

# *The review of drugs against diseases caused by stomach acid\**

## *– a summary*

Authors: Doctor of Medical Science, Anders Wessling and Ph.D. Douglas Lundin

\* PPIs, H2 antagonists and antacids.

# 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 carrying out a review?***

When Sweden introduced new regulations for reimbursement in October 2002 it was not practically possible to evaluate all medicines overnight in light of these new regulations. The LFN is now conducting a review of approximately 2 000 medicines to ascertain the eligibility for reimbursement of these medicines going forward. Each and every medicine will be evaluated in accordance with the new rules and will either retain or lose reimbursement status.

### ***More health per crown***

Our purpose is to extract as much health as possible for every tax crown allocated to medicines. We will remove the medicines not delivering enough value in relation to their cost. But this does not mean that we shall only have cheap medicines in the pharmaceutical benefits system. If a medicine gives enough positive effects on the health and quality of life of people in general and from a social-economic perspective as a whole, then it may also be expensive.

### ***Three principles for decisions***

When making decisions on reimbursement of a medicine we evaluate its cost-effectiveness, that is to say we weigh the benefits of the medicine against the cost. In this evaluation, cost-effectiveness must be considered together with two other principles: the needs and solidarity principle meaning that those in the greatest medical need shall have more healthcare resources than other patient groups, and the human value principle meaning that healthcare shall respect the equal value of all people.

### ***49 groups to be evaluated***

During the review we will evaluate medicines therapeutic area by therapeutic area. In total the review comprises 49 pharmaceutical groups and they are reviewed in the order of sales volume for each group in 2003. The medicines which turned over most come first. The two initial groups, medicines against migraine and medicines for diseases caused by stomach acid, are however pilot groups chosen based on other criteria. The review of the migraine group was presented in February 2005.

### ***Extensive research and investigation***

Before a decision is made we carry out an extensive investigation and an analysis of data regarding medical effect and cost-effectiveness which we have earlier requested from the companies regarding a specific medicine. We also go through the scientific and health-economic literature for the group of medicines which is to be evaluated. Sometimes we also need to construct our own health-economic models. Each review is concluded with the publication of a final report. The report contains, amongst other things, an account of the present level of knowledge for the group in question. The report is also available in summary form, which is printed separately.

### ***Evaluated externally***

The collation of knowledge regarding medical effect and health-economic documentation which we present in the final report has been scrutinized by external medical experts. The report has also been sent for comments to the Swedish Council on Technology Assessment in Healthcare (SBU), the Medical Products Agency and the National Board of Health and Welfare. The companies in question, the county councils' pharmaceutical benefit group and the Swedish Association of People with Stomach and Bowel diseases (Riksförbundet för Mag- och Tarmsjuka) have also commented on the report.

## ***The review of drugs against diseases caused by stomach acid***

The LFN has evaluated medicines for diseases caused by acid in the stomach. We have evaluated the proton pump inhibitors launched at the end of the eighties and which today completely dominate treatment. The first one developed in the world was Losec, which contains the substance omeprazole. We have also evaluated the older generation of medicines that reduce production of stomach acid, so-called H2 antagonists. In this evaluation medicines from the earlier generations are also included, such as those which neutralise stomach acid and protect mucous membranes.

This evaluation is a part of the LFN's review of the entire range of medicines available on the reimbursement list. In it we evaluate if presently prescribed medicines should also be reimbursed in the future. Each and every medicine is evaluated individually and consequently retains or loses its reimbursement status. Our purpose is to extract as much health as possible for every "tax crown" used for medicines. This is the second therapeutic group of medicines from the review to be presented. The first group was presented in February 2005 regarding medicines against migraine.

This is a summary of the final report on the review of medicines for diseases caused by stomach acid and the decisions that have been made.

