

A review of medicines for lowering blood pressure

Summary

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TLV

TANDVÅRDS- OCH
LÄKEMEDELSFÖRMÅNSVERKET

The LFN has changed name to the TLV

On the 1st of September 2008 we changed name to the TLV,
the Dental and Pharmaceutical Benefits Agency

We decide if pharmaceutical products and dental care procedures shall be subsidized.



Why is the LFN conducting a review?

On adopting new reimbursement rules in October of 2002, it was not practically possible to review all medicines according to the new rules. Therefore, the LFN is now conducting a review of approximately 2,000 medicines to see if they should continue to be given reimbursement status in the future. Each of the medicines will be tried according to the new rules and will either retain or lose reimbursement status.

More health per tax crown

The purpose of the new reimbursement rules is to allow the Swedish population to extract as much health value as possible for every tax crown allocated to medicines. We eliminate those medicines that do not show sufficient effectiveness in relation to what they cost. However, this does not mean that we aim only to have inexpensive medicines in the medical reimbursement system. If a medicine has positive effects on a person's health and quality of life, and on a socio-economic level as a whole, then it may also be worth paying for.

Three principles for making decisions

In reimbursement decisions for a medicine, we shall, among other things, evaluate whether or not it is cost-effective. This means that we weigh the effectiveness of the medicine against its cost. We also incorporate other principles into our evaluation: the needs and solidarity principle, which means that those who have the greatest medical needs shall receive more of our healthcare resources than other patient groups; and the human value principle, which means that we must respect the equal value of all individuals.

49 groups to be reviewed

In this review we are testing medicines in one therapeutic area after another. The review encompasses a total of 49 groups of medicines and the order in which they are tested is determined by how large the sales figures were for each respective group in 2003. The medicines that sold the most will be reviewed first.

Extensive research and groundwork

Before any decision is made, we perform a comprehensive investigation and analysis of data on medical effect and cost-effectiveness which we request from pharmaceutical companies in regard to their medicines. We also review the scientific, medical, and health economic literature available for the group of medicines to be reviewed. In addition, we sometimes need to construct our own health economic models. We publish each completed review in a final report. The report documents the existing body of scientific knowledge for the group in question. Where possible, the agency also reports on an evaluation of each medicine's cost-effectiveness. We also prepare a synopsis of the report to be printed separately.

Assessment by independent external experts

The assembled knowledge in regard to medical effect and health economic documentation which we present in the final report has been assessed by independent external medical experts. The report has also been circulated for comments to the SBU (The Swedish Council on Technology Assessment in Health Care), Medical Products Agency and the National Board of Health and Welfare. The companies and patient organisation groups concerned, as well as the county councils' pharmaceutical reimbursement group, have also had the opportunity to give input.

If you are interested in the entire report then it is available for download in Swedish at www.lfn.se. You can also order it from the LFN. The English version of the entire report will be available shortly.

A review of medicines for lowering blood pressure

The LFN (Läkemedelsförmånsnämnden) has concluded a review of medicines used to treat hypertension. In total the review covered approximately fifty pharmaceutical substances and a large range of products (original brands, generics and parallel imports) already part of the pharmaceutical reimbursement scheme.

This review is part of our ongoing evaluation of the entire list of medicines approved for pharmaceutical reimbursement. In it we establish whether a drug already reimbursed, should also be reimbursed in the future. Each medicine is evaluated and will either retain or lose its reimbursement status. The purpose of the exercise is to extract as much health as possible for every tax crown expended on medicines. This is the fourth therapeutic group to be presented. In earlier reviews we have treated the results from medicines against migraine, stomach acid and asthma, chronic obstructive pulmonary disease (COPD) and coughing.

Six groups of hypertension drugs

The treatment of hypertension today consists of medicines which affect the body in many different ways. The same medicine is used to treat a number of different diseases such as hypertension, heart failure, arrhythmia and the prevention of migraine. A number of medicines are also available as a fixed combination substance. The medicines used to treat hypertension are often divided into groups. These are:

- anti-hypertensive substances
- diuretics
- betablocking medicines
- calcium channel blockers
- ACE inhibitor
(angiotensin converting enzyme)
- ARB (angiotensin-receptor-blockers)

Many companies decreased their price in order to retain reimbursement

One finding from our review is that prices vary greatly for many medicines used for treating hypertension despite having a similar effect. Many companies have chosen to decrease their prices in connection with our review in order to retain reimbursement status. These price decreases represent a savings of approximately 115 million Skr per year.

