

# MEDICATIONS

## How they work and why you need them

Dr John McDermott, described the huge variety of medications used to lower blood sugar and abolish the symptoms of diabetes at the Diabetes Ireland National Spring Meeting in Kilkenny, writes

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**W**hen someone is diagnosed with diabetes the aim is to abolish symptoms and try to reduce the long-term complications. This means that various medications are used to reach glucose targets.

Other medications, mainly statins, are used to help people reach cholesterol targets. And blood pressure medications are used to reach blood pressure targets.

"While nobody likes taking tablets, there is very good evidence that they work and significantly reduce the risk of diabetes complications," Dr John McDermott, Consultant Endocrinologist, Connolly Hospital, Dublin, told the recent Diabetes Ireland National Spring Meeting, held in Kilkenny.

The newly diagnosed person with type 2 diabetes may leave their first appoint-

ment at the diabetes clinic with a range of medications. This may include things like Glucophage, Lipitor, Tritace and aspirin.

And when they return for review a couple of years later, even though they may feel well, more medication like Diamicon and Natrilix may be added to the mix.

### Why so many tablets?

Dr McDermott said this barrage of medication lead people to ask:

- Why so many tablets and treatments for diabetes?
- How do they work?
- Are they good for you?
- Why take them if feeling well?

The simple answer is that these medications help to:

- Abolish the symptoms of diabetes
- Reduce the risk of blindness, kidney disease and amputation
- Reduce the risk of heart attack and stroke.

For people without diabetes, the naturally occurring insulin in their body keeps their blood sugar normal. It keeps sugar production in the liver at a healthy level and allows body tissues to use the available sugar. People with type 1 diabetes have no insulin; and people with type 2 diabetes have 'insulin resistance' and can't use the available insulin effectively.

### Symptoms of diabetes

High blood sugar leads to:

- High sugar in the urine
- Excessive urination
- Thirst
- Weight loss
- Blurred vision.

There is a wide variety of glucose lowering medications available. They act in different ways and are effective at reducing diabetes symptoms.

### Glucophage

This medication reduces the glucose being released from the liver and helps insulin to work better. The advantages are it:

- Can help with weight loss
- Has a low risk of causing hypos (episodes of dangerously low blood sugars)
- Is safe
- Is cheap.

The disadvantages are:

- It can have gastrointestinal effects
- Cannot be used for people who have advanced kidney disease.

### Diamicon and Amaryl

These medications boost the release of insulin from the pancreas. The advantages are they are:

- Safe
- Effective.

The disadvantages are that people taking them may:

- Have hypos
- Gain weight.

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Dr John McDermott: one of the speakers at the recent Diabetes Ireland National Spring Meeting held in Kilkenny

## Actos, Avandia

These medications help insulin to work better. The advantages of Actos are that it might be able to reduce the incidence of heart attacks and improve cholesterol.

The disadvantage with these medications is that some research has shown there has been excess heart failure with both medications and heart attacks in people taking Avandia. Recent studies have shown a slightly increased risk of bladder cancer with Actos.

## Januvia, Onglyza, Galvus

These medications boost your insulin levels. They are called DPP4 inhibitors. DPP4 is an enzyme that breaks down the hormone in your body called GLP1, blocking this enzyme, which results in an insulin increase. This allows your blood sugars to drop.

The advantages of these medications is they don't cause weight gain.

"The disadvantage is that they're not very powerful so if your blood sugar is quite high they're not going to get you down to where you want to be. Now the converse of that is that if your blood sugar is only a little bit above where you want it they might well get you down to target," said Dr McDermott.

Also, as these medications are rela-

COMMONLY PRESCRIBED INSULINS			
	Short-acting duration	Long-acting duration	Mixed duration
Conventional insulin	ActRapid Humulin R	Insulatard Humulin N	Mixtard Humulin Mix
Analogue insulin	Novorapid Humalog, Apidra	Lantus Levemir	Novomix Humalog Mix

tively new, their long-term safety has not yet been established.

## Byetta, Victoza, Bydureon

These medications are GLP1 analogues. GLP1 is a hormone that can increase the amount of insulin released. It also slows the emptying of the stomach so people feel fuller when eating.

These effects of the medication can help weight loss, which is a major advantage of this type of medication. These medications are also less likely to cause low blood sugars (hypos) that some other treatments.

"A disadvantage is that they do cause nausea and vomiting in some people, especially at the start of treatment, but most people manage to continue to take them," said Dr McDermott.

Another drawback is that they have to be given by injection.

"Again, most people have no problems with injecting once they've taken the decision to choose these medications," said Dr McDermott.

