VI.2 ELEMENTS FOR A PUBLIC SUMMARY

VI.2.1 Overview of Disease Epidemiology

Hypercholesterolemia (or hyperlipidaemia) refers to high blood cholesterol levels. Cholesterol is a waxy, fatty substance (also known as lipid) that the body needs the appropriate amounts of to work properly. It is obtained from food and is also made by the liver. There are a few different types of cholesterol, including:

- Total cholesterol (all the cholesterol combined; Total-C)
- Low-density lipoprotein cholesterol (LDL-C): also called “bad” cholesterol because it is the main source of cholesterol build up and blockage in the blood vessels.

- High-density lipoprotein cholesterol (HDL-C) also called “good” cholesterol because it helps keep cholesterol from building up in the blood vessels.
- Triglycerides: are types of fat found in blood. Body uses them for energy.

High blood cholesterol levels, particularly high LDL-C and triglyceride levels, may lead to a build-up of cholesterol and fat along the inner walls of the blood vessels of the heart (coronary heart disease) and brain (cerebrovascular disease) which increases the risk of heart disease and stroke.

The most common cause of hypercholesterolemia is an interaction between genes and dietary and other factors, such as smoking and physical inactivity. This is called primary non-familial hypercholesterolemia. Primary non-familial hypercholesterolemia affects about 34% of men (ranging from 21% - 41% in different regions) and 40% in women (ranging from 26% - 47% in different regions). [Ref. 5.4: 03QJDC]

Homozygous and heterozygous familial hypercholesterolaemia (HoFH and HeFH) are genetic diseases which are passed down from parents which cause very high levels of bad cholesterol. The defect makes the body unable to remove LDL-C from the blood. Most people with FH inherit a defective gene for FH from only one parent and are therefore called heterozygous (HeFH). Rarely, a person may inherit the genetic defect from both parents and thus have homozygous FH (HoFH). About 1 per 500 people [Ref. 5.4: 03PJWM, 03QJFY, 03QJFZ] and 1 per 1,000,000 [Ref. 5.4: 03QJFZ] people have HeFH and HoFH respectively. It is more commonly found in Afrikaner, French Canadians, Ashkenazi Jews, and Lebanese populations [Ref. 5.4: 03QKW2]. The rates of HeFH and HoFH are the same for both men and women. Individuals with familial hypercholesterolemia tend to get coronary artery disease at earlier ages and those with HoFH tend to have a decreased life span.

Homozygous sitosterolaemia (phytosterolaemia) is a very rare inherited genetic disorder. In normal individuals, plant sterols (present in small amounts in fruits, vegetables, nuts, seeds, and cereals) are poorly absorbed and usually removed by the digestive system. However, in this disorder, excessive absorption and decreased removal of dietary plant sterols takes place. The blood cholesterol levels may be normal or raised; however, plant sterols are elevated which increases the risk of coronary heart disease. It is not known how many people are affected by this disorder, but it is likely to be a few hundred to a few thousand worldwide.

The potential health risk due to all type of hypercholesterolaemia includes risk of heart attack, stroke, chest pain (angina), reduced blood flow to heart (ischaemic heart disease), and death related to heart and blood vessel (cardiovascular) problems. According to the World Health Organization over 30% of deaths worldwide are related to cardiovascular disease [Ref. 5.4: 03QJG9]. Cardiovascular disease causes nearly half of all deaths in Europe [Ref. 5.4: 03QJD3].

Ezetimibe/simvastatin is also used toreduce the risk of cardiovascular events in patients with coronary heart disease and a history of a heart attack or unstable angina.Coronary heart disease (CHD) is a result of plaque buildup in the arteries that supply oxygen-rich blood to your heart. The buildup of plaque occurs over many years as a result of

hypercholesterolemia and leads to blockages restricting blood flow to the heart. If the flow of oxygen-rich blood to your heart muscle is reduced or blocked, angina or a heart attack can occur. Angina is chest pain or discomfort. A heart attack occurs if the flow of oxygen-rich blood to a section of heart muscle is cut off causing damage to the heart. About 6.2% of adults in the United States [Ref. 5.4: 042MCN] and 5.7% of men and 3.5% of women in the UK [Ref. 5.4: 04CGKK] have CHD.