Three active substances lose reimbursement

In total approximately 46 pharmaceutical substances retain reimbursement. For 23 of these substances the reimbursement granted is restricted. In total society is estimated to save approximately 30 million Skr per year for the three medicines which will no longer be part of the reimbursement scheme. The choice to restrict reimbursement for a number of products depends on one of two things: either there are cheaper alternatives within the system or there are patient groups with special needs who cannot use the cheaper alternatives. Our estimates show that there is a further 250 million Skr which can be released into the system if givers of healthcare follow our restrictions for angiotensin-receptor-blockers (ARB).

General and restricted reimbursement

There are two types of reimbursement within the pharmaceutical reimbursement scheme:

- **General reimbursement means that a medicine receives reimbursement for the whole of its approved area of use.**
- **Limited reimbursement means that a medicine is reimbursed only for a specific area of use or a specified patient group.**

It is important that the county councils develop a support mechanism for prescribers to make it easier for doctors to follow restrictions so that decisions coming from the LFN are able to contribute to a cost-effective use of medicines.

Total potential savings of almost 400 million Skr

This review represents a total potential savings of 400 million Skr. The decisions come into force on the 1st of September 2008 regardless of whether they have been appealed or not. It is only if a court repeals a decision that the medicine in question has the possibility to reenter the benefits system. A list of the decisions which have been appealed will be available on our website at www.lfn.se.

Medicines and substances for treating high blood pressure which either lose reimbursement or receive restricted reimbursement from the 1st of September 2008

Table 1: Three medicines lose reimbursement completely.

Active substance	Therapeutic group	Original product
Lerkanidipine	Calcium channel blocker	Zanidip
Cilazapril	ACE inhibitor	Inhibace, Inhibace Comp
Trandolapril and verapamil	ACE inhibitor, combination	Tarka

Table 2: Medicines which have lost their reimbursement and where another product containing the active substance will be available within the benefits system.

Active substance	Therapeutic group	Original product
Isradipine*	Calcium channel blocker	Lomir
Nifedipine, long-acting*	Calcium channel blocker	Adalat Oros
Kinapril**	ACE inhibitor	Accupro, Accupro Comp

* The substances will still be available in a reimbursed version, but on restriction (see Table 5).

** The substance will still be available on reimbursement, even though the original brand Accupro loses its reimbursement.

Table 3: All ARBs get limited reimbursement.

Active substance	Therapeutic group	Original product
Losartan*	ARB	Cozaar, Cozaar Comp, Cozaar Comp Forte
Eprosartan*	ARB	Teveten, Teveten Comp
Valsartan*	ARB	Diovan, Diovan Comp
Irbesartan*	ARB	Aprovel, CoAprovel
Kandesartan*	ARB	Atacand, Atacand Plus
Telmisartan*	ARB	Micardis, Micardis Plus
Valsartan and amlodipin	ARB, combination	Exforge
Restriction: ARB is reimbursed only for patients who have tried but cannot use ACE inhibitors or as a complement to an ACE inhibitor.		

* Also as fixed combinations containing hydrochlorotiazide.

Table 4 All beta blockers get limited reimbursement.

Active substance	Therapeutic group	Original product
Pindolol	Beta blockers	Viskén
Propranolol	Beta blockers	Inderal, Inderal Retard
Metoprolol	Beta blockers	Seloken, Seloken Zoc
Atenolol	Beta blockers	Tenormin
Bisoprolol	Beta blockers	Emconcor
Karvedilol	Beta blockers	Kredex
Restriction: For newly commenced treatment of hypertension the above beta blockers are reimbursed only if patients have first tried other groups of medicines.		
Labetalol	Beta blockers	Trandate
Restriction: Labetalol is reimbursed only for treatment of hypertension during pregnancy.		

Table 5: Four calcium channel blockers get limited reimbursement.

Active substance	Therapeutic group	Original product
Isradipine, long-acting	Calcium channel blocker	Lomir SRO
Restriction: Long-acting Isradipine (Lomir SRO) is reimbursed only for treatment of hypertension during pregnancy.		
Nifedipine	Calcium channel blocker	Adalat
Restriction: Short-acting Nifedipine (Adalat) is reimbursed only for treatment of hypertension during pregnancy and for the treatment of Morbus Raynaud.		
Verapamil	Calcium channel blocker	Isoptin, Isoptin Retard
Diltiazem	Calcium channel blocker	Cardizem, Cardizem Retard, Coramil, Unotard
Restriction: For treatment of hypertension, diltiazem and verapamil are reimbursed only if the patient cannot use vasodilating calcium channel blockers.		