### ***The LFN's decisions***

The LFN has decided in the review of medicines against illnesses caused by stomach acid that the following medicines shall be reimbursed:

- Generic omeprazole.
- Pantoloc (pantoprazole).
- Nexium (esomeprazole) gets limited reimbursement. Only reimbursed for diagnosed ulcers in the oesophagus or where generic omeprazole or other proton pump inhibitors has not given satisfactory treatment results.
- Nexium HP, a combined product of Nexium and antibiotics, may keep its reimbursement as earlier.
- Cytotec (misoprostol) gets limited reimbursement for prevention of ulcers caused by antiinflammatory medicines (NSAID)

Medicines which lose their reimbursement status are Lanzo (lansoprazole), Pariet (rabeprazole), Losec and Losec Mups, Losec Medartuum, all H2 antagonists, Andapsin (sucralfate), Gaviscon (alginic acid) and Novaluzid (aluminium, magnesium). A number of companies have however appealed the LFN's decision regarding discontinued reimbursement. Therefore a number of medicines, despite the LFN's decision, may retain their reimbursement status until the courts have ruled on the matter. This is the case for Lanzo, Losec Medartuum, Andapsin as well as the H2 antagonists Acinil (cimetidine), Famotidin Hexal (famotidine), Artonil (ranitidine), Inside Brus (ranitidine), Ranitidin Hexal, Ranitidin Merck NM, Ranitidin Recip and Ranitidin Sandoz.

### ***Decisions release 175 million Swedish crowns***

Continuing to reimburse generic omeprazole, while not reimbursing other equal but more expensive medicines, means that patients receive the same effects from treatment at a cost that may be approximately 175 million crowns lower. The money released through this may be used for new innovative treatment methods or for other areas of urgent need within the healthcare sector.

The decisions enter into force, unless appealed, from

the 1st of May, 2006. Following this the medicines which have been removed from the benefits scheme are not reimbursed. If the decisions regarding one or more medicines are appealed by the companies in question, then the relevant medicines will continue to be reimbursed until the case has been resolved in court.

**Sales of almost 900 million crowns**

The medicines in the group had a turnover of almost 900 million Swedish crowns within the pharmaceutical benefits scheme. This answers for almost four percent of the total sales within the benefits system. Sales in terms of both crowns and volume have increased steadily over the past 30 years. This is mainly due to the introduction of new pharmaceuticals. In 1978 sales in the group were 86 million crowns. The major part of this consisted of medicines which neutralised hydrochloric acid. Since then both H2 antagonists and proton pump inhibitors have been introduced. Sales value increased steadily up till roughly a year ago when Losec (omeprazole) lost its patent and generic omeprazole entered the market at a considerably lower price. Sales in crowns decreased then somewhat, while the actual sales volume continued to increase.

**Proton pump inhibitors dominate**

Proton pump inhibitors dominate treatment completely today and have a market share of 93 percent. After Losec (omeprazole) four similar products have been launched on the Swedish market. H2 antagonists have a market share of approximately five percent. The rest of the market consists of medicines which neutralise stomach acid and protect the mucous membranes.

**Medicines for diseases caused by acid in the stomach**

In the review of medicines for diseases caused by acid in the stomach we have divided the medicines into three groups: *proton pump inhibitors*, *H2 antagonists* and *others*.

H2 antagonists and proton pump inhibitors are medicines which inhibit the production of acid in the stomach. Proton pump inhibitors have a greater acid-reducing effect than H2 antagonists and also give better treatment results. The medicines in the group called *Others* are currently not used very much. They are still partly used for the same conditions as the proton pump inhibitors and the H2 antagonists. The studies available show that these older medicines are not a good alternative to proton pump inhibitors and H2 antagonists, either in terms of treatment or cost.

The medicines in this group are used for a large range of illnesses and symptoms arising from stomach acid:

**Peptic ulcers**

- Duodenal ulcers
- Gastric ulcers
- Ulcers caused by anti-inflammatory medicines (NSAID)
- Prevention of ulcers when treated with anti-inflammatory medicines (NSAID)

**Heartburn (acid reflux, GERD)**

- Heartburn without ulcers in the oesophagus (non-erosive GERD)
- Heartburn with ulcers in the oesophagus (erosive GERD)

In the past a lot of the medicines prescribed for treating stomach acid were used for treating peptic ulcers. Peptic ulcers make up a small part of this today. A very large part is used for treating diseases caused by stomach acid leaking into the oesophagus and giving symptoms such as heartburn which sometimes can cause ulcers in the oesophagus.

The medicines are not only used for treatment of peptic ulcers and for diseases arising when acid enters the oesophagus. They are probably used erroneously outside their approved areas of use for functional dyspepsia. This is symptoms not caused by stomach acid but which are difficult to distinguish from symptoms resulting from stomach acid.