VI.2.2 Summary of Treatment Benefits

Despite the diversity of available therapies, a significant proportion of the hypercholesterolemic population fail to reach target circulating LDL-C concentrations, or drug interactions and safety issues preclude long-term treatment needed to reduce the risk of CHD. These issues underlie the continued search for effective, conveniently administered, and better-tolerated drugs. Ezetimibe, an orally active selective inhibitor of dietary and biliary cholesterol absorption, is a lipid-lowering agent that has been approved as monotherapy or to be given in combination with statins for the treatment of familial and non-familial hypercholesterolemia. Ezetimibe is also approved as adjunctive therapy for the treatment of homozygous familial sitosterolemia. Inegy is a marketed combination tablet containing ezetimibe, an orally active selective inhibitor of dietary and biliary cholesterol absorption, and simvastatin, an HMG-CoA reductase inhibitor.

An extensive clinical program has been conducted with ezetimibe administered alone, and in combination with statins. Ezetimibe either as monotherapy or co-administered with a statin significantly reduced total cholesterol (total-C), low-density lipoprotein cholesterol (LDL-C), apolipoprotein B (Apo B), and triglycerides (TG) and increased high-density lipoprotein cholesterol (HDL-C) in patients with hypercholesterolaemia.

The clinical trial experience supporting the efficacy on the combination of ezetimibe/simvastatin is based on data from 12 blinded coadministration studies, of varying design, which provide data on >6000 patients who received ezetimibe coadministered or as a combination tablet with simvastatin. Approximately 23,963 patients overall have been exposed to ezetimibe + simvastatin (combination or coadministration) in clinical trials.

The efficacy of the different dose-strengths of ezetimibe/simvastatin (10/10 to 10/80 mg/day) was studied in a clinical study that included all available doses of ezetimibe/simvastatin and all relevant doses of simvastatin. Ezetimibe/simvastatin significantly lowered total and LDL cholesterol, TG as well as other fatty substances (apolipoprotein B, non-HDL cholesterol) and a specific protein (C-reactive protein) which measure inflammation in body. Further analysis showed ezetimibe/simvastatin significantly increased HDL cholesterol compared with pill without medicine.

One clinical study conducted in children involved 142 boys and 106 girls with onset of menstruation, 10 to 17 years of age with HeFH who were randomised to receive ezetimibe /simvastatin combination or simvastatin alone. It was noted that ezetimibe /simvastatin combination significantly reduced total and LDL cholesterol, Apo B, and non-HDL cholesterol as compared to simvastatin alone.

The Study of Heart and Renal Protection (SHARP) was conducted including 9438 patients with long term kidney disease, a third of who were on a process by which blood is purified with the help of machine or fluids (dialysis) at start of study. A total of 4650 patients received ezetimibe /simvastatin combination and 4620 received pill without medicine. After one year, including patients no longer taking study medication, a maximum of reduction in LDL cholesterol was observed with ezetimibe /simvastatin combination as compared to simvastatin alone and pill without medicine. Ezetimibe /simvastatin combination significantly reduced the risk of major blood vessel related events.

IMPROVE-IT was a randomized, double-blind, parallel group, multicenter study of ezetimibe/simvastatin (combination tablet) versus simvastatin monotherapy, designed to assess the clinical benefit of the 2 therapies in the incidence of the composite endpoint in a stabilized acute coronary syndrome (ACS) subject population. Subjects were initially randomized in a 1:1 ratio to receive either ezetimibe/simvastatin 10/40 mg or simvastatin 40 mg daily and subsequently uptitrated in a blinded manner to ezetimibe./simvastatin 10/80 mg or simvastatin 80 mg daily based on LDL-C levels. The primary composite endpoint was CV death, non-fatal MI, documented unstable angina that requires admission into a hospital, and all coronary revascularization with either PCI or CABG occurring at least 30 days after randomized treatment assignment, and non-fatal stroke. IMPROVE-IT randomized a total of 18,144 subjects with stabilized high-risk ACS. The protocol-defined intent-to-treat (ITT) population included 9,067 subjects in the ezetimibe/simvastatin group and 9,077 subjects in the simvastatin monotherapy group. All subjects were to be followed for a minimum of 2.5 years. The median length of follow-up for the primary endpoint in the ITT population was 56.9 mos (4.7 years). Overall, the trial achieved 104,135.0 patient-years of follow-up for all-cause mortality. The study met its primary and all secondary composite efficacy endpoints and based on the design of the study, these benefits are attributable to ezetimibe. Specifically, ezetimibe/simvastatin treatment significantly reduced the incidence of the following endpoints, compared to treatment with simvastatin monotherapy:

- the composite endpoint of death due to all causes, major coronary events, and non-fatal stroke.
- the composite endpoint of death due to coronary heart disease (CHD), non-fatal myocardial infarction (MI), and urgent coronary revascularization with either percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG) occurring at least 30 days after randomization.
- the composite endpoint of cardiovascular death, non-fatal MI, documented unstable angina that requires admission into a hospital, all revascularization (including both coronary and non-coronary) occurring at least 30 days after randomization, and non-fatal stroke.