Table 6: One ACE inhibitor gets limited reimbursement.

Active substance	Therapeutic group	Original product
Fosinopril	ACE inhibitor	Monopril
Restriction: Fosinopril is reimbursed only for patients with severe kidney function problems.		

Table 7: One diuretic gets limited reimbursement.

Active substance	Therapeutic group	Original product
Torsemide	Diuretic	Torem
Restriction: Torsemide is reimbursed only for patients needing loop-diuretics but who cannot use furosemide.		

Table 8: Three antihypertensive agents get limited reimbursement.

Active substance	Therapeutic group	Original product
Metyldopa	Antihypertensive agents	Aldomet
Restriction: Metyldopa is reimbursed only for treatment of hypertension during pregnancy.		
Moxonidine	Antihypertensive agents	Physiotens
Doxazosin	Antihypertensive agents	Alfadiil
Restriction: For treatment of hypertension doxazosin and moxonidine are reimbursed only if the patient has first tried other groups of medicines.		

These medicines turnover approximately 2 billion Skr

Sales of hypertension drugs within the benefits system reached 2.4 billion Skr in 2007 and are dominated by ARB drugs which stand for approximately 40 percent of sales value.

Socio-economic costs amount to some billions

Treatment of a particular disease does not only consist of costs for medicines. The disease can also cause other costs for society. Hypertension itself does not lead to high costs for society. However the diseases avoided by treating hypertension do lead to high costs. Examples of such diseases are stroke and heart failure which cost society a number of billions of Skr annually.

Principles for granting reimbursement

When judging if a medicine shall be included in the pharmaceutical benefits system we take the three principles detailed in the law on pharmaceutical benefits into account.

The three principles are:

- cost-effectiveness principle
- need and solidarity principle
- human value principle

We must evaluate if the use of a medicine is cost-effective, meaning that we weigh the utility of the medicine against the cost. We shall also observe the other two principles. The need and solidarity principle means that those in greatest medical need shall have more of healthcare resources than other patient groups. The human value principle means that the healthcare system shall have respect for the equal value of all people.

Similar effect – price comparisons sufficient

The health economic literature shows that the value of treating hypertension easily matches the cost of the treatment. However, we make decisions on individual products. Therefore we are interested in how effective the medicines included in the review are when compared to each other.

The medical literature shows that effects and side-effects are in the main similar for the different medicines when used in treating high blood pressure. Therefore comparing the cost of the pharmaceutical is enough to judge the cost-effectiveness for each medicine. The cost-effectiveness analysis in this review is as a result reduced to in many parts being a cost comparison.

Important with a wide range of products

There is a great need for a wide range of medicinal products which treat hypertension. One reason for this is that many patients need more than one medicine to treat their blood pressure. Often the same patient needs drugs from a number of different groups of medicines. At the level of the individual different patients can respond in different ways to treatment using the same medicine.

If we were to interpret the cost-effectiveness principle too narrowly then this would mean that we would only have one medicine left in many therapeutic groups. This would not however lead to a cost-effective use of the medicines. There is great value in having access to a number of different medicines in the same group. To a large extent this is why we let prices vary somewhat and have introduced a pricing corridor.

This means that we accept a higher price for a hypertension drug if the company marketing it can show that the medicine is a cost-effective alternative even at a higher price. A medicine which is considerably better than the others may be allowed a price which is over and above the pricing corridor.

Reasoning behind decisions

In the following sections we briefly account for the decisions where we have changed the reimbursement status of the medicine in question, in other words the medicine which has lost its reimbursement or received limited reimbursement. If you would like a more detailed picture of the other decisions then there is more information in the final report available on our website. There you can also read more on each individual decision.

Following all of the price decreases and with the price variance we allow using the pricing corridor most of the medicines retain their reimbursement. Only three active substances disappear completely from the benefits scheme while 23 of them get a limited reimbursement.

Of the 23 restrictions most of the medicines are in the groups of medicines known as ARB and beta blockers. All medicines within these two groups get limited reimbursement.

The three active substances which disappear from the scheme are a calcium channel blocker, an ACE inhibitor and a combination substance. There is also one original substance which disappears but there will be an alternative left within the system for this. This is for the ACE inhibitor Accupro which costs too much compared to the cheaper copies.