The various diseases caused by stomach acid result in symptoms, and in some cases damage of varying degrees of severeness. An untreated peptic ulcer can develop into a very serious – in extreme cases life-threatening

*Table. Proton pump inhibitors dominate heavily. Sales stomach-related drugs within the pharmaceutical benefits system during 2005.*

Type of medicine	Medicine (substance)	Sales in million crowns
Proton pump inhibitors	Losec and generic omeprazole	331
	Lanzo (lansoprazole)	236
	Nexium (esomeprazole)	192
	Pantoloc (pantoprazole)	50
	Pariet (rabeprazole)	15
	<b>Total</b>	<b>824</b>
H2 antagonists	Zantac, Ranitidin, Inside Brus and Artonil (ranitidine)	33
	Pepcodin and Famotidin (famotidine)	8
	Acinil, Tagamet (cimetidine)	5
	<b>Total</b>	<b>46</b>
Others	Gaviscon (alginic acid)	10
	Andapsin (sucralfate)	5
	Novaluzid (magnesium hydroxide and more)	3
	Cytotec (misoprostol)	2
	<b>Total</b>	<b>20</b>
<b>Total</b>	<b>891</b>	

– condition, while milder forms of the disease with mainly heartburn can be fairly uncomplicated and possible for the patient to treat themselves. The argument for always treating peptic ulcers is convincing and that proton pump inhibitors result in the best medical effect when treating peptic ulcers is hardly in question. When the peptic ulcer bacteria, *Helicobacter pylori*, are present, then proton pump inhibitors should be combined with suitable antibiotics so that the patient is freed of the bacteria and the consequent risk of a relapse is reduced.

More serious forms of heartburn, in particular when ulcers form in the oesophagus, demand a more powerful blocking of acid and should be treated with proton pump inhibitors. For patients with milder forms of heartburn a satisfactory result can also be achieved with medicines with lesser inhibiting effects on acid. This means that H2 antagonists can be an alternative treatment for milder symptoms.

### ***Over-zealous treatment for uncomplicated symptoms***

In our opinion one of the reasons for the drastically increased use of proton pump inhibitors is that doctors write prescriptions for rather uncomplicated conditions. This approach costs a lot of tax money, which can be better utilised for treatments of diseases where the patient's difficulties and possible health benefits are greater. In other words, milder forms of heartburn result in so small changes in quality of life that the treatment as a rule should not be reimbursed.

It is however difficult to see how a limitation of reimbursement to only more serious conditions can be implemented in practice. One possibility is that the patient would have to undergo endoscopy. This means the insertion of a flexible instrument to the oesophagus so that the mucous membranes can be inspected. In this way one can confirm that the leakage of acid to the oesophagus has led to ulcers and that treatment should therefore be reimbursed.

The problem is however that the severeness of symptoms seems to be independent of the existence of peptic ulcers. Heartburn without ulcers can cause as much discomfort for the patient as if there had been an ulcer in the oesophagus. The impact of a reimbursement limitation like this would therefore be low. Another problem is that general endoscopy in this manner would be costly. And it is therefore uncertain whether any tax money would be saved.

### ***Proton pump inhibitors are mostly cost-effective***

In the review we have first compared the cost-effectiveness for the various groups of medicines to each other. This

means that the effect of the treatment has been compared to the cost of the treatment. Proton pump inhibitors are the most effective treatment for as good as all conditions. H2 antagonists may cost less, but a lower treatment cost cannot compensate in most cases for the difference in treatment effect. Proton pump inhibitors are therefore the most cost-effective alternative for most conditions.

### ***Proton pump inhibitors cost-effective for ulcers***

The great majority of health-economics literature draws the conclusion that proton pump inhibitors are the cost-effective alternative when treating peptic ulcers. That is to say, using proton pump inhibitors gives a better medical effect and justifies the higher price, regardless of whether the ulcer is duodenal or gastric.

It is unclear if it is cost-effective to treat patients with acid-inhibiting drugs to prevent ulcers caused by the use of anti-inflammatory drugs. For patients at a high risk of getting ulcers it may be cost-effective. In this case it must be possible to identify patients who are at a high risk of getting ulcers due to this usage of anti-inflammatory drugs. This is not very easy in practice. It is not entirely clear either which type of medicine would then be the most cost-effective treatment: proton pump inhibitors, H2 antagonists or Cytotec (misoprostol). Cytotec is however the medicine which has shown a preventative effect for serious ulcers.