VI.2.3 Unknowns Relating to Treatment Benefits

Ezetimibe/simvastatin has not been studied in:

- pregnant and breast feeding women. There is no clinical data available on the use of this product during pregnancy. It is not known if ezetimibe is secreted into human breast milk.
- children less than 18 years of age. The clinical experience in children and adolescent patients (aged 10-17 years old) is limited. There is insufficient data on safety and effectiveness this product in children below 10 years of age. Experience in children who have not achieved sexual maturation is limited.

VI.2.4 Summary of Safety Concerns

Important Identified Risks

Important identified risks are safety issues or undesirable effects for which there is sufficient proof of an association or link with the use of this medicine.

Table 71 provides information on the important identified risks and their preventability.

Table 71 Summary of Important Identified Risks

Risk	What is known	Preventability
Muscle injury (Rhabdomyolysis/ Myopathy)	▪ Muscle disease is a rare but known effect of statins, including simvastatin. ▪ It may be mild to severe, ranging from muscle pain, tenderness and weakness to muscle inflammation (myositis) and muscle breakdown (rhabdomyolysis). ▪ In clinical studies, most cases of muscle disease and related muscle events were mild to moderate in severity. The majority of such events resolved with stopping of treatment. ▪ The risk of muscle disease and muscle breakdown is dose related for simvastatin. ▪ The exact mechanism of muscle injury is not known. ▪ It is not completely known which patients are at greatest risk of developing muscle injury with ezetimibe/simvastatin use.	▪ Patients should promptly report signs and symptoms of muscle disease to their doctor, should these occur. ▪ Creatine kinase is an enzyme that is released by damaged muscle that doctors can test for to help in checking for muscles problems.

Table 71 Summary of Important Identified Risks

Risk	What is known	Preventability
	However, muscle injury may occur more frequently in patients who: - are elderly (age ≥65) - have uncontrolled hypothyroidism - have kidney problems - are women - have a personal or familial history of hereditary muscular disorders - have a previous history of muscular toxicity during treatment with cholesterol lowering medicines called "statins" (like simvastatin, atorvastatin, and rosuvastatin) or fibrates (like gemfibrozil and benzafibrate) - abuse alcohol	
Abnormal liver function (Abnormal liver function)	▪ Increased liver enzymes (transaminases) is a common (may affect up to 1 in 10 treated patients) side effect. ▪ Reports of serious liver injury and liver inflammation (hepatitis) have been very rare. In clinical studies, most cases of abnormal liver function tests were mild to moderate in severity, and resolved with stopping of treatment. ▪ The mechanism by which abnormal liver function associated with ezetimibe/simvastatin use occurs is not known. ▪ It is not clearly known which patients are at risk of developing abnormalities in liver function with ezetimibe. However,	▪ Ezetimibe/simvastatin can be used with caution in patients with liver impairment. ▪ Ezetimibe/simvastatin should not be used in patients with active liver disease or with unexplained persistent increases in liver function tests higher than 3 times the upper limit of normal. ▪ It is recommended to perform liver function tests before starting treatment with ezetimibe/simvastatin and whenever required during treatment. ▪ Immediately contact your doctor if any symptoms of liver problems such as feeling tired or weak, dark colored urine, pale colored stool, loss of appetite or

Table 71 Summary of Important Identified Risks

Risk	What is known	Preventability
	abnormal liver function may occur more frequently in patients who: - are of advanced age - are men - have a large waist circumference - consume alcohol in large amounts - are receiving treatment with certain medicines (such as painkillers, anti-seizure medicines, anti-tubercular medicines, herbal medications, or use illicit drugs) - have liver disease (such as fatty liver disease, hepatitis B and C and other forms of liver inflammation) - have certain medical conditions (such as autoimmune diseases, haemochromatosis, Wilson's disease, congestive heart failure, coeliac disease, hypothyroidism, Addison's disease and glycogen storage disease).	yellow discoloration of the skin or eyes occur.
Allergic reactions (Hypersensi-tivity)	▪ Allergic reactions can occur with any medicine and are known to occur with ezetimibe/simvastatin use. ▪ Events of rash, itching and hives are an uncommon side effect (may affect up to 1 in 100 patients). ▪ Events of life threatening allergic reactions and swelling of the face, lips, tongue and/or throat which may cause difficulty in breathing or swallowing have been reported in	▪ Ezetimibe/simvastatin should not be used by patients who are allergic to ezetimibe or simvastatin or any of the components of the medicinal product. ▪ Patients who develop signs and symptoms of serious allergic reactions such as whole body reaction (anaphylaxis), difficulty breathing or swelling of the

