of the reimbursement status of medicinal products as well as the Danish Medicines Agency's guidelines of 4 July 2006 for evaluation and comparison of medicinal products in reassessments of reimbursement

status. A link to these documents can be found at www.dkma.dk > Companies > General reimbursement > Reassessment of reimbursement status for medicinal products (the fact box).

Reassessment

In connection with the introduction of the reassessment of the reimbursement status of medicinal products in 2005, it was decided that the reimbursement status of all medicinal products should be reassessed regularly. The reimbursement status granted to the medicinal products following this decision will thus be reassessed in connection with this regular reassessment procedure.

In addition, the Danish Medicines Agency can initiate ad hoc reassessments, e.g. when receiving new information about inappropriate consumption, new treatment recommendations, changes in price etc. The Danish Medicines Agency monitors the development in consumption and prices comprised by this decision.

Information

Doctors and pharmacies will be informed of the content of this decision via articles in professional journals etc. Other stakeholders will receive a notification referring to the Danish Medicines Agency's website. All decisions with appendices for medicinal products in ATC groups C02, C03, C07, C08 and C09 as well as an overview of the current and future reimbursement status for all medicinal products comprised by these decisions will be available at the website.

Complaints

This decision may be appealed to the Danish Ministry of Health and Prevention, Slotsholmsgade 10-12, 1216 Copenhagen K, Denmark. However, the Ministry cannot reassess the Danish Medicines Agency's scientific evaluation.

Yours sincerely,



Elisabeth Thomsen

Appendix II/C09: Price and consumption list of agents acting on the renin-angiotensin system, individual substances

Average lowest price of treatment per day for hypertension calculated over six price periods (for the period 22 September to 14 December 2008)

1. ATC	2. Active substance/ group	3. Number of persons treated		4. Dose used (mg) ¹	5. Pharmaceutic form	6. Strength(s) (mg)	7. Avg. lowest unit price(s) (DKK)	8. Avg. lowest price of treat. per day (DKK)
		2006	2007					
C09AA	Ace inhibitors, plain							
		259,199	277,082					
C09AA01	Captopril	5,683	4,953	50 ²³⁶	Tablets	25	0.39	0.78
C09AA02	Enalapril	133,929	145,522	20 - 40 ⁴⁵	Tablets	20	0.36	0.36 - 0.72
C09AA03	Lisinopril	11,519	12,165	20 ⁴⁵	Tablets	20	1.37	1.37
C09AA04	Perindopril	31,747	33,214	4 - 8 ⁴⁵	Tablets	4	3.80	3.80 - 7.60
	Perindopril	31,747	33,214	5 - 10 ⁴⁵	Film-coated tablets	5 / 10	5.42 / 7.17	5.42 - 7.17
C09AA05	Ramipril	56,126	62,372	5 - 10 ⁴⁵	Tab./capsules	5 / 10	0.53 1 0.89	0.53 - 0.89
C09AA06	Quinapril	1,306	1,158	20 - 40 ⁴⁵	Film-coated tablets	20	4.40	4.40 - 8.80
C09AA07	Benazepril	343	300	20 - 40 ⁴⁵	Film-coated tablets	20	11.38	11.38 - 22.76
C09AA09	Fosinopril	382	285	40 ⁴⁵	Tablets	20	6.41	12.82
C09AA10	Trandolapril	22,070	20,489	4 ⁴⁵	Capsules/hard cap.	2	0.67	1.34
C09CA	Angiotensin II antag. plain							
		124,151	136,667					
C09CA01	Losartan	48,366	50,693	50 - 100 ⁴⁵	Film-coated tablets	50 / 100	7.36 / 10.13	7.36 - 10.13
C09CA02	Eprosartan	3,428	3,489	600 ⁴⁵	Film-coated tablets	600	6.34	6.34
C09CA03	Valsartan	11,116	12,782	80 - 160 ⁴⁵	Film-coated tablets	80 / 160	7.62 / 10.98	7.62 - 10.98
C09CA04	Irbesartan	14,650	15,440	150 - 300 ⁴⁵	Film-coated tablets	150 / 300	7.40 / 11.01	7.40 - 11.01
C09CA06	Candesartan	36,371	42,135	8 - 16 ⁴⁵	Tablets	8 / 16	5.29 / 6.73	5.29 - 6.73
C09CA07	Telmisartan	9,649	10,683	40 - 80 ⁴⁵	Tablets	40 / 80	7.16 / 8.84	7.16 - 8.84
C09CA08	Olmesartanmedoxomil	2,311	3,095	20 - 40 ⁴⁵	Film-coated tablets	20 / 40	6.23 / 7.51	6.23 - 7.51
C09CA	Renin inhibitors	-	-					
C09XA02	Aliskiren	-	-	150 ³	Film-coated tablets	150	11.22	11.22