Medicines leaving the benefits system

In this section we briefly account for the reasons behind the decision to exclude the three active substances from the benefits system.

Lercanidipine (Zanidip), cilazapril (Inhibace and Inhibace Comp) as well as trandolapril and verapamil (Tarka)

Treatment using Lercanidipine, cilazapril and trandolapril and verapamil are not cost-effective compared to well-documented and cheaper medicines. The prices are too high in comparison to the alternatives.

The pharmaceutical companies Meda, Roche and Abbott Scandinavia have not submitted any documentation showing that their medicines have a better effect than other similar medicines and which supports the high price the companies want to charge.

Medicines losing reimbursement but where the substance remains in the benefits system

In this section we account for the reasons behind decisions for medicines losing their reimbursement but which in some form will remain in the benefits system.

Isradipine (Lomir) and long-acting Nifedipine (Adalat Oros)

The prices for Isradipine and long-acting Nifedipine are too high. A general treatment using these substances is therefore not cost-effective compared to well-documented and cheaper medicines. Lomir and Adalat Oros will therefore be excluded from the benefits system. However it is important to reimburse these active substances for a limited group of patients (see below).

Kinapril (Accupro)

The price for the original medicine Accupro is too high and treatment using this medicine is not cost-effective compared to better-documented and cheaper medicines. A generic form of kinapril at a lower price will be retained in the reimbursement system.

Medicines attaining limited reimbursement

In this section we account briefly for the medicines where we have chosen to limit reimbursement, either as a second line treatment or for patient groups with special needs.

All ARB medicines get limited reimbursement

All ARB medicines get limited reimbursement. ARB shall be reimbursed for patients who have tried but cannot use ACE inhibitors or as a complement to ACE inhibitors.

The prices for ARB medicines are too high for a general treatment using these substances to be considered cost-effective compared to well-documented and cheaper medicines. There are however smaller groups of patients where treatment with ARB medicines can be cost-effective compared to cheaper alternatives.

When treating patients with an uncomplicated form of hypertension calcium antagonists or a low dose of thiazide should be tried before treating the patient with ARB drugs.

Limited reimbursement for all beta blockers

All beta blockers will receive limited reimbursement on a group level. When commencing treatment for hypertension the medicines shall only be reimbursed for patients who have first tried other groups of medicines and not achieved their treatment objectives.

The SBU (Statens Beredning för Medicinsk Utvärdering) and Medical Products Agency (MPA) have concluded that beta blockers are not as good as the other large therapeutic groups for the treatment of high blood pressure. These conclusions are also supported in a number of newly published studies and meta-analyses.

Despite these findings beta blockers have a well-documented effect and an accepted place in therapy. For some patients who have tried some of the other therapeutic groups to lower blood pressure but not achieved the treatment objective, it may be both urgent and cost-effective to use beta blockers. Many patients also use beta blockers to treat a number of other conditions. Beta blockers have demonstrated a good effect for treatment of conditions such as angina, heart failure and arrhythmia and will continue to be reimbursed for these conditions.

There is one exception to this where a beta blocker has its own restriction. This is for labetalol (Trandate) where we judge it to be important to reimburse the medicine for pregnant women. The MPA presents labetalol in its treatment recommendations "Treatment of hypertension during pregnancy" from 1996 as an alternative for treatment of hypertension during pregnancy.

Four calcium channel blockers receive limited reimbursement

In total reimbursement will be restricted for four different active substances in this class. Long-acting Isradipine (Lomir SRO) will only be reimbursed for treatment of hypertension during pregnancy. Nifedipine (Adalat) will also be restricted but here the restricted use is for pregnant women and patients suffering from Morbus Raynauds disease.

In their treatment recommendations in "Treatment of hypertoni during pregnancy" from 1996 the MPA indicate Isradipine and Nifedipine as alternatives for treatment of hypertension in connection with pregnancy.

Adalat is one of very few medicines approved for treatment under the indication Morbus Raynauds disease. This is an important condition to treat. The condition means the patient's fingers and possibly toes turn blueish, lose feeling and can be damaged permanently.

General treatment using Isradipine and Nifedipine is however not cost-effective in comparison with well-documented and cheaper medicines as the prices for these substances are too high.

For treatment of hypertension verapamil (Isoptin and Isoptin Retard) and diltiazem (Cardizem, Cardizem Retard, Cardizem Unotard and Coramil) will only be reimbursed for patients who cannot use the calcium channel blockers amlodipine or felodipine. The prices for these medicines are too high and for that reason general treatment using these substances are not cost-effective in comparison with well-documented and cheaper medicines.