Table 71 Summary of Important Identified Risks

Risk	What is known	Preventability
	patients taking ezetimibe/simvastatin or medicines containing the active ingredients ezetimibe or simvastatin. ▪ In clinical studies most cases of allergic reactions with ezetimibe/simvastatin were mild to moderate and resolved upon stopping the medicine.	face, lips, tongue or throat should immediately stop taking ezetimibe/simvastatin and seek medical attention.
Drug interaction with medicines used to prevent blood clots (warfarin, phenprocoumon, acenocoumarol or fluindione; these medicines are also referred to as anticoagulants)	▪ A study in healthy adults showed no significant effect on warfarin levels and prothrombin time with co- administration of ezetimibe. There have been post-marketing reports of increased International Normalized Ratio (INR) in patients who had ezetimibe added to warfarin or fluindione. Most of these patients were also on other medications. Prothrombin time and INR are blood tests used to monitor patients taking warfarin ▪ The effect of ezetimibe/simvastatin on the prothrombin time has not been studied.	▪ If warfarin, another coumarin anticoagulant, or fluindione is administered along with ezetimibe/simvastatin, the INR or prothrombin time should be appropriately monitored to reduce the risk of bleeding events associated with these drugs. ▪ Patients should talk to their doctor/pharmacist about any other medicines they are taking or might be taking.
Drug interaction with medicine often used in organ transplant patients to prevent organ rejection (ciclosporin)	▪ Clinical studies have shown an increased level of ezetimibe in renal transplant patients taking ezetimibe and ciclosporin. In a study of healthy subjects administration of ezetimibe and ciclosporin resulted in an increase in the level of ciclosporin.	▪ Interactions can be prevented by avoiding the use of ezetimibe/simvastatin at the same time as ciclosporin. ▪ Side effects due to this interaction can be prevented by monitoring of the concentration of ciclosporin in the blood. ▪ Patients should talk to their doctor/pharmacist about any other medicines they are taking or might be taking.

Important Potential Risks

Important potential risks are safety issues or undesirable effects for which there is some basis for suspicion of a link with the use of medicine of interest, but this association has not been confirmed.

Table 72 provides information on the important potential risks identified with the medicinal product.

Table 72 Summary of Important Potential Risks

Risk	What is known
Inflammation of the pancreas (pancreatitis)	• How pancreatitis may occur with the use of ezetimibe/simvastatin is unknown. • Promptly contact your doctor if you notice the following signs and symptoms of pancreatitis: pain in the upper part of the abdomen that radiates to the back; swelling and tenderness of the abdomen; nausea and vomiting, fever and increased heart rate. • General risk factors for pancreatitis include age, alcohol use, obesity, gallstones and hypertriglyceridemia.
Gallbladder inflammation/gallstones (Cholecystitis/cholelithiasis)	• Signs and symptoms of gallbladder inflammation and gallstones are sharp, cramping, dull or steady pain in the upper abdomen; clay-colored stools, fever, nausea and vomiting and yellowing of the skin and whites of the eyes (jaundice). • General risk factors for gallstones/gallbladder inflammation are: - family history of gallstones/gallbladder disease - advanced age - female gender - overweight or obesity - recent rapid weight loss - physical inactivity - metabolic syndrome (high blood sugar, high blood pressure, high triglyceride levels and a large waistline).
Interstitial lung disease	• Interstitial lung disease refers to a group of diseases that affect the interstitium (a lace-like network of tissues that is present in the lungs and provides support to the lungs' air sacs) of the lungs. In interstitial lung disease, thickening of the interstitium occurs due to inflammation, scarring or extra fluid. • Interstitial lung disease associated with ezetimibe/simvastatin use is very rare. • Signs and symptoms of interstitial lung disease are shortness of breath, cough and weight loss.