Notes/explanations:

1	Unless otherwise stated, the dose can be given once a day
2	Divided into two daily doses
3	DDD value (WHO)
4	Equieffective dose from IRF's background note
5	Recommended by IRF
6	Not recommended by IRF

Name and form of medicinal product

ATC	Name	Form
C09AA01	Capoten	tablets
	Captol	tablets
	Captopril 'Actavis'	tablets
	Captopril 'Alpharma'	tablets
	Captopril 'Merck NM'	tablets
	Captopril 'Stada'	tablets
C09AA02	Corodil	tablets
	Enacodan	tablets
	Enalapril '1A Farma'	tablets
	Enalapril 'Actavis'	tablets
	Enalapril 'Krka'	tablets
	Enalapril 'Merck NM'	tablets
C09AA03	Enalapril 'Sandoz'	tablets
	Lisinopril 'Actavis'	tablets
	Lisinopril 'Arrow'	tablets
	Lisinopril 'Mylan'	tablets
	Lisinopril 'Ranbaxy'	tablets
C09AA04	Lisinopril 'Sandoz'	tablets
	Lisinopril 'Stada'	tablets
	Asyntilsan	tablets
	Coverex	tablets
	Coversyl	tablets
	Coversyl Arginine	film-coated tablets
	Coversyl Novum	film-coated tablets
	Prestarium	film-coated tablets

C09AA05	Ramipril '1A Farma'	tablets
	Ramipril 'Actavis'	capsules, hard
	Ramipril 'Actavis'	tablets
	Ramipril 'Copyfarm'	tablets
	Ramipril 'HEXAL'	tablets
	Ramipril 'Ranbaxy'	film-coated tablets
	Ramipril 'ratiopharm'	tablets
	Ramipril 'Sandoz'	tablets
	Ramipril 'Stada'	tablets
	Triatec	capsules, hard
	Triatec	tablets
C09AA06	Accupro	film-coated tablets
	Accupro	tablets
	Quinapril 'Actavis'	film-coated tablets
	Quinapril 'Alternova'	film-coated tablets
C09AA07	Cibacen	film-coated tablets
C09AA09	Fosinopril natrium 'Teva'	tablets
C09AA10	Odrik	capsules, hard
	Trandolapril 'Actavis'	capsules, hard
	Trandolapril 'Alternova'	capsules, hard
	Trandolapril 'Arrow'	capsules, hard
	Trandolapril 'Merck NM'	capsules, hard
	Trandolapril 'Orifarm'	capsules, hard
C09CA01	Cozaar	film-coated tablets
	Cozaar startpakke	film-coated tablets
	Lorzaar	film-coated tablets
	Losaprex	film-coated tablets
C09CA02	Teveten	film-coated tablets
	Tevetenz	film-coated tablets
C09CA03	Diovan	film-coated tablets
	Diovane	film-coated tablets
C09CA04	Aprovel	film-coated tablets
	Aprovel	tablets
	Karvea	tablets
C09CA06	Amias	tablets
	Atacand	tablets

	Ratacand	tablets
C09CA07	Kinzalmono	tablets
	Micardis	tablets
C09CA08	Benetor	film-coated tablets
	Olmetec	film-coated tablets
C09XA02	Rasilez	film-coated tablets

Appendix III/C09: Price and consumption list of agents acting on the renin-angiotensin system, combination products

Average lowest unit price calculated over six price periods (for the period 22 September 2008 to 14 December 2008)

