Ezetimib Stada 10 mg tablets

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PUBLIC SUMMARY OF THE RISK MANAGEMENT PLAN

VI.2 Elements for a Public Summary

Ezetimib Stada 10 mg tablets

VI.2.1 Overview of disease epidemiology

Having high cholesterol/lipids in the blood is one of the major risk factors for a heart attack and stroke. Cholesterol builds up in artery walls and thereby restricts the blood flow to the heart / brain respectively. Low density lipoprotein (LDL) (so called 'the bad cholesterol') and high-density lipoprotein (HDL) ('the good cholesterol') can be measured to predict one's risk of developing complications. Depending on the origin of high blood cholesterol, hypercholesterolaemia can be classified as a primary non-familiar one (not caused by an underlying disease, but rather by risk factors (e.g. smoking, unhealthy diet)) or primary familiar one (caused by an underlying genetic condition, e.g. homozygous familial hypercholesterolaemia (HoFH) and homozygous sitosterolaemia (phytosterolaemia)).

Prevention of cardiovascular events

Cardiovascular disease (CVD), an illness involving the heart and/or the blood vessels, is considered to be the leading cause of death worldwide. According to the European Society of Cardiology, CVD causes over 4 million deaths in Europe every year, and 1.9 million deaths in the European Union (EU). CVD has been associated with advanced age, male gender, obesity, high blood pressure, hyperlipidemia and diabetes mellitus amongst other factors; however, the main causes are considered to be lifestyle factors (such as smoking, lack of physical activity, bad diet) that lead to clogging of arteries (atherosclerosis). Therefore, measures for prevention of CVD are currently targeting mainly lifestyle and diet. In patients with a history of CVD, ezetimibe in combination with statins (a type of lipid-lowering medication) are found provided incremental benefit in reducing the primary composite endpoint of cardiovascular death compared with simvastatin alone.

Primary hypercholesterolaemia (non-familiar)

Risk factors for high blood cholesterol are smoking, unhealthy diet (high in fat), lack of exercise, obesity and drinking alcohol in excessive amounts. A lot of patients do not just have high cholesterol in blood – most patient will have high blood pressure and potentially also diabetes. The chances of developing high blood cholesterol increase with age; hypercholesterolemia is also more common in men younger than 55 years and in women older than 55 years. People of Indian, Pakistani, Bangladeshi and Sri Lankan descent are at increased risk of having a heart attack.

Primary hypercholesterolaemia (familiar)

Primary familial hypercholesterolaemia (including homozygous familial hypercholesterolaemia (HoFH) and homozygous sitosterolaemia (phytosterolaemia)) is caused by a gene alteration causing high cholesterol blood levels. Patients with these genetic alterations tend to have high blood cholesterol from birth, rather than late in life. There is a 1 in 2 (50%) chance that a child or sibling (brother or sister) of someone with familial hypercholesterolaemia will also have the condition. These conditions are rare -

prevalence of HoFH is estimated to be between 1 in 160,000 to 1 in 1,000,000 people,[1] whereas that of homozygous sitosterolaemia (phytosterolaemia) is estimated to be less than 1 in 1,000,000 people.

VI.2.2 Summary of treatment benefits

Ezetimib Stada is a medicine to lower increased levels of cholesterol in your blood.

Cholesterol is one of several fatty substances found in the bloodstream. Your total cholesterol is made up mainly of LDL and HDL cholesterol.

LDL cholesterol is often called “bad” cholesterol because it can build up in the walls of your arteries forming plaque. Eventually this plaque build-up can lead to a narrowing of the arteries. This narrowing can slow or block blood flow to vital organs such as the heart and brain. This blocking of blood flow can result in a heart attack or stroke.

HDL cholesterol is often called “good” cholesterol because it helps keep the bad cholesterol from building up in the arteries and protects against heart disease.

Triglycerides are another form of fat in your blood that may increase your risk for heart disease.

Ezetimib Stada lowers levels of total cholesterol, "bad" cholesterol (LDL cholesterol), and fatty substances called triglycerides in the blood. In addition, Ezetimib Stada raises levels of "good" cholesterol (HDL cholesterol).

Ezetimibe, the active ingredient of Ezetimib Stada works by reducing the cholesterol absorbed in your digestive tract.

Ezetimib Stada adds to the cholesterol-lowering effect of statins, a group of medicines that reduce the cholesterol your body makes by itself.

It is used for patients who cannot control their cholesterol levels by cholesterol lowering diet alone. You should stay on your cholesterol lowering diet while taking this medicine.

Ezetimib Stada is used in addition to your cholesterol lowering diet if you have:

- a raised cholesterol level in your blood (primary hypercholesterolaemia [heterozygous familial and non-familial])
    - together with a statin, when your cholesterol level is not well controlled with a statin alone
    - alone, when statin treatment is not suitable or is not tolerated
- a hereditary illness (homozygous familial hypercholesterolaemia) that increases the cholesterol level in your blood. You will also be prescribed a statin and may also receive other treatments
- a hereditary illness (homozygous sitosterolaemia, also known as phytosterolaemia) that increases the levels of plant sterols in your blood

Ezetimib Stada does not help you lose weight.