Table 72 Summary of Important Potential Risks

Risk	What is known
Group of allergic reactions to simvastatin (simvastatin hypersensitivity syndrome)	• Simvastatin "hypersensitivity syndrome" is not a defined disease but rather a collection of common symptoms and miscellaneous diseases. • The overall incidence of simvastatin hypersensitivity syndrome is very rare. • Simvastatin hypersensitivity syndrome is a reaction that includes some of the following: hypersensitivity (allergic reactions including swelling of the face, lips, tongue and/or throat which may cause difficulty in breathing or swallowing and requires treatment immediately), pain or inflammation of the joints, inflammation of blood vessels, unusual bruising, skin eruptions and swelling, hives, skin sensitivity to the sun, fever, flushing, shortness of breath and feeling unwell, lupus-like disease (including rash, joint disorders, and effects on white blood cells).
Diabetes (New-onset diabetes/Impaired glucose metabolism)	• Signs and symptoms of diabetes are: - urinating more often than usual - feeling very thirsty - feeling hungry (even though the patient eats often) - tiredness - blurry vision - cuts/bruises that are slow to heal, tingling - weight loss - tingling - pain or numbness in the hands or feet • Risk factors for the development of new-onset diabetes include: - older age - obesity - family history of diabetes - a history of diabetes diagnosed during pregnancy - impaired glucose metabolism - physical inactivity - high fat diet • Patients may be able to reduce the risk of new-onset diabetes by losing weight, becoming physically active and eating a healthy balanced diet.
Stroke due to bleeding in the brain (Haemorrhagic stroke)	• Haemorrhagic stroke is caused by a blood vessel that breaks and bleeds into the brain.

Table 72 Summary of Important Potential Risks

Risk	What is known
	• How haemorrhagic stroke occurs in association with ezetimibe/simvastatin is unknown. • Sign and symptoms of haemorrhage stoke may include severe headache – sometimes in a specific area, nausea and vomiting, neck stiffness, dizziness, seizures or change in mental state (irritability, confusion and unconsciousness). • Risk factors for haemorrhage stroke include: - older age - high blood pressure - use of blood thinners (such as warfarin) and antiplatelet medicines (such as aspirin and clopidogrel) - smoking - kidney dialysis - use of certain drugs such as cocaine, amphetamines and phenylpropanolamine • Patients may be able to reduce their general risk of haemorrhagic stroke by keeping their blood pressure well under control and by stopping smoking.

Missing Information

Missing information is information about the safety of a medicine or pill which is not available at the time of submission of a particular risk management plan.

Examples of missing information include populations not studied (e.g. pregnant women or patients with severe renal impairment) or where there is a high likelihood of off-label use (pill used for indication other than what it is approved for).

Table 73 provides missing information with the medicinal product.

Table 73 Summary of Missing Information

Missing information	What is known
Use in pregnancy and breastfeeding (Exposure during pregnancy and lactation)	• Ezetimibe/simvastatin has not been studied in pregnant and breastfeeding women; also there is no clinical data available on the use of this product during pregnancy. • It is not known if Inegy is secreted into human breast milk. • Ezetimibe/simvastatin should not be used during pregnancy or while breast feeding.
Use in children (Limited clinical trial experience in children 10 – 17 years of age. No clinical trial experience in children less than 10 years of age.)	• Clinical experience with Inegy in pediatric and adolescent patients (aged 10-17 years old) is limited. • Ezetimibe/simvastatin is not recommended for use in children below age 10 due to insufficient data on safety and efficacy. Experience in children who have not achieved sexual maturation is limited.

VI.2.5 Summary of Risk Minimization Measures by Safety Concern

All medicines have a Summary of Product Characteristics (SPC) which provides physicians, pharmacists and other healthcare professionals with details on how to use the medicine, the risks and recommendations for minimizing 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 minimization measures.

The SPC and the PL for Ezetimibe/Simvastatin can be found on your local Health Authority website.

This medicine has no additional risk minimization measures.

