

Type 2 diabetes: How do glinides compare to other medications?



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People who have type 2 diabetes no longer make enough insulin and/or have become resistant to the insulin that their body makes. This means that the sugar in their blood can no longer be properly transported into the cells of their body, so they have high blood sugar levels (hyperglycaemia). Typical signs of severe hyperglycaemia include extreme thirst, going to the toilet a lot, tiredness and itching. The bigger problem, though, is that very high blood sugar levels damage small blood vessels over time, causing damage to important organs like the eyes and kidneys. People with type 2 diabetes also have a higher risk of cardiovascular (heart and circulation) diseases such as heart attacks and strokes.

Many people who have type 2 diabetes are able to control their blood sugar without using medication, for example by doing more exercise and losing some weight if they are overweight. If that is not enough to make a difference, tablets that help to reduce blood sugar levels (so-called oral diabetes medications) can be used. Some people with type 2 diabetes need insulin injections too.

How glinides work and how they are used

There are a lot of different medications that aim to lower blood sugar. The most common oral diabetes medications are metformin and sulfonylureas. These are considered to be the first-choice drugs for this purpose. A number of other medications are now also available, including the so-called glinides.

Glinides work in a similar way to sulfonylureas: they lower blood sugar by stimulating beta cells to release insulin. Beta cells are found in the pancreas, where they produce insulin.

Two glinides, called nateglinide and repaglinide, are currently approved for use in Germany. They are available on the market under the names Starlix (nateglinide) and NovoNorm (repaglinide). These medications have been approved to be used in slightly different ways in Germany: nateglinide is only allowed to be used in combination with metformin, and only in people who have already tried (unsuccessfully) to lower their blood sugar using metformin

alone. Repaglinide can also be used on its own (as a monotherapy).

Researchers from the University of Düsseldorf and the German Institute for Quality and Efficiency in Health Care (IQWiG – the publisher of this website) summarised the current evidence about the two glinides that have been approved for use in Germany. The German Federal Joint Committee (G-BA) commissioned them to find out whether nateglinide and repaglinide are effective treatments for people with type 2 diabetes, and whether they offer any advantages compared to other treatments and strategies that aim to lower blood sugar. The G-BA is the national decision-making body of the German healthcare system, including the health insurance funds, hospitals, community-based doctors, dentists and psychotherapists.

Blood sugar levels alone are not suitable evaluation criteria

In order to assess the advantages and disadvantages of glinides, we need long-term trials which look at treatment outcomes that are important to people with diabetes, such as preventing the loss of vision. The ability of medication to lower blood sugar levels is not necessarily a benefit in itself. Past experience has shown that laboratory values do not necessarily reflect whether a medication really has a true benefit – for example, whether it can prevent diabetes complications such as damage to the eyes or kidneys. So the IQWiG researchers did a specific search for trials that looked at important criteria like these.

Adverse effects are also taken into consideration when evaluating drugs. Because oral diabetes medications aim to lower blood sugar levels, there is always a risk that blood sugar levels could drop too low (hypoglycaemia, or “a hypo”). Signs of hypoglycaemia include paleness, shaking and poor concentration. Severe hypoglycaemia can lead to the loss of consciousness so it is a serious complication. Slight weight gain is another adverse effect of some medications that aim to lower blood sugar levels.

Advantages and disadvantages of glinides not clear

The researchers looked through medical databases and also asked the companies that make the medications whether there were any other trials. Trials were only included in their analysis if the glinides were used in a way that has been approved by regulatory authorities in Germany. They found 10 reliable trials of the two

glinides. Eight of those trials compared repaglinide with sulfonylureas, metformin or a placebo in a total of 1,700 participants. There were only two trials of nateglinide, involving about 730 participants. One of these trials compared nateglinide and metformin with a placebo and metformin, and the other trial compared a combination of nateglinide and metformin with a sulfonylurea and metformin.