1. ATC	2. Active substance/group	3. Number of persons treated		4. Pharmaceutic. form	5. Strength (mg)	6. Avg. lowest unit price (DKK)
		2006	2007			
C09BA	ACE inhibitors and diuretics	53,471	66,648			
C09BA01	Captopril and hydrochlorothiazide	267	255	Tablets	50+25	5.76
	Captopril			Tablets	50	0.44
	Hydrochlorothiazide	----- Not marketed in Denmark -----				
C09BA02	Enalapril and hydrochlorothiazide	33,428	42,139	Tablets	20+12,5 / 20+6	0.32 5.93
	Enalapril			Tablets	20	0.36
	Hydrochlorothiazide	----- Not marketed in Denmark -----				
C09BA03	Lisinopril and hydrochlorothiazide	6,188	6,878	Tablets	10+12,5 / 20+12,5	3.51 0.87
	Lisinopril			Tablets	10 / 20	0.31 1.37
	Hydrochlorothiazide	----- Not marketed in Denmark -----				
C09BA04	Perindopril and indapamide	7,097	8,095	Tablets	5+1,25	8.60
	Perindopril			Tablets	4	3.80
	Perindopril			Film-coated tablets	5	5.42
	Indapamide			Prolonged-rel. tab.	1.5	1.85
	Indapamide			Film-coated tablets	2.5	1.67
C09BA05	Ramipril and hydrochlorothiazide	6,909	9,699	Tablets	5+25	0.89
	Ramipril			Tablets	5	0.53
	Hydrochlorothiazide	----- Not marketed in Denmark -----				
C09BB	ACE inhibitors and calcium ch. blockers	-	-			
C09BB	Perindopril and amlodipine	-	-	Tablets	5+5 / 5+10	5.42 / 5.42
C09BB	Perindopril and amlodipine	-	-	Tablets	10+5 / 10+10	7.17 / 7.17
	Perindopril			Tablets	4	3.80
	Perindopril			Film-coated tablets	5 / 10	5.42 7.12
	Amlodipine			Tablets	5 / 10	0.26 0.32

1. ATC	2. Active substance/group	3. Number of persons treated		6. Pharmaceutic. form	7. Strength (mg)	8. Avg. lowest unit price (DKK)
		2006	2007			
C09DA	Angiotensin II antagonists and diuretics	86,431	97,643			
C09DA01	Losartan and hydrochlorothiazide	39,371	42,249	Film-coated tablets	50+12,5 / 100+12,5	7.68 / 12.37
	Losartan and hydrochlorothiazide			Film-coated tablets	100+25	8.45
	Losartan			Film-coated tablets	50 / 100	7.36 10.13
	Hydrochlorothiazide	----- Not marketed in Denmark -----				
C09DA02	Eprosartan and hydrochlorothiazide	1,451	1,923	Film-coated tablets	600+12,5	6.55
	Eprosartan			Film-coated tablets	600	6.34
	Hydrochlorothiazide	----- Not marketed in Denmark -----				
C09DA03	Valsartan and hydrochlorothiazide	14,399	16,717	Film-coated tablets	80+12,5 / 160+12,5	7.72 / 9.94
	Valsartan and hydrochlorothiazide			Film-coated tablets	160+25 / 320+12,5	10.99 / 16.07
	Valsartan and hydrochlorothiazide			Film-coated tablets	320+25	16.07
	Valsartan			Film-coated tablets	80 / 160	7.62 / 10.98
	Valsartan			Film-coated tablets	320	16.07
	Hydrochlorothiazide	----- Not marketed in Denmark -----				
C09DA04	Irbesartan and hydrochlorothiazide	10,677	11,602	Film-coated tablets	150+12,5 / 300+12,5	7.56 / 9.56
	Irbesartan and hydrochlorothiazide			Film-coated tablets	300+25	12.07
	Irbesartan			Film-coated tablets	150 / 300	7.40 / 11.01
	Hydrochlorothiazide	----- Not marketed in Denmark -----				
C09DA06	Candesartan and hydrochlorothiazide	15,502	17,319	Tablets	8+12,5 / 16+12,5	7.19 / 9.04
	Candesartan			Tablets	8 / 16	5.29 / 6.73
	Hydrochlorothiazide	----- Not marketed in Denmark -----				
C09DA07	Telmisartan and hydrochlorothiazide	5,767	7,406	Tablets	40+12,5 / 80+12,5	7.45 / 7.42
	Telmisartan and hydrochlorothiazide			Tablets	80+25	11.61
	Telmisartan			Tablets	40 / 80	7.16 8.84
	Hydrochlorothiazide	----- Not marketed in Denmark -----				
C09DA08	Olmesartan and hydrochlorothiazide	526	1,551	Film-coated tablets	20+12,5 / 20+25	6.23 6.23
	Olmesartan			Film-coated tablets	20	6.23
	Hydrochlorothiazide	----- Not marketed in Denmark -----				