[1] Singh S, Bittner V. Familial hypercholesterolemia--epidemiology, diagnosis, and screening. Curr Atheroscler Rep. 2015;17(2):482

VI.2.3 Unknowns relating to treatment benefits

The safety and efficacy of ezetimibe in children below 6 years of age has not been established. No data are available.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Muscle pain, tenderness and weakness caused by muscle death (Rhabdomyolysis / Myopathy)	Muscle pain, tenderness and weakness caused by muscle death may occur in patients taking ezetimibe. This risk increases if a statin is also taken.	Contact your doctor **immediately** if you experience unexplained muscle pain, tenderness, or weakness.
Abnormal liver function	Liver problems, which can be detected by doing a blood test, affect up to 1 in 10 people treated with ezetimibe. Some of the symptoms may include abdominal pain and swelling, chronic fatigue, swelling of the ankles and yellowish skin and eyes.	Your doctor should do a blood test before you start taking Ezetimib Stada with a statin. This is to check how well your liver is working. Your doctor may also want you to have blood tests to check how well your liver is working after you start taking Ezetimib Stada with a statin. If you have moderate or severe liver problems, Ezetimib Stada is not recommended.
Allergic reactions (Hypersensitivity)	Allergic reactions, including swelling of the face, lips, tongue, and/or throat that may cause difficulty in breathing or swallowing (which requires treatment right away) have been reported in general use.	Tell your doctor about all your medical conditions including allergies. Contact your doctor **immediately** if you experience swelling of the face, lips, tongue, and/or throat, unusual skin reactions or any trouble with breathing.
Drug interaction with blood thinners, such as warfarin (Drug interaction with warfarin, another coumarin anticoagulant or fluindione)	Concomitant administration of ezetimibe (10 mg once daily) had no significant effect on efficacy and safety of warfarin in a study of twelve healthy adult males. However, there have been post-marketing reports of increased International Normalised Ratio (INR) in patients who had ezetimibe added to warfarin or fluindione. If ezetimibe is added to warfarin, fluindione or another blood thinner, INR should be appropriately monitored.	Tell your doctor or pharmacist if you are taking, have recently taken or might take a blood thinner. Your doctor may need to perform INR test to establish whether concomitant use of ezetimibe and a blood thinner is safe.

Drug interaction with an immunosuppressant drug, ciclosporin (Drug interaction with ciclosporin)	When taken together with ezetimibe, cislosporin (an immunosuppressant drug commonly used in organ transplant patients) can lead to an increase in ezetimibe exposure and therefore to an ezetimibe overdose.	Tell your doctor or pharmacist if you are taking, have recently taken or might take ciclosporin. Your doctor will monitor your ciclosporin concentrations if you are taking ezetimibe and ciclosporin concomitantly.

Important potential risks

Risk	**What is known (Including reason why it is considered a potential risk)**
Inflammation of the gallbladder / gallstones (Cholecystitis/ Cholelithiasis)	Patients treated with ezetimibe may be at an increasd risk of developing inflammation of the gallbladder and/or gallstones. The frequency of occurrence is unknown.
Inflammation of the pancreas (Pancreatitis)	Patients treated with ezetimibe may be at an increased risk of developing inflammation of the pancreas. The frequency of occurrence is unknown.

Missing information

Risk	**What is known**
Exposure during pregnancy	There is no experience from the use of Ezetimib Stada without a statin during pregnancy. Ask your doctor for advice before using Ezetimib Stada if you are pregnant.
Limited exposure in children less than 6 years of age	The safety and efficacy of ezetimibe in children below 6 years of age has not been established. No data are available.
Long-term efficacy of ezetimibe to reduce morbidity and mortality in adulthood in patients below 17 years	The long-term efficacy of therapy with ezetimibe in patients below 17 years of age to reduce morbidity and mortality in adulthood has not been studied.
Safety and efficacy of ezetimibe administration with fibrates	The safety and efficacy of ezetimibe administered with fibrates (another group of medicines used to lower cholesterol levels) have not been established.

VI.2.5 Summary of risk minimisation measures by safety concern

All medicines have a Summary of Product Characteristics (SPC) which provides physicians, pharmacists and other health care professionals with details on how to use the medicine, the risks and recommendations for minimising them. An abbreviated version of this in lay language is provided in the form of the package leaflet (PL). The measures in these documents are known as routine risk minimisation measures.

This medicine has no additional risk minimisation measures.

VI.2.6 Planned post authorisation development plan

No post-authorisation studies have been imposed or are planned.

VI.2.7 Summary of changes to the Risk Management Plan over time

Not applicable.