

LIPID DISORDERS

The review of medicines for treating lipid disorders

A summary



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Why carry out pharmaceutical reviews?

This is a summary of the TLV's review of lipid disorders and is the sixth pharmaceutical review of the total of 49 therapeutic groups which the TLV has divided the groups up into. On adopting new reimbursement rules in October of 2002, it was not practically possible to review all medicines according to the new rules overnight. Therefore, the TLV 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 or be granted restricted reimbursement.

More health for our money

The purpose of the new reimbursement rules is to extract as much health as possible for every tax crown expended on medicines. We remove 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 pharmaceutical 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 expensive.

Three principles for our decisions

In reimbursement decisions for a medicine, we shall 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 therapeutic groups to be reviewed

In this review we are evaluating medicines in one therapeutic area after another. The review encompasses a total of 49 groups of medicines and the order in which they are tried 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. At www.tlv.se/genomgang we present the therapeutic groups being reviewed right now, the medicines included in those reviews and more.

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. 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.

The review of medicines for treating lipid disorders

Decisions for exclusion from the benefits system:

- Lipitor in the strength 10 mg and Crestor in the strength 5 mg lose their reimbursement.
- Lescol, Lescol Depot and Pravachol lose their reimbursement.
- Zocord loses its reimbursement status for all packages except 80 mg in packs of 49 tablets.

Generic pravastatin and simvastatin retain their reimbursement (individual products and packages containing one of these substances lose their reimbursement).

Decision on restricted reimbursement:

- Crestor and Lipitor in other strengths are reimbursed as a new treatment only if generic simvastatin has been tried and the patient has not reached the treatment objectives. Patients who have previously used Lipitor 10 mg and Crestor 5 mg respectively shall also first have tried simvastatin, before higher doses of Lipitor and Crestor may be prescribed on reimbursement.
- Ezetrol is reimbursed if generic simvastatin has been tried and the patient has not achieved the treatment objectives, or if it has been established the patient does not tolerate statins.
- Questran and Questran Loc loses its reimbursement status for treatment of lipid disorders, but retains reimbursement for diarrhoea and pruritis.

The decisions come into effect from the 1st of June, 2009.

The TLV's conclusions in brief

Generic simvastatin (pharmaceutical copies containing the substance simvastatin) shall be used as a first line treatment. On comparison between generic simvastatin and the other statins simvastatin is always the cheapest, and thereby the most cost-effective treatment alternative.

There is a large price difference between the cheapest and most expensive statin. Based on the current body of knowledge our conclusion is that when statins are used in doses which decrease LDL cholesterol by the same amount, then the risk for cardiovascular disease is decreased to the same degree. This is regardless of which of the statins is used.

Lipitor and Crestor at low strengths are not a cost-effective treatment alternative compared to simvastatin, as it costs so much more to achieve the same decrease in the level of LDL cholesterol.

It is not cost-effective to use cholesterol absorption inhibitors, bile acid sequestrants fibric acids or medicines containing nicotinic acid in general. The patients who do not achieve sufficient effect or cannot tolerate statins may need to switch to one of these medicines or use them as a supplementary medicine. It is only for these patients that treatment with the remaining medicines can be cost-effective.

The decisions in this review mean that pharmaceutical costs can decrease by approximately 170 million Swedish crowns per annum.

We have evaluated medicines which decrease the risk of arteriosclerosis

In this review we have evaluated medicines which decrease the risk of arteriosclerosis. For people with a high occurrence of LDL cholesterol statins are the obvious first line treatment alternative: they are effective, well-documented, well-tolerated and cheap – assuming that one of the most cost-effective ones is used.

Besides statins, which dominate sales in this group, we have also evaluated cholesterol absorbing inhibitors, bile acid sequestrants, fibric acids and nicotinic acid in this therapeutic group. They may be used by patients who cannot tolerate or get insufficient effect from statins.

Treatment against lipid disorders is aimed at decreasing the risk of arteriosclerosis. Arteriosclerosis causes the majority of cardiovascular disease in the industrialized world.