1. ATC	2. Active substance/group	3. Number of persons treated		6. Pharmaceutic. form	7. Strength (mg)	8. Avg. lowest unit price (DKK)
		2006	2007			
C09DB	Angiotensin II antagonists and calcium ch.	-	3,279			
C09DB01	Valsartan and amlodipine	-	3,279	Film-coated tablets	80+5 / 160+5	7.83 / 11.33
	Valsartan and amlodipine			Film-coated tablets	160+10	11.49
	Valsartan			Film-coated tablets	80 / 160	7.62 / 10.98
	Amlodipine			Tablets	5 / 10	0.30 / 0.39

Name and form of medicinal product

ATC	Name	Form
C09BA01	Capozid	tablets
	Capozide	tablets
C09BA02	Corodil Comp.	tablets
	Enacecor	tablets
	Enalapril hydrochlorothiazide 'Teva'	tablets
	Enalapril/hydrochlorothiazide 'Actavis'	tablets
	Enalapril/hydrochlorothiazide 'Ratiopharm'	tablets
	Enalapril/hydrochlorothiazide '1A Farma'	tablets
	Enalapril/hydrochlorothiazide 'Krka'	tablets
	Synerpril	tablets
C09BA03	Lisinoplus	tablets
	Lisinopril hydrochlorothiazide 'ratiopharm'	tablets
	Lisinopril/hydrochlorothiazide 'Alternova'	tablets
	Lisinopril/hydrochlorothiazide 'Sandoz'	tablets
	Lisinopril/hydrochlorothiazide 'Copyfarm'	tablets
	Lisinopril-hydrochlorothiazide 'Actavis'	tablets
C09BA04	Coversyl Arginine Plus	film-coated tablets
	Coversyl Comp Novum	film-coated tablets
	Coversyl Comp.	tablets
C09BA05	Ramipril/hydrochlorothiazide '1A Farma'	tablets
	Ramipril/hydrochlorothiazide 'ratiopharm'	tablets

	Ramipril/hydrochlorothiazide 'Actavis'	tablets
	Ranid	tablets
	Triatec Comp.	tablets
C09BB	Coversical	tablets
C09DA01	Cosaar Plus	film-coated tablets
	Cozaar Comp.	film-coated tablets
	Cozaar Comp. Forte	film-coated tablets
	Cozaar Comp.	film-coated tablets
	Cozaar Comp. 100 mg/12.5 mg	film-coated tablets
	Cozaar Comp. Forte	film-coated tablets
	Cosaar Plus	film-coated tablets
	Fortzaar	film-coated tablets
	Forzaar	film-coated tablets
	Losazid	film-coated tablets
C09DA02	Teveten Comp.	film-coated tablets
C09DA03	Co-Diovan 160 mg/12.5 mg	film-coated tablets
	Co-Diovan Forte 160 mg/25 mg	film-coated tablets
	Corixil	film-coated tablets
	Cotareg	film-coated tablets
	Cotareg 160 mg/12.5 mg	film-coated tablets
	Cotareg 80 mg/12.5 mg	film-coated tablets
	Co-Vals Forte	film-coated tablets
	Diovan Comp.	film-coated tablets
	Diovan Comp. 160 mg/12.5 mg	film-coated tablets
	Diovan Comp. 160 mg/25 mg	film-coated tablets
	Diovan Comp. 320 mg/12.5 mg	film-coated tablets
	Diovan Comp. 320 mg/25 mg	film-coated tablets
	Diovan Comp. 80 mg/12.5 mg	film-coated tablets
	Kalpress Plus Forte	film-coated tablets
C09DA04	CoAprovel	film-coated tablets
	CoAprovel	tablets
	Karvezide	tablets
C09DA06	Atacand Plus	tablets
	Atacand Zid	tablets
	Atazid	tablets
	Hytacand	tablets

	Ratacand Plus	tablets
	Ratacand Zid	tablets
C09DA07	Kinzalkomb	tablets
	MicardisPlus	tablets
	PritorPlus	tablets
C09DA08	Benetor Comp.	film-coated tablets
	Olmotec Plus	film-coated tablets
C09DB01	Exforge	film-coated tablets