The trials included data about the following criteria:

- blood sugar levels
- the frequency of hypoglycaemia
- the frequency of other adverse effects
- changes in body weight

Glinides were shown to have a similar effect to other medications in all four criteria. In the two trials that compared metformin and repaglinide, the people who took metformin lost about 2 kilos, whereas the weight of those people who took repaglinide stayed the same. It is not clear, however, whether this difference is big enough to affect people's health. None of the trials provided data on quality of life or satisfaction with the treatment.

Overall, the trials did not consider the adverse effects of glinides enough, so it is not possible to say how they compare to other medications.

The important questions remain unanswered

None of the trials included in the analysis aimed to find out whether glinides could prevent damage to blood vessels and important organs, such as the eyes and kidneys. And none of the trials lasted longer than 14 months. The IQWiG researchers consider this to be too short to be able to assess the long-term benefits and harms of glinides. It takes a very long time for high blood sugar levels to cause damage to the small blood vessels in the eyes and kidneys. So, in order to be able to assess the effects of medications that lower blood sugar levels, trials that last several years are needed.

Although repaglinide and nateglinide have been on the market since 1998 and 2001 respectively, research in this area is still in its infancy. Unlike most other oral diabetes medications, repaglinide is allowed to be used in people

with type 2 diabetes who have severe renal insufficiency (kidney failure). But more research is needed into this area of use too.

This additional information has been provided by the U.S. National Library of Medicine:

In the U.S., both nateglinide and repaglinide can be used on their own as monotherapy, or in combination with other types of medication to treat type 2 diabetes.

Author: German Institute for Quality and Efficiency in Health Care (IQWiG)

Note

This health information is a summary of a scientific report published by IQWiG. It is not an assessment of the right to have health care services reimbursed by statutory health insurance funds in Germany. By law, decisions about the reimbursement of diagnostic and therapeutic procedures can only be made by the German Federal Joint Committee (G-BA). The Federal Joint Committee takes IQWiG reports into consideration in its decision-making process. You can find information about the decisions of the German Federal Joint Committee on its English-language website, www.english.g-ba.de (URL: <http://www.english.g-ba.de>) .

Glossary

evidence

Evidence is what we call scientific proof from well-conducted, good-quality scientific trials that have been carefully designed to answer specific questions. Depending on the types of questions, different scientific research methods (types of study) are most appropriate to find reliable answers to these questions. Randomized controlled trials (RCTs), for example, are the best way to get reliable evidence on the effectiveness of medical treatments (interventions). This type of study, however, is not the best form of evidence for all possible questions, and does not provide the best answers to all kinds of questions, either. Epidemiological studies, for example, are very suitable for establishing well-founded proof for the spreading of a disease in the population.

pancreas

The pancreas is 12 to 18 cm long and lies in a horizontal position in the upper abdomen below the stomach. It produces a digestive juice with digestive enzymes in it, which is released into a duct inside the pancreas. This duct then leads into the intestine. There the enzymes help to break down fat, for example. The pancreas also contains the islets of Langerhans with different cells that produce hormones for the metabolism. Unlike the enzymes, the hormones are not released into the intestine, but into the blood. Alpha cells produce Glucagon, beta cells produce insulin and delta cells somatostatin. These are the three most important hormones for regulating glucose metabolism.

Sources

German Institute for Quality and Efficiency in Health Care (IQWiG). *Glinides in the treatment of diabetes mellitus type 2. Final report A05-05C. Version 1.0.* Cologne: IQWiG. April 2009. [Executive summary (URL: http://www.iqwig.com/download/A05-05C_Executive_Summary_Glinides_in_the_treatment_of_diabetes_mellitus_type_2.html)] [Full text (URL: http://www.iqwig.de/download/A05-05C_Abschlussbericht_Glinide_zur_Behandlung_des_Diabetes_mellitus_Typ_2.html) – in German]

The German Institute for Quality and Efficiency in Health Care (IQWiG)

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Evidence basis of our health information

Our information is based primarily on systematic reviews of the effects of health care. Systematic reviews are necessary to gain an objective picture of health care. In order to do this, a clear question is formulated. Researchers then find all the relevant studies that could answer this question. They then evaluate those studies.

You can find a list of the evidence and other scientific literature on which this information is based at **www.informedhealthonline.org**

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