Lipid disorders contribute to arteriosclerosis

Lipid disorders reflect what we eat but are also hereditary. Other diseases such as metabolic disorders and kidney disease can also result in lipid disorders. Lipids are necessary for building up the cells in the body and for producing some hormones. They are also an important part of the body's energy store. There are mainly three types of blood fats, or lipids: LDL cholesterol, HDL cholesterol and triglycerides.

High levels of LDL cholesterol in the blood can be stored in the walls of the arteries and contribute to arteriosclerosis. HDL cholesterol however protects against arteriosclerosis by transporting cholesterol away from the arterial walls. High levels of triglycerides may also contribute to arteriosclerosis.

Statins dominate sales

Statins are the group of medicines which dominate sales. They stand for approximately 85 percent of the sales value, comparable to 632 million crowns in 2008.

More than half of all Swedish women and men suffer from lipid disorders. In the older age groups the proportion of people with lipid disorders is bigger than in the younger age groups.

The price of statins varies greatly

There is a wide spread in price between the cheapest and most effective statin. Based on the current body of knowledge our conclusion is that when statins are

used in doses which decrease the level of LDL cholesterol equally, then the risk for cardiovascular disease decreases proportionally. This is regardless of which of the statins is used.

For this reason generic simvastatin (pharmaceutical copies containing the active substance simvastatin) should be used as a first line treatment. Comparisons between generic simvastatin and other statins show that simvastatin is namely always the cheapest alternative and therefore the most cost-effective alternative.

Both pravastatin and simvastatin are available in generic form. Generic competition has meant that prices for these drugs have sunk to extremely low levels compared to the other statins. Achieving a 40 percent decrease of the levels of LDL cholesterol costs from 0.50 Skr per day on generic simvastatin, to 8 Skr per day on Lipitor (atorvastatin), or 10 Skr per day on Crestor (rosuvastatin).

More than one statin is needed to choose from

It is relatively common to experience mild side-effects when using statins. These side-effects, such as muscle pains, occur for all statins and changing to another statin does not always solve this problem. However, sometimes patients who cannot tolerate one statin can manage another statin better.

There is a need for more than one statin to choose from so that it is possible to switch to another statin when experiencing difficulties from side-effects. Due to this need we have introduced a pricing corridor which encompasses both pravastatin and simvastatin.

A pricing corridor means that medicines which are equally beneficial are allowed to have differing prices. The size of the pricing corridor indicates how much the cost difference between the most expensive and cheapest equal alternative may vary. This reflects the value we believe having a range of selection within a chosen therapeutic area has.

Some statins lose their reimbursement

Generic pravastatin and simvastatin are to continue to be reimbursed. But there are individual products, containing some of these active substances, which lose their reimbursement status because the price does not fall within the pricing corridor.

Furthermore, there are some package sizes which will not be reimbursed. The reason for this is that the price for these packages does not fall within the pricing corridor.

Zocord loses reimbursement for all packages excepting one which is within the pricing corridor and may therefore remain in the reimbursement scheme.

Lescol and Lescol Depot as well as Pravachol (pravastatin) lose their reimbursement status.

Lipitor 10 mg and Crestor 5 mg lose reimbursement

Lipitor 10 mg and Crestor 5 mg lose their reimbursement. At low strengths these medicines are not cost-effective treatment alternatives compared to generic simvastatin. This is due to it costing so much more to achieve the same decrease in the levels of LDL cholesterol.

As it is possible to achieve the same decrease of LDL cholesterol using simvastatin it is notable that half of the approximately 90 000 patients who currently use Lipitor use the lowest strength of 10 mg. If all patients who today use Lipitor 10 mg instead use generic simvastatin then the bill for pharmaceuticals would be almost 120 million Swedish crowns lower annually.

Crestor and Lipitor in other strengths get restricted reimbursement

Crestor in the strengths 10 mg, 20 mg and 40 mg and Lipitor in the strengths 20 mg, 40 mg and 80 mg are reimbursed for new treatment only if the patient has tried generic simvastatin and not reached the treatment objectives. That a patient does not reach the treatment objectives may either depend on the level of LDL cholesterol not being decreased enough, or that the patient does not tolerate treatment with generic simvastatin.

