

DIABETES

The review of medicines used for treating diabetes

A summary

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Decisions made by the TLV in the review of diabetes medicines

This is a summary of the TLV's review of medicines used for treating diabetes in regard to medicines which are part of the ATC groups A10 and H04.

This review covers pharmaceuticals solely and is primarily based on scientific material from the MPA and the National Board of Health and Welfare. Medical devices and other aids such as insulin pumps and test strips were not subject to this review.

The following medicines lose their reimbursed status:

Therapeutic group	Medicine	Active substance
Sulfonylureas (SU)	Daonil	Glibenclamide
Meglitinides	Starlix	Nateglinide
Combination drugs	Avaglim	Glimepiride and rosiglitazone

The following medicines are restricted (for type 2 diabetes) to patients where other insulin treatment is not sufficient to reach the treatment objectives due to recurring hypoglycemic episodes. However, they shall be part of the pharmaceutical benefits system for type 1 diabetes:

Therapeutic group	Medicine	Active substance
Long-acting insulin analogues	Lantus	Insulin glargin
Long-acting insulin analogues	Levemir	Insulin detemir

The following medicines are not reimbursed for new courses of treatment:

Therapeutic group	Medicine	Active substance
Sulfonylureas (SU)	Glibenklamid Recip	Glibenclamide

The following medicines retain general reimbursement status:

Therapeutic group	Medicine	Active substance
Rapid-acting human insulin	All	All
Rapid-acting insulin analogues	All	All
Intermediate-acting human insulin (NPH)	All	All
Intermediate-acting insulin with rapid onset (2-step)	All	All
Biguanides	Generic metformin	Metformin
Sulfonylureas (SU)	Mindiab	Glipizide
Sulfonylureas (SU)	Generic glimepiride	Glimepiride
Sulfonylureas (SU)	Amaryl	Glimepiride
Hypoglycemia drugs	Glucagon Novo Nordisk	Glucagon

The following medicines are restricted to patients who have first tried metformin, SUs or insulin, or where these options are not suitable:

Therapeutic group	Medicine	Active substance
Alpha-glucosidase inhibitors	Glucobay	Acarbose
Glitazones	Avandia	Rosiglitazone
Glitazones	Actos	Pioglitazone
DPP-4 inhibitors	Januvia	Sitagliptine
DPP-4 inhibitors	Galvus	Vildagliptine
Meglitinides	NovoNorm	Repaglinide
GLP-1 analogues	Byetta	Exenatide
Combination drugs	Avandamet	Metformin and pioglitazone
Combination drugs	Competact	Metformin and pioglitazone
Combination drugs	Janumet	Metformin and sitagliptine
Combination drugs	Eucreas	Metformin and vildagliptine

The decisions in this review come into force on the 1st of March 2010.

Summary

In the review of medicines used for treating diabetes (diabetes mellitus) we have only reviewed medicines. Medical devices and other aids are not part of the review. Our work is primarily based on material from the MPA and National Board of Health and Welfare. Our conclusions are that Sweden uses medicines cost-effectively to treat diabetes, with a few exceptions. Our decisions come into force on 1st of March, 2010.

Diabetes – the disease

In Sweden there are approximately 350 000 diabetes patients currently undergoing pharmaceutical treatment. Diabetes is classed as one of the most widespread diseases in the world. Diabetes arises due to a disturbance in the body's production of insulin in the pancreas. Insulin regulates the level of glucose, which is a sugar, in the blood. The result is that cells cannot absorb as much glucose and that sugar levels in the blood therefore rise to dangerous levels. There are two primary types of diabetes: type 1 diabetes and type 2 diabetes.

Approximately 50 000 people in Sweden suffer from type 1 diabetes which often appears in juveniles and is partly hereditary. Approximately 300 000 people in Sweden suffer from type 2 diabetes and this disease often afflicts adults and may be hereditary but can also be due to lifestyle. For example, obesity, stress and smoking can increase the risk of getting type 2 diabetes.

Treating diabetes

Type 1 diabetes and type 2 diabetes are treated in different ways. In both cases the treatment objective is to decrease acute and long-term complications arising from the disease such as kidney disease and cardiovascular disease. Type 1 diabetes is treated with different forms of insulin which are injected into the body. Insulins exist in two forms. There is human insulin (produced biosynthetically using recombinant DNA technology) and insulin analogues (produced by altering the structure of insulin somewhat, resulting in the make-up of the insulin changing). The insulins are available in different versions each offering varying degrees of onset. There are insulins available which are rapid-

acting, intermediate-acting (NPH insulins), intermediate-acting with rapid onset and insulins which are long-acting.

Type 2 diabetes is primarily treated using various diabetes medicines in tablet form (peroral medicines). Substances included in this group include, besides biguanides (metformin) and SUs (sulfonylureas), alpha-glucosidase inhibitors (acarbose), glitazones, DPP-4 inhibitors, meglitinides, GLP-1 analogues and hypoglycemia medicines.

Insulin drugs and metformin or SUs respectively are the first-line choice depending on the type of diabetes. They are effective, well-documented, cheap and most patients can tolerate the side-effects.

The total market for diabetes medicines is 1.2 billion Skr in Sweden

During 2008 diabetes medicines were sold to a total value of 1.2 billion Swedish crowns. Insulin made up 925 million crowns of this value and long-acting insulin analogues made up almost 300 million crowns of the total.

Peroral diabetes medicines were sold to a value of almost 260 million crowns. Of these drugs metformin turned over most at approximately 100 million crowns, followed by repaglinide which turned over approximately 35 million crowns and rosiglitazone which turned over 25 million crowns.