For treatment of angina the medicines shall continue to be reimbursed.

One diuretic gets limited reimbursement

Torasemide shall only be reimbursed for patients needing loop-diuretics but who cannot use furosemide. The price for torasemide cannot be supported in view of the availability of cheaper diuretics and ACE inhibitors. General treatment with this substance is not cost-effective in comparison with well-documented and cheaper medicines.

It is however important to be able to offer loop diuretics as a treatment alternative for some patients. In the cases where these patients cannot take furosemide then torasemide is the only approved treatment alternative left. Within this limited group it is reasonable for torasemide to receive continued reimbursement.

One ACE inhibitor gets limited reimbursement

Monopril is only reimbursed for patients with seriously decreased kidney function. The medicine is the only alternative for patients with decreased kidney function if treatment is necessary using an ACE inhibitor. General treatment using Monopril is however not cost-effective in comparison to well-documented and cheaper medicines.

Three antihypertensive agents get limited reimbursement

Methyldopa (Aldomet), Moxonidine (Physiotens) and Doxazosin (Alfadil) all get limited reimbursements. The medicines are not cost-effective compared to other well-documented and cheaper blood pressure decreasing medicines.

Aldomet shall only be reimbursed for hypertension during pregnancy while Physiotens and Alfadil, when they are used to lower blood pressure shall only be reimbursed for patients who have first tried other groups of medicines but not reached their treatment objectives.

In their treatment recommendations "Treatment of hypertoni during pregnancy" from 1996 the MPA presents Methyldopa as a medicine without any known deformity-inducing effects.

The medicine also adds a further effect mechanism for the treatment of hypertension and is possible to combine with all of the five larger therapeutic groups. This makes moxonidine a further possibility for combination treatment.

The Medical Products Agency recommends the use of alpha blockers (doxazosin) in its treatment recommendations from 2006 as an alternative complementary therapy when the patient has tried the larger therapeutic groups. There may therefore be some patients who need doxasozin as a treatment option in complex cases.

What constitutes a cost-effective medicine?

When the LFN decides whether or not a medicine should be given reimbursement status, we shall, among other things, evaluate whether or not the medicine is cost-effective. Or, put more simply, if the medicine is worth its price, if treatment with the medicine costs an amount of money that is reasonable for society in relation to the healthcare benefits that the medicine delivers. The size of the cost of a medicine is therefore not a good measure of whether or not we are using the right medicine or even a sufficient amount of it. What is important, on the other hand, is that use of a medicine is cost-effective, not just for healthcare, but for society as a whole. To investigate how cost-effective a medicine is gives us a foundation for being able to prioritize and therefore use resources in the best way.

Benefits weighed against costs

What then, does it mean, for use of a medicine to be cost-effective? First of all, it does not mean that all inexpensive medicines are cost-effective, while more expensive ones are not. When determining whether or not a medicine is cost-effective, all the expenses associated with the medicine being used must first be totaled. There is, first and foremost, the cost of the medicine. But costs can also arise if the patient has to visit a doctor to receive the medicine, or if any other additional healthcare assistance is needed, as well as any side-effects that the medicine might cause.

This total cost is weighed against the benefit that the medicine provides, primarily in the form of healing, alleviation,

and increased quality of life for the patient. One must also account for the fact that use of the medicine may also entail savings in other areas of healthcare, in that the patient does not need to visit the doctor as often, avoids hospitalization, operations, etc. However, all this is still not enough to gain a societal perspective. We also have to account for whether or not a medicine allows a patient to work and earn a living and contribute to our common welfare instead of being on medical leave or even being placed on early retirement. In this case, benefits go to the individual in production, and to the state, who then avoids fees for sick leave and early retirement. If the patient is older, it is possible that use may lead to the individual's being able to take better care of himself or herself and thereby require less assistance from elderly care services or relatives. This is also a socio-economic benefit on the plus side of a cost-effectiveness analysis.

Does not need to lead to cost-savings

It sometimes happens that the positive effects of a medicine are so great that they entirely compensate for the medicine's costs. Then it can be said that the treatment is cost-saving. But we do not make such high demands to consider use of a medicine to be cost-effective; in other words that it has a reasonable cost when seen in relation to the effect and therefore should be given reimbursement status. That people are healthy, without pain, and able to live a more normal life by taking a medicine, has a great value for which we are prepared to pay.