### ***Proton pump inhibitors for acute and serious symptoms in the oesophagus***

Proton pump inhibitors are cost-effective in the acute treatment of diseases which arise from acid entering the oesophagus. They are also cost-effective for continuous treatment when the condition is serious.

### ***H2 antagonists cost-effective for milder conditions in the oesophagus***

For milder conditions, where the patient experiences enough relief from H2 antagonists, the treatment is cost-effective as they are cheaper than proton pump inhibitors. We believe however that milder forms of heartburn bring about such small losses in quality of life that treatment with H2 antagonists should not be reimbursed.

### ***No cost-effectiveness for functional dyspepsia***

For the condition functional dyspepsia none of the medicines are cost-effective as acid-inhibiting drugs have no effect. Despite this it is probable that a considerable amount of acid-inhibiting medicine is being prescribed on the reimbursement scheme for this condition.

**Generic omeprazole most cost-effective**

So far we have discussed the cost-effectiveness for each of the three drug groups we have reviewed. As there are a number of different drugs in each group it is not enough to know which type of drug is most cost-effective for the various conditions. To be able to make a decision on reimbursement it is also important to know if the various drugs within a group differ when it comes to cost-effectiveness.

Our review shows that Lanzo (lansoprazole), Pantoloc (pantoprazole) and Pariet (rabeprazole) are not cost-effective in relation to the various generic omeprazole. Nexium (esomeprazole) is cost-effective in comparison to the generic omeprazole for patients with more serious forms of ulcers in the oesophagus, especially in the acute phase of the treatment.

We have not found any scientific evidence indicating that the five drugs have different levels of effect. An exception to this is Nexium where there is some evidence indicating a better effect in certain situations. The reason for this is that Nexium is given in higher doses than the other drugs in the group. At the same time as the other proton pump inhibitors are similar when it comes to effect of treatment, the price differences are very large on the Swedish market. The cost of treatment can be everything from 20 percent to 200 percent higher if a patient uses any other proton pump inhibitor other than generic omeprazole.

**Pricing band comparable to more than 25 percent**

Amongst the proton pump inhibitors there are four drugs which have the same positive medical effect for the average patient. These are Losec (omeprazole), Pariet (rabeprazole), Pantoloc (pantoprazole) and Lanzo (lansoprazole).

Simultaneously there exists a very large price difference between the cheapest version of Losec, generic omeprazole products and any of the other three drugs.

If we make a narrow interpretation of the principle stating that a drug must be cost-effective in order to receive reimbursement then it would mean that Lanzo, Pantoloc and Pariet would lose their reimbursement status as they have a higher price but do not have any added medical effect.

Do medicines with the same medical effect then have to cost exactly the same? We believe that there are good grounds for price differences if there is a need of a range of choices, in other words to have access to more than one drug. People can react differently to a drug both in terms of effect and side-effects. On the other hand it is not reasonable for society to pay an exorbitant amount for a wide range of product choices. This is why we use

a pricing band which is to encourage and leave room for even small differences between drugs in a particular area. The size of the pricing band is reflected by the value we believe a wide range of product choices has in the area in question.

We believe the need for a wide range of products within the area of diseases related to excess stomach acid to be small relative to other areas. We use a pricing band of one crown which is equal to a little more than 25 percent. Lanzo, Pariet and Pantoloc may all be just over 25 percent more expensive than the generic omeprazole and still keep their reimbursement status.

**Which drugs will remain in the pharmaceutical reimbursement system?**

Generic omeprazole and Pantoloc (pantoprazole) will retain their reimbursement status.

Further Nexium (esomeprazole) will have limited reimbursement status and the same is true of Cytotec (misoprostol).

Because companies have appealed the LFN's decisions regarding discontinued reimbursement, a number of medicines will retain their reimbursement status until the courts have ruled on the matter. These medicines are the PPI's Lanzo (lansoprazole) and Losec Medartuum. This is also the case for the H2 blockers Acinil (cimetidine), Famotidin Hexal (famotidine), Artonil (ranitidine), Inside Brus (ranitidine), Ranitidin Hexal, Ranitidin Merck NM, Ranitidin Recip and Ranitidin Sandoz. Also the decision to cease reimbursing Andapsin (sucralfate) has been appealed.