Prices vary across the range of diabetes drugs

The daily price for insulin depends on the weight of the patient and the dose required to achieve an effect. Price comparisons are therefore difficult to carry out.

Rapid-acting insulin analogues vary in price

between 8 and 21 crowns per day. The price for intermediate-acting insulins with rapid onset varies between 7 and 16 crowns per day. NPH insulin costs between 4 and 13 crowns per day. The long-acting insulin analogues on the market cost between approximately 8 and 19 crowns per day. Metformin and SUs cost approximately 3 crowns and 1 crown respectively per day and other peroral diabetes drugs cost between 7 crowns and 15 crowns per day, if one excludes the drug Byetta which costs 32 crowns per day.

A range of alternatives is needed

It is common that the patient suffers side-effects due to their diabetes treatment. Examples of side-effects include a blood sugar level which is too low (hypoglycemia) and weight gain. The various drugs employed have varying tendencies to lead to these side-effects and the patients are affected to varying degrees of severity. Switching to another drug does not always solve the problem with regard to side-effects but a patient who does not tolerate a certain diabetes drug may tolerate another better. For this reason it is important to have a number of treatment alternatives available in order to be able to offer quality diabetes care.

Some peroral diabetes drugs lose their reimbursement status

The medicine Starlix containing the active substance nateglinide loses its reimbursement. Patients who take this medicine must review their medication together with their doctor. The medicine Daonil (glibenclamide) which belongs to the SUs group loses its reimbursement. The active substance, however, is retained in the

system in generic form.

The combination drug Avaglim loses its reimbursement. The active substances however are retained but as separate substances.

Furthermore, there are some package sizes which will no longer be reimbursed. The reason for this is that prices for these packages are judged to be too high in comparison with the other packages which are part of the reimbursement system.

Most medicines get restricted reimbursement

The long-acting insulin analogues, Lantus and Levemir, are restricted (for type 2 diabetes) to patients where other insulin treatment is not sufficient to reach the treatment objectives due to recurring hypoglycemic episodes. However, they shall be part of the pharmaceutical benefits system for type 1 diabetes. Glibenclamid Recip (glibenclamide) is not reimbursed for new courses of treatment.

Glucobay (acarbose), Avandia (rosiglitazone), Actos (pioglitazone), Januvia (sitagliptine), Galvus (vildagliptine), NovoNorm (repaglinide), Byetta (exenatide) and the combination drugs Competact, Janumet and Eucreas are only reimbursed for patients who have first tried metformin, SUs or insulin, or where these treatments are not suitable.

The TLV's decisions free up funds

Decisions made in the review mean that the cost for pharmaceutical reimbursements decreases by at least 12 million crowns per year.

The purpose of our reviews is to extract as much health as possible for each tax crown expended on medicines.

Agency collaboration within the area of diabetes

The Medical Products Agency (MPA), the SBU, the National Board of Health and Welfare and the TLV have collaborated in producing scientific base material for the healthcare sector within the area of diabetes.

The Medical Products Agency (MPA) has produced recommendations for the pharmaceutical treatment of diabetes, the SBU has evaluated the utility value, risks and costs associated with some methods used in treating patients, the National Board of Health and Welfare has produced national guidelines for diabetes care and the TLV has made decisions on the reimbursement of diabetes drugs.

The four agencies have, within their remits, collaborated in order to provide the healthcare system with a shared source of scientific base evidence and knowledge. The purpose of this collaboration has been to provide a more complete overview of how diabetes care should be structured.

At the TLV we have used the summary produced by the SBU and the National Board of Health and Welfare as a basis for our decisions in regard to pharmaceutical reimbursement. We have gathered and collated the health economic literature on diabetes drugs. This literature constitutes a part of the National Board of Health and Welfare's base scientific documentation for the Swedish national guidelines. Furthermore, the TLV and representatives from other agencies participated in the expert workshop which the MPA organised in order to produce recommendations for the pharmaceutical treatment of diabetes. This workshop used scientific literature from the National Board of Health and Welfare as its point of departure.

Why the TLV is carrying out a review of medicines used to treat diabetes

On adopting new reimbursement rules in 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 medicines within various therapeutic areas 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. This review is the seventh pharmaceutical review from a series of 49 which we are assigned to carry out.

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 eliminate those medicines that do not show sufficient utility 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.

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.

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 thus 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 use of the medicine 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, which 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 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.

Facts in brief on diabetes and the TLV's review

Diabetes

- 350 000 people in Sweden have diabetes.
- 50 000 people in Sweden have diabetes type 1.
- 300 000 people in Sweden have diabetes type 2.
- Diabetes drugs turned over approximately 1.2 billion Skr in 2008.
- Insulin drugs turned over 925 million crowns in 2008.
- Other diabetes drugs turned over almost 260 million crowns. The largest drug here in terms of sales volume was metformin.

Decisions

- The medicine Starlix containing the active substance nateglinide loses its reimbursement status. Its cost is too high compared to the medical efficacy of the medicine.
- The medicine Daonil loses its reimbursement status, however the active substance glibenclamide remains in its generic form. The original brand drug is too expensive compared to the price offered by its generic alternative.
- A number of other medicines receive restricted reimbursement.
- The decisions in this review come into effect on the 1st of March, 2010.

Information material

- More information on this review is available (in Swedish) on www.tlv.se/diabetes and www.tlv.se/databas. An English translation of the full report is ongoing and will be available at the start of 2010.
- Information on the TLV's pharmaceutical reviews is available on www.tlv.se/genomgang and may also be ordered by mailing registrator@tlv.se

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