“PCSK9 inhibitor” is a general term for a new kind of medicine that helps to lower cholesterol in the blood.

Why were these drugs developed?
PCSK9 is a protein that is made in our liver. Doctors have been studying people who naturally produce a lot of this PCSK9 protein and some that produce very little. They have found out that having more PCSK9 protein tends to cause life-long high cholesterol and early heart disease. Those people that have less PCSK9 protein tend to have life-long low cholesterol and much less heart disease. Knowing how this protein affects cholesterol and heart health has led to this new medicine - the PCSK9 inhibitor - being developed.

How do they work?
PCSK9 inhibitors all act on the PCSK9 protein, which is produced by liver cells.

Receptors on the surface of liver cells, called LDL receptors, remove cholesterol from our blood. The more working LDL receptors we have, the easier it is for us to keep our blood cholesterol low. However the PCSK9 protein increases the breakdown of these LDL receptors.

So PCSK9 inhibitors:
- Target and disable the PCSK9 protein making it less able to breakdown LDL receptors
- Help increase the number of working LDL receptors on the surface of liver cells
- Help the liver to catch more LDL particles, with their cholesterol cargo, and remove them from our blood

How are these drugs given and how often should I take them?
Most medicines for cholesterol lowering are given as tablets but PCSK9 inhibitors are different. The first ones to be developed are a kind of medicine called a monoclonal antibody or MAB. All MABs are made in a laboratory under very strict controls. Once in the body they find and attach themselves to specific proteins produced by cells in our bodies. Each MAB targets just one particular protein - PCSK9 inhibitors target the PCSK9 protein.

Monoclonal antibodies (MABs) cannot be taken as tablets, capsules or liquids. They have to be injected using a pre-filled pen or syringe. The good news is that PCSK9 inhibitors only need to be given once every 2 to 4 weeks. Most people won’t need to attend a hospital or GP surgery to receive the treatment because doctors and nurses will help them learn how to give the medicine all by themselves.

Will I need a PCSK9 inhibitor?
Statins are still the preferred treatment for lowering cholesterol. Ezetimibe, a cholesterol absorption inhibitor, may also be prescribed, either alone or with a statin. These medicines are safe and effective at lowering cholesterol and are generally well tolerated. Only a few people will need a PCSK9 inhibitor.

Doctors, who look after people with blood fat conditions, believe that PCSK9 inhibitors could be very helpful for people with high levels of cholesterol in their blood who are at high risk of early heart disease.

These include:
- People who have already had a heart attack or have cardiovascular disease (CVD) but cannot lower their LDL-cholesterol enough using other medicines
- People who have a condition called FH and who are not reaching their target cholesterol levels on other routine treatments. FH stands for familial hypercholesterolaemia. It is an inherited problem which results in very high levels of cholesterol in the blood.

NICE (The National Institute for Health and Care Excellence) issued guidance for doctors in 2016 about the types of people who could be given a PCSK9 inhibitor.
PCSK9 Inhibitors

Are there any side effects?
All medicines can have side effects but the good news is that PCSK9 inhibitors appear to be well tolerated by most people. We know this from the clinical studies that have been carried out. The commonest side effects reported (affecting less than 1 in 10 but more than 1 in 100 people) included flu like symptoms, cold, nausea, back and joint pain, injection site reactions and muscle related pain.

How effective are PCSK9 inhibitors?
PCSK9 Inhibitors seem to be very effective. Clinical studies have shown that they can cut LDL cholesterol levels by more than half. They can also be safely used alongside other cholesterol lowering treatments such as statins. Early data also suggests that there are fewer heart attacks and strokes amongst people that have taken these medicines compared to people on a dummy (placebo) drug.

How will I know they are working for me?
PCSK9 inhibitors are prescribed by a specialist doctor working in a lipid clinic. These doctors have a variety of names including lipidologist, chemical pathologist, clinical biochemist, cardiologist, diabetologist or endocrinologist. Their job includes helping to find people who might benefit from a PCSK9 inhibitor, decide on how much to give and monitor how well it works. Usually they will carrying out a repeat blood test after 2 to 3 months to check how well the medicine is working. Once the doctor is pleased with the progress made cholesterol levels will be checked less often; usually about once a year.

What are the names of PCSK9 inhibitors?
Two PCSK9 inhibitors are currently available in the UK and others are in the process of being developed. The ones are can be used in the UK are Evolocumab and Alirocumab. They are sold under the brand names Repatha and Praluent.

Two other PCSK9 inhibitors are still being developed. They are not yet licensed for use. They work by helping to reduce the amount of PCSK9 our bodies make.

How much is usually prescribed?
Repatha (evolocumab): every 2 weeks - 140mg
Praluent (alirocumab): every 2 weeks in either 75mg or 150mg

Tell me more
PCSK9 stands for Proprotein Convertase Subtilisin/Kexin type 9. PCSK9 is produced by cells in our liver and to a smaller extent by cells in our intestine, kidneys and brain. It is a key regulator of LDL receptor levels and will strongly bind to LDL receptors. It is this binding process which results in the LDL receptor being destroyed.

Normally the LDL receptor is continuously re-used. But when PCSK9 is present it will bind to it and take it into the cell for destruction, stopping the receptor from being re-used. So the presence of PCSK9 increases the chances that the LDL receptor will be destroyed. The result is fewer LDL receptors available on the liver cell surface to pick up circulating LDL cholesterol. When this happens LDL cholesterol levels, in the blood, increase.

NICE Guidance on Evolocumab can be found here: www.nice.org.uk/guidance/ta394/ifp/chapter/What-has-NICE-said
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