The medicines losing their reimbursement status from the 1st of May, 2006 are PPI's Pariet (rabeprazole), Losec and Losec Mups. For H2 antagonists Tagamet (cimetidine), Pepcidin (famotidine), Peptan (famotidine), Famotidin Stada, Zantac (ranitidine), Zantac Brus, Ranitidin Medartuum, Ranitidin Pliva, Ranitidine Ranbaxy and Ranitidin Stada lose their reimbursement status. This is also the case for Gaviscon (alginic acid) and Novaluzid (aluminium, magnesium).

In the following section an overview is given for the decisions the board has made in the review of drugs against diseases caused by stomach acid.

**Decisions regarding proton pump inhibitors****Continued reimbursement of generic omeprazole**

There is today a number of companies who sell generic omeprazole under various brands. All of these products will continue to be reimbursed. However, Losec and Losec Mups do not accommodate the pricing band we use and will therefore no longer be reimbursed. The parallel-im-

ported Losec Medartuum does not either accommodate the pricing band and loses reimbursement status. The company has however appealed the LFN's decision meaning that Losec Medartuum retains reimbursement until the courts have ruled on the matter.

One of the main principles for the reimbursement system is that it shall be product-based, that is to say reimbursement should be connected to the drug. In the cases where we have granted continued reimbursement of proton pump inhibitors we have done this without any limitations, although we believe that milder forms of heartburn should not be reimbursed. The reason for this is that we could not see a form in which a limitation like this could be enforced in practice.

#### ***Continued reimbursement for Pantoloc after decreased price***

The company has decreased the price of Pantoloc (pantoprazole) by up to five percent on various packages in order to accommodate the pricing band. Pantoloc will therefore receive continued reimbursement.

For all proton pump inhibitors we believe, in accordance with the reasoning outlined above, that milder forms of heartburn should not be reimbursed.

#### ***Company appeals discontinued reimbursement for Lanzo***

Lanzo (lansoprazole) by large achieves the same treatment results as Losec and generic omeprazole. The price for Lanzo is however too high to accommodate the pricing band of 25 percent which covers the generic omeprazole. The company has appealed the LFN's decision regarding discontinued reimbursement and Lanzo may therefore retain its reimbursement status until the courts have ruled on the matter.

#### ***No reimbursement for Pariet***

Pariet (rabeprazole) by large achieves the same treatment results as Losec and generic omeprazole. The price for Pariet is however too high to accommodate the pricing band of 25 percent which covers the generic omeprazole.

#### ***Limited reimbursement of Nexium***

Nexium's (esomeprazole) reimbursement is limited to patients where ulcers in the oesophagus have been diagnosed or where generic omeprazole or other proton pump inhibitors have not achieved a satisfactory result.

Nexium achieves by and large equal results to Losec or any of the generic omeprazole products when used for treating diseases related to stomach acid. An exception to this is the treatment of heartburn with ulcers in the oesophagus where Nexium in higher doses gave a better treatment outcome.

The treatment costs which can be calculated are higher for Nexium than for generic omeprazole. Only in the treatment of heartburn with ulcers in the oesophagus is the higher cost offset by a better treatment outcome. In other cases the treatment gives the same effect but is more expensive.

This could justify a limitation of reimbursement to patients where a doctor has diagnosed an ulcer in the oesophagus. However, in the everyday work of a doctor access to endoscopy and pH measurement tools are limited and thus speaks against a limitation like this. These diagnostic measures are crucial to being able to ascertain the presence of ulcers in the oesophagus of a patient.

This means that in practice the treatment is based on the symptoms described to the doctor by the patient. If the doctor finds that it is most probably stomach acid entering the patient's oesophagus which is the problem, then the condition is treated with acid-inhibiting drugs. If the patient responds to the treatment then the diagnosis is considered to have been correct.

Because of this there will be an option to prescribe Nexium in the reimbursement system to patients who do not respond satisfactorily to treatment with generic omeprazole or other proton pump inhibitors and where the cause for the unsatisfactory treatment could be insufficient acid suppression.

#### ***Reimbursement for Nexium HP***

Nexium is also available in a combination pack, Nexium HP. This is Nexium in combination with antibiotics, and is used when treating ulcers with the simultaneous eradication of the *Helicobacter pylori* bacteria. The price for Nexium HP is equal to the price for a generic omeprazole product and antibiotics sold as individual products.

#### ***No reimbursement of H2 antagonists***

H2 antagonists have less treatment effect than proton pump inhibitors. The treatment costs for H2 antagonists are lower, but the difference in treatment costs can in most cases not compensate for the difference in treatment outcomes.