Patients who earlier used Lipitor 10 mg and Crestor 5 mg respectively shall also first have tried simvastatin, before higher doses of Lipitor and Crestor may be prescribed on reimbursement.

We cannot motivate switching the most severely ill patients on the highest doses of Crestor (20–40 mg) and Lipitor (40–80 mg) to simvastatin. For this reason the restriction only applies to new treatments.

This should not be interpreted as that our stance is that everyone currently being treated with Crestor and Lipitor should remain on this treatment. On the contrary we believe that patients treated with in particular Crestor 10 mg and Lipitor 20 mg and who have not previously tried simvastatin should switch to simvastatin 40 mg.

The reason for this is that many of these patients can achieve a satisfactory treatment using simvastatin 40 mg at a considerably lower treatment cost.

Other medicines are cost-effective only in some cases

It is not cost-effective with general use of cholesterol absorption inhibitors, bile acid sequestrants, fibric acids or medicines containing nicotinic acid. The patients who do not get enough of an effect or do not tolerate statins may need to switch to one of these medicines or use them as a supplementary treatment. It is only for these patients that treatment with the other medicines can be cost-effective.

Ezetrol (ezetimibe) is due to this only reimbursed if generic simvastatin has been tried and the patient has not achieved the treatment objectives, or if it can be established that the patient cannot tolerate statins. For the bile acid sequestrants Questran and Questran Loc (cholestyramine) they cost more than Lestid (colestipol). Therefore they are not cost-effective in comparison to Lestid. Questran and Questran Loc lose their reimbursement for the treatment of lipid disorders but are reimbursed going forward for diarrhoea and pruritis.

The bile acid sequestrant Lestid, fibric acids and medicines containing nicotinic acid also retain reimbursement. The reason they do not receive a formal restriction is that these medicines are already used today where statins cannot be used or where treatment with only statins is not enough.

What makes a cost-effective medicine?

When we try whether or not a medicine should be granted reimbursement, we shall evaluate whether or not the medicine is cost-effective or, put more simply, if the medicine is worth its price. That is if treatment with the medicine costs an amount of money reasonable for society in relation to the healthcare benefits that the medicine delivers. How large the cost of a medicine is, is therefore not a good measure of whether or not we are using the right medicine or even a sufficient amount of it. However what is important, is that the use of a medicine is cost-effective, not just for healthcare, but for society as a whole. Investigating how cost-effective a medicine is gives us a foundation for being able to prioritize and therefore use our resources in the best possible way.

The value derived is balanced against the cost incurred

What then, does it mean, for use of a medicine to be cost-effective? Firstly, it does not mean that all inexpensive medicines are cost-effective, while more expensive ones are not. When determining if a medicine is cost-effective, all the expenses associated with the medicine being used must first be added up. There is, first and foremost, the cost of the medicine. However, costs can also arise due to the patient visiting a physician to receive the medicine, if any other additional healthcare assistance is needed, as well as any side-effects that the medicine may cause.

This total cost is weighed against the benefit that the medicine provides, primarily in the form of healing, alleviation of pain and increased quality of life for the patient. One must also consider 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 hospitalisation, 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 sick leave or even being forced into early retirement. Here 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 of the medicine 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

Cost-savings are not obligatory

Sometimes 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 reimbursed. That people are healthy, without pain, and able to live a more normal life by taking a medicine constitutes a great value for which society is prepared to pay.

The TLV aspires to communicate clearly

In order to communicate our findings as clearly and effectively as possible, we strive to write concisely, avoid obscure specialist terminology and to explain difficult but necessary terms.

In 2005 the Swedish Parliament (riksdagen) ruled that the language used in the public services should be carefully chosen, simple and understandable. The term "klarspråk (plain language)" had taken root. The objective of this initiative is to increase transparency for citizens. Obscure language should not be an obstacle in participating in society and public rulings.

The TLV, Dental and Pharmaceutical Benefits Agency, has reviewed the therapeutic group of medicines used for treating lipid disorders. This review was presented in February 2009. This is a summary of the report and is available for download at our website www.tlv.se/blodfett
The review may also be ordered via registrator@tlv.se.

It is possible to read about other completed and ongoing reviews at www.tlv.se/genomgang.

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