VI.2 Elements for a public summary

VI.2.1 Overview of disease epidemiology

Acute coronary syndrome (ACS) is a condition in which patients have symptoms from a blockage of the blood vessels that supply oxygen to the heart. The most common symptom is chest pain, often spreading down the left arm or the jaw, and may seem more like pressure in the chest. Patient may also feel sick to their stomach and have sweating.

Men tend to be diagnosed more often than woman. Patients have an average age of approximately 65 in men and approximately 71 in women at the time of diagnosis.

Percentage of Patients with ACS
In European countries, approximately 26 to 60,6 adults per 10,000 have ACS.
In non-European countries approximately 50 to 202 adults per 100,000 have ACS.

VI.2.2 Summary of treatment benefits

Since the first approval of prasugrel in 2009, it has been used by more than 2.1 million patients world-wide. Prasugrel is taken together with another platelet aggregation inhibitor to prevent atherothrombotic events (problems causes by blood clots and hardening of the arteries) in patients with ACS who are undergoing percutaneous coronary intervention (PCI). Acute coronary syndrome is a group of conditions that includes unstable angina (a severe type of chest pain) and heart attack. Percutaneous coronary intervention is an operation used to unblock narrowed coronary arteries (blood vessels in the heart).

In one main study, prasugrel, given as a 60-mg starting dose followed by 10-mg "maintenance" dose, was compared with clopidogrel (another inhibitor of platelet aggregation); both medicines were taken in combination with another platelet aggregation inhibitor. The study involved almost 14,000 adults with ACS who were about to undergo PCI. The main measure of effectiveness was reduction in the total number of cardiovascular (CV) deaths (deaths due to problems in the heart or blood vessels), heart attacks, or strokes. The patients were followed up for an average of 14.5 months.

Prasugrel was more effective than clopidogrel at reducing the total number of CV deaths, heart attacks, or strokes. At the end of the study, 9% of the patient taking prasugrel had died from CV causes or has a heart attack or stroke (643 out of 6813) compared with 11% of the patients taking clopidogrel (781 out of 6795).

VI.2.3 Unknowns relating to treatment benefits

There is not much information about prasugrel use in children, women who are pregnant or breastfeeding, patients with other kinds of severe heart disease, or patients with advanced liver disease. Doctors should think carefully about whether prasugrel is needed in these patient populations because the benefit of taking prasugrel is unknown.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	**What is known**	**Preventability**
Bleeding **(haemorrhage)** including: - Bleeding in the skull (**intracranial haemorrhage**) or stroke (blood flow to a part of the brain stops) - Bleeding in the stomach or intestine (**gastrointestinal haemorrhage**) - Bleeding in the eye (**intraocular haemorrhage**) - Nosebleeds (epistaxis) - Bleeding related to medicinal procedures (**percutaneous coronary intervation-related haemorrgahe, coronary artery bypass graft**	Medication like prasugrel can increase bleeding. The bleeding risk is greater in people who are 75 years of age or older, people who weigh less than 60 kg, and people who are taking other medications that may increase their risk of bleeding. The risk of bleeding is also greater for people with major injuries, recent surgery, a history of bleeding in the stomach or intestine, and/or severe liver or kidney disease.	You should not take prasugrel if you have severe bleeding, a history of stroke, or history of mini stroke. If you are 75 years of age or older, you need to ask your doctor if the benefits of prasugrel outweigh the risk pf prasugrel because of your agre. If your doctor does prescribe prasugrel and you are 75 years of age or older, then you should only be taking a 5-mg daily dose of prasugrel. If you weigh less than 60 kg, then you should only be taking a 5-mg daily dose. Because of this increased bleeding risk on prasugrel, it should be stopped at least 7 days before any planned

haemorrhage, and other procedure-related haemorrhage)		surgery or dental procedure. It is very important to tell your doctor if you are being treated with clopidogrel (a medicine that keeps your blood from clotting), warfarin (a blood thinner), or not-steroidal anti-inflammatory drugs for pain and fever (such as ibuprofen naproxen, etoricoxib). If these medicines are taken with prasugrel, it can increase your risk of bleeding. If you have any other possible medical conditions that could cause increased bleeding, you should be sure to tell your doctor before your start taking prasugrel.
Prasugrel should be used as directed on the drug label. It is recommended that prasugrel is used only after doctor knows by X-rays that you can be treated without surgery for clogged blood vessels that provide oxygen to your heart. If prasugrel is given before this time, there could be greater risk of bleeding.	Some doctors give patients prasugrel before learning if they can be treated without surgery for clogged blood vessels that provide oxygen to the heart. If this happens, then the risk of bleeding may be increased.	Prasugrel should be used as directed on the drug label. It is recommended that prasugrel is used only after a doctor knows by X-ray that you can be treated without surgery for clogged blood vessels that provide oxygen to your heart. If prasugrel is givne before this time, the risk of bleeding could be higher.
Allergic reactions **(hypersensitivity),** presenting hives or itchy	Allergic reactions have been seen in patients who had allergic reactions to other	You should not take prasugrel in you are allergic to prasugrel or any