For diseases caused by excess stomach acid it is crucial that more serious diseases are treated with medicines with more powerful suppression of stomach acid production so that the treatment outcome can become satisfactory. The opposite is also true that a satisfactory treatment outcome for milder conditions can be achieved with a less powerful drug.

The differences in treatment outcomes and cost-effectiveness can therefore vary between various diseases and the seriousness of symptoms. H2 antagonists can

therefore be a cost-effective treatment alternative to generic omeprazole in the treatment of milder conditions of heartburn. We however believe that for illnesses where treatment with H2 antagonists could be an option, the disease gives so small losses in quality of life that the treatment should not be reimbursed.

A number of companies have appealed the LFN's decisions regarding discontinued reimbursement. This means many H2 antagonists may retain their reimbursement status until the courts have ruled on the matter (see list on page 3).

### **Other drugs**

#### **Limited reimbursement of Cytotec**

We find that Cytotec (misoprostol) may continue to be eligible for reimbursement in preventive treatment with anti-inflammatory drugs. Cytotec is a drug that has proven preventative effects on serious ulcers. Health economic studies do not exist, but in our estimation the treatment cost is reasonable in relation to the treatment outcomes.

#### **No reimbursement for Gaviscon**

Gaviscon (alginic acid) will not continue to be reimbursed.

Proton pump inhibitors are the leading treatment alternative in terms of both effect and cost for treating heartburn with ulcers in the oesophagus. Milder forms of heartburn cause such small losses in quality of life that the treatment should not be reimbursed.

#### **No reimbursement for Novaluzid**

Novaluzid (aluminium, magnesium) is as a rule used for milder forms of heartburn. We however believe that the diseases where Novaluzid is a treatment option result in such small losses in quality of life, that the treatment should not be reimbursed.

#### **Company appeals discontinued reimbursement for Andapsin**

This drug has shown equal results in the treatment of ulcers and prevention of ulcers as H2 antagonists. The treatment costs for Andapsin (sucralfate) is however not only considerably higher than for H2 antagonists, but is also higher than for generic omeprazole. Therefore there is no reason for Andapsin to retain its reimbursement status.

The company has appealed this decision and Andapsin therefore retains its reimbursement status until the courts have ruled on the matter.

## **What constitutes a cost-effective medicine?**

When the LFN makes a decision on which medicine to reimburse we evaluate amongst other things if the medicine is cost-effective. That is to say if a medicine gives value for money or, if the medicine costs society a reasonable amount of money in relation to the health gains made through using it. The actual size of the drugs bill is not a good measure of if we are using enough medicines or even the right ones. The crucial aspect here is that the medicine is cost-effective, not just for the healthcare sector, but for society as a whole. Finding out how cost-effective a medicine is gives us a foundation for priority-setting and through this use our resources in the best way possible.

### **The utility value is weighed against the cost**

What does "cost-effective usage of a medicine" mean?

To begin with it does not mean that all cheap medicines are cost-effective and that expensive ones are not. When we estimate the cost-effectiveness of a medicine we pool all of the costs associated with using the medicine. This is primarily the actual cost of the product. But costs can also be related to visits to the doctor in order to get the medicine, possible further healthcare measures, the side-effects of the medicine and other aspects.

Then we balance this total cost against the value extracted from using the medicine, mainly in the form of being cured, easing of symptoms and increased life quality for the patient. But we also include the fact

that usage of the medicine may involve savings in other areas within the healthcare sector because, for instance, the patient does not need to see a doctor as often, does not have to be hospitalised, or operated on and so on. This is not enough however to get a societal perspective. We also include if the medicine means the patient can work and support herself and contribute to our common welfare instead of being sick-listed and perhaps forced into early retirement. This benefits private persons, production and the state which avoids the sick-listing costs and early retirement. If the patient is older perhaps the treatment means that he can manage better without as much help from the municipality's elderly care services or relatives. This is also counted as a benefit from a social-economic perspective which is put on the plus side of the cost-effectiveness analysis.

### **Does not have to lead to savings**

Sometimes it is so that the positive effects of a medicine are so great that they easily compensate for all costs. Then it is said that the treatment is a cost-saving. But we do not make such high demands in order to consider the use of a medicine cost-effective. That is to say, to have a reasonable cost in relation to the effect and therefore be reimbursed. That people get well, do not experience pain and can live a more normal life through using a medicine is important enough so that society is willing to pay for it.