As with the DPP4 inhibitors, these medications are relatively new to widespread use, so long-term effects have not been established.

## Insulin

Insulin is still the most powerful agent available in the treatment of diabetes. It is also extremely safe. The disadvantages are that it can lead to an increased risk of low blood sugars (hypos) compared to other medications.

It also has to be given by injection and can lead to significant weight gain in a lot of people.

"When you're on insulin you do need to monitor your blood sugars much more

## COMMONLY PRESCRIBED STATINS FOR CHOLESTEROL

Generic name (active ingredient)	Brand name
Fluvastatin	Lescol
Atorvastatin	Lipitor
Simvastatin	Zocor
Rosuvastatin	Crestor
Pravastatin	Lipostat

frequently than some of the other medications I spoke about," said Dr McDermott.

## Reducing complications

It is very important to remember that while you can have diabetes and feel perfectly well, you can have blood sugar levels that are just a little above normal but are still doing damage. This can lead to complications at a later stage. A trial called the DCCT plotted the link between HbA1c and diabetes complications. It showed that the higher the HbA1c the higher the risk for complications. In order of risk, from highest to lowest were:

- Diabetic retinopathy (diabetic eye disease)
- Nephropathy (kidney disease)
- Severe NPDR (early stage diabetic eye disease)
- Neuropathy (damage to the nervous system)
- Microalbuminuria (early stage kidney disease).

## HbA1c targets

This is what HbA1c targets are all about – avoiding developing these serious complications of diabetes.

"In general the target is to have the HbA1c at 7% or below. Some people say

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6.5% or as low as can be safely achieved. The targets do need to be individualised to the particular patient.

“So this may explain why, even if you’re feeling well, your doctor is adding glucose-lowering medications to your existing medications in order to try to get your HbA1c down to target and thereby reduce the risk of complications down the line,” said Dr McDermott.

### Common treatment scenarios

Dr Dermott outlined a common treatment scenario for someone newly diagnosed with type 2 diabetes.

- Start off on a low dose of Glucophage when they are first diagnosed
- If at their next visit their HbA1c is not at the target the Glucophage would be increased
- If at the third visit the HbA1c was still not on target, the doctor might consider adding Diamicon, Januvia, Onglyza, Trajenta, Galvus or Actos
- The doctor could also consider prescribing GLP analogues that need to be injected, like Victoza, Byetta or Bydureon.
- Finally, the doctor would consider putting the patient on insulin.

How and when these medicines are prescribed depends on the circumstances of each patient, said Dr McDermott.

### Different types of insulin

Insulin can be divided into:

- Analogue insulin
- Human insulin.

And then into:

- Short-acting insulin
- Long-acting insulin.

### Analogue and human insulins

With analogue insulin, the insulin has been altered in the manufacturing process to change its absorption characteristics. For example, the company may change a molecule in the insulin so that when you inject it under the skin you absorb it slowly.

Or they may change another molecule so you absorb it quickly.

This means that analogue insulins are not identical to normal human insulin – they are modified slightly to change the way they work and how they are absorbed.

### Short-acting insulin

Actrapid and Humulin R are examples of older conventional short-acting human insulin. NovoRapid, Humalog and Apidra are examples of the newer short-acting analogue insulins.

Short-acting insulins are given before a meal to cover the rise in blood sugar that happens after a meal, said Dr McDermott.

### Long-acting insulins

Insulatard and Humulin N are examples of the older conventional long-acting human insulins.

Lantus and Levemir are examples of the newer long-acting analogue insulins.

### Insulin mixes of long and short-acting

Some insulins prescribed are a mixture

## COMMONLY PRESCRIBED BLOOD PRESSURE MEDICATION

### ACE-inhibitors

Generic name (active ingredient)	Brand name
Lisinopril	Zestril
Ramipril	Tritace
Perindopril	Coversyl
Quinapril	Accupro
Enalapril	Innovace
Captopril	Capoten
Cilazapril	Vascae

### ARBs (angiotensin receptor blockers)

Generic name	Brand name
Losartan	Cozaar
Irbesartan	Aprovel
Eprosartan	Teveten
Olmesartan	Omesar
Valsartan	Diovan
Telmisartan	Micardis
Candesartan	Blopress, Atacand

of fast-acting and long-acting insulin and these are also taken before meals.

Mixtard and Humulin are examples of the older conventional mixed insulins.

Novomix and Humalog Mix are examples of the newer mixed insulin analogues.

### Short-acting insulin analogues

The advantage of fast-acting insulin analogues is people tend to have less hypos after meals when taking them. They are also more rapid than others to start working.