welts on the skin or swelling of the face including lips, tongue, and throat that can affect your breathing **(angioedema)**	medications like prasugrel.	ingredients of prasugrel, or if you are allergic to any medications that are like prasugrel.
Low platelet count – platelets are a part of blood that help in blood-clotting **(thrombocytopaenia)**	Low platelet count has been seen in patients who take prasugrel or other medications like prasugrel. This can cause people to bleed more easily.	The risk of low platelet count with prasugrel can be lessened by minimasing bleeding risks as described above in the section regarding bleeding.
Blood clots form in small blood vessels throughout the body **(thrombotic thrombocytopaenic purpura)**	Thrombotic thrombocytopenic purpura (TTP) has been seen with medications that are like prasugrel (clopidogrel and ticlopidine), and has been seen very rarely with prasugrel use. There small blood clots can cause numerous small red spots on the skin called “petechiae”. There small blood clots can damage many organs including kidneys, heart, and brain.	There is no known was to avoid TTP while taking prasugrel or medications like prasugrel. If you think that you may have this condition, you shoul tell your doctor immediately.

Important potential risks:

Risk	**What is known (Including reason why it is considered a potential risk)**
Damage to the liver caused by taking prasugrel **(drug-induced hepatic injury)**	None of the studies with prasugrel have shown that use of prasugrel causes liver damage. However, because liver damage is a risk with many medications, and because similar medications have caused changes in liver lab results, it is considered a potential risk for prasugrel.
Healthcare professional	Patients who have had a prior stroke or mini stroke are at an

decision to use prasugrel with a history of stroke or mini stroke **(potential off-label use in patients with prior TIA/stroke)**	increased risk for bleeding in the skull (intracranial hemorrhage) or stroke (blood flow to a part of the brain stops) when using prasugrel.
Cancer of the colon or rectum (parts of the large intestine) **(colorectal cancer)**	There have been patients treated with prasugrel who have been diagnosed with cancer of the colon or rectum. Many of these cancers are found because the patient has some bleeding from their colon or rectum while on prasugrel. Bleeding like this can happen more frequently while on prasugrel due to the expected effect of the drug. While it seems like the bleeding risk on prasugrel is the reason for finding these cancers, it is not known if prasugrel increases the risk for cancer growth.

Missing information

Risk	**What is known**
Use of prasugrel along with blood thinners **(concomitant use with fibrinolytics other thienopyridines, warfarin) and/or frequent use of anti-inflammatory medications (NSAIDs (non-ASA))**	Because prasugrel can cause bleeding, it should not be used at the same time as blood thinners or other medications that can cause bleeding such as anti-inflammatory medications.
Use in children **(Use in paediatric population)**	Prasugrel should not be used in children below age 18 because it has not been studied.
Use in pregnant and breastfeeding women **(Use in pregnancy and lactation)**	No clinical study has been done in pregnant or breastfeeding women. Therefore, prasugrel should not be used in these patients.
Patient who do not have symptoms or evidence of a heart attack treated by a procedure to open clogged vessels **(Use in subjects without clinical manifestation of ACS)**	Prasugrel has not been studied in these patients.
Patients who have severe heart disease who cannot be treated with a procedure or surgery **(Use in subjects with severely**	Prasugrel has not been studied in these patients.

compromised cardiac status (cardiogenic shock, class IV CHF, refractory ventricular arrhythmia))	
Patients with severe liver disease **(Use in subjects with severe hepatic impairment)**	Prasugrel should not be used in patients with severe liver disease because they have a greater risk of bleeding.

VI.2.5 Summary of risk minimisation measures by safety concern

All medicines have a Summary of Product Characteristics (SmPC) 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.

The Summary of Product Characteristics and the Package leaflet for this product can be found at the agency's EPAR page.

This medicine has special conditions and restrictions for its safe and effective use (additional risk minimisation measures). Full details on these conditions and the key elements of any educational material can be found in Annex II of the product information which is published in agency's EPAR page; how they are implemented in each country however will depend upon agreement between the manufacturer and the national authorities.

These additional risk minimisation measures are for the following risks:

Bleeding (Haemorrhage) in patients ≥ 75 years of age and patients weighing < 60 kg

Risk Minimisation Measure(s): Additional actions taken to reduce bleeding events for patients 75 years of age or older and patients who weigh less than 60 kg are provided by teaching health care professionals (doctors and nurses) the right way to use prasugrel in these patients.
Objective and Rationale To teach health care providers so that patients are treated with the best dose of medication for each patient.

VI.2.6 Planned post authorisation development plan

Not applicable. No postauthorisation studies are planned.

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

Not applicable, this is the first Risk management plan.