VI.2.6 Planned Post-Authorization Development Plan

VI.2.6.1 List of Studies in post-authorization development plan

Table 74 List of Studies in Post-Authorization Development Plan

Actions	Objectives	Efficacy Concerns Addressed	Milestones/Exposure	Study Status	Milestones/ Calendar Time
Clinical Study P04103 IMPROVE-IT (IMProved Reduction of Outcomes: Vytorin Efficacy International Trial)	A randomized, active-control, double-blind study of subjects with stabilized high-risk acute coronary syndrome. The primary objective was to evaluate the clinical benefit of ezetimibe/simvastatin combination 10/40 mg compared with Simvastatin 40 mg. Clinical benefit is defined as the reduction in the risk of the occurrence of the composite endpoint of CV death, non-fatal MI, documented unstable angina that requires admission into a hospital, and all coronary revascularization with either PCI or CABG occurring at least 30 days after randomized treatment assignment, and non-fatal stroke.	IMPROVE-IT assessed the incremental clinical benefit of ezetimibe when taken with simvastatin, compared to simvastatin monotherapy, in the risk reduction for the occurrence of CV outcomes	Randomized 18,144 patients. The primary endpoint event occurred in 5314 patients, meeting projected number of events. All patients followed for a minimum of 2.5 years and the median follow-up for mortality was greater than 6 years.	Completed	FPE: Oct 2005 Study Completion Sep-2014 CSR: Mar-2015

VI.2.6.2 Studies which are a condition of the marketing authorisation

None of the above studies is a condition of the marketing authorization.

VI.2.7 Summary of Changes to the Risk Management Plan Over Time

Table 75 Major Changes to the Risk Management Plan

RMP Version	Date	Safety Concerns	Comment
1.1	13-JUN-2012	Important Identified Risks: • Muscle injury (Rhabdomyolysis/myopathy) • Abnormal liver function • Allergic reaction (Hypersensitivity) • Drug interaction with warfarin, another coumarin anticoagulant, or fluindione • Drug interaction with ciclosporin • Drug interaction with potent CYP3A4 Inhibitors, including itraconazole, telithromycin, ketoconazole, erythromycin, clarithromycin, HIV protease inhibitors, nefazodone • Drug interaction with fusidic acid • Drug interaction with grapefruit juice • Drug interaction with dilitazem • Drug interaction with verapamil • Drug interaction with amlodipine • Drug interaction with fibrates • Drug interaction with niacin • Drug interaction with danazol • Drug interaction with amiodarone Important Potential Risks: • Pancreas inflammation (Pancreatitis) • Gallbladder inflammation/ gallstones (Cholecystitis/cholelithiasis) • Interstitial lung disease • Group of allergic reactions to simvastatin (Simvastatin hypersensitivity syndrome) • Diabetes (New onset diabetes)/impaired glucose metabolism • Cancer (Malignancy) • Stroke due to bleeding in the brain (Haemorrhagic stroke)	None

Table 75 Major Changes to the Risk Management Plan

RMP Version	Date	Safety Concerns	Comment
		• Drug interaction with colchicine Important Missing Information: • Use in pregnancy and breastfeeding (Exposure during pregnancy and lactation) • Use in children: limited clinical trial experience in children 10-17 years of age. No clinical trial experience in children less than 10 years of age.	
2.0	24Mar2015	Removal of cancer (malignancy) as an Important Potential Risk Relocation of drug interactions under identified/potential interaction(s) with other medicinal products, food, and other substances in the main body of the RMP.	Based on results of completed trial (IMPROVE-IT). Template change
2.1	01Oct2015		Version 2.1 is an administrative update and includes the previously recognized (version 1.1) important identified risks of drug interaction with ciclosporin and drug interaction with warfarin, another coumarin anticoagulant, or fluindione in the appropriate sections of the document.
2.2	29Feb2016		Version 2.2 is an administrative update regarding the indication for use.

Key Points

- This medication is used to reduce blood cholesterol levels in patients with raised cholesterol level in blood or elevated fat levels in blood. It may also be used to reduce the risk of cardiovascular events in patients with coronary heart disease and a history of acute coronary syndrome.
- Muscle injury is a known risk associated with the use of ezetimibe/simvastatin. Patients should be alert to such symptoms as unexplained muscle pain, tenderness or weakness and seek medical attention immediately, should these occur.
- Abnormal liver function is a known risk associated with the use of ezetimibe/simvastatin. Periodic blood tests to check liver function are recommended during treatment with ezetimibe/simvastatin.
- This medication should not be used by patients with active liver disease or with unexplained persistent increases in liver function tests higher than 3 times the upper limit of normal.
- This medicine should not be used by those who have a history of allergic reactions to ezetimibe, statins or any inactive ingredient of the drug product.
- Gallstones, gallbladder inflammation, pancreas inflammation, diabetes and haemorrhagic stroke have occurred in patients using ezetimibe/simvastatin.
- This medicine should not be used by pregnant or breastfeeding women and by children less than 10 years of age.