“With the older fast-acting insulin you had to inject and then wait for half an hour before eating which was a major inconvenience,” said Dr McDermott.

### Long-acting insulin analogues

The advantage of long-acting insulin analogues is that they reduce the risk of hypos in the middle of the night compared to the older human insulins.

### Heart attack risk in diabetes

The risk of heart attack is a significant complication for people who have diabetes.

The five major risk factors for heart attack in anyone are:

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- Cholesterol
- Blood pressure
- Smoking
- Family history
- Diabetes.

People with type 2 diabetes often have high blood pressure and high cholesterol. So they have three out of these five major risk factors. The result is that cardiovascular disease is the leading cause of death among people who have diabetes.

"It's fairly clear from that that we need to be very aggressive at controlling these risk factors as best we can," said Dr McDermott. "There's nothing we can do about family history – if it's there it's there. Smoking is up to you! But we as doctors can aggressively target cholesterol and blood pressure as well as being aggressive in our diabetes treatment. This is why there are specific targets for cholesterol and blood pressure in diabetes," he said.

### Cholesterol in diabetes

LDL (low-density lipoprotein) is the 'bad' cholesterol. In general the target is to have it below 2.6. The higher your LDL, the higher your risk of heart attack.

HDL (high density lipoprotein) is the 'good' cholesterol which reduces your risk of having a heart attack. For people with diabetes the targets are to have HDL above 1 in a man and 1.3 in a woman.

Triglycerides are another 'bad' cholesterol and the target is to have them below 1.7.

"But it is also important to note that even if the cholesterol numbers are normal, the type of cholesterol can be harmful.

"One way of explaining it is if you have diabetes and your risk of heart attack is high then even if your cholesterol is normal getting it down lower will reduce your risk of heart attack. So this explains why some people who have got a perfectly normal cholesterol profile still end up being on a cholesterol tablet," said Dr McDermott.

### Statins (cholesterol medication)

Statins block the action of an enzyme



responsible for the manufacture of cholesterol. They are the most common prescribed tablets worldwide and are safe and effective, said Dr McDermott. They work well at achieving targets and can reduce LDL by 30-60% and therefore reduce the risk of heart attack (see 'Commonly prescribed statins' panel).

### Blood pressure in diabetes

"Up to 40% of people with newly diagnosed type 2 diabetes have high blood pressure. The big United Kingdom Prospective Diabetes Study showed that blood pressure control is actually just as important as the sugar control in diabetes," said Dr McDermott.

Blood pressure control is important not only in terms of reducing risk of heart attack and stroke, but also in terms of reduction in eye disease and kidney disease.

"So it is a mistake just to focus on the sugars in diabetes, the blood pressure is just as important. As we have a blood sugar target and a cholesterol target we also have a blood pressure target.

"The target in general is 130 over 80mmHg. High blood pressure is a condition that does not cause symptoms and this explains why you might be feeling perfectly well, but you're being put on blood pressure tablets – often more than one blood pressure tablet," said Dr McDermott.

The most commonly used blood pressure medications include: Micardis,

Natrilix, Centyl, Zestril, Cozaar, Istin, Dilzem, Tritace, Teveten, Emcor, Omesar, Cardura, Accupro, Betaloc, Amlid, Zanidip, Frumil.

### ACE-inhibitors and ARBs

Two types of blood pressure tablets are ACE-inhibitors and angiotensin receptor blockers (ARBs).

These are considered the first tablets to try when trying to gain blood pressure control in someone who has diabetes.

"There's very good evidence that they are effective at blood pressure lowering and also at reducing complications in diabetes. They could help reduce the risk of eye disease in diabetes and they have also been shown to protect the kidneys," said Dr McDermott.

Angiotensin receptor blockers work in a similar way to ACE-inhibitors and they're also quite commonly used in type 2 diabetes.

### Other blood pressure medications

While ACE-inhibitors and ARBs are the first things prescribed to treat blood pressure in people with diabetes, the average person with diabetes needs three separate blood pressure tablets to reach targets, said Dr McDermott.

"In recent years a great development has been the development of combination pills whereby you can combine two medications in the one pill. They certainly help in terms of improving compliance and making it easier to take the medications.

"So, an example would be Coversyl Plus which is an ACE-inhibitor combined with a diuretic tablet and Co-Diovan which is an angiotensin receptor blocker combined with a diuretic tablet," said Dr McDermott.

### Medications can protect you

Many medications are available to lower blood sugar and abolish diabetes symptoms. So to reduce your complications, use medications as needed to reach glucose targets, cholesterol targets and blood pressure targets, urged Dr McDermott.