Part VI. Summary of the Risk Management Plan

Summary of risk management plan for Cyramza (ramucirumab)

This is a summary of the risk management plan (RMP) for Cyramza. The RMP details important risks of Cyramza, how these risks can be minimised, and how more information will be obtained about Cyramza's risks and uncertainties (missing information).

Cyramza's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Cyramza should be used.

This summary of the RMP for Cyramza should be read in the context of all this information, including the assessment report of the evaluation and its plain-language summary, all of which is part of the European Public Assessment Report (EPAR).

Important new concerns or changes to the current ones will be included in updates of Cyramza's RMP.

I. The medicine and what it is used for

Cyramza is authorised for the treatment of advanced gastric cancer or gastro-oesophageal junction adenocarcinoma, metastatic colorectal cancer, locally advanced or metastatic non-small cell lung cancer, and hepatocellular carcinoma (see SmPC for the full indication). It contains ramucirumab as the active substance and it is given by intravenous infusion.

Further information about the evaluation of Cyramza's benefits can be found in Cyramza's EPAR, including in its plain-language summary, available on the EMA website, under the medicine's webpage.

http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/002829/human_med_001825.jsp&mid=WC0b01ac058001d124

II. Risks associated with the medicine and activities to minimise or further characterise the risks

Important risks of Cyramza, together with measures to minimise such risks and the proposed studies for learning more about Cyramza's risks, are outlined below.

Measures to minimise the risks identified for medicinal products can be:

- Specific information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to patients and healthcare professionals;
- Important advice on the medicine's packaging;
- The authorised pack size — the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly;
- The medicine's legal status — the way a medicine is supplied to the patient (e.g., with or without prescription) can help to minimise its risks.

Together, these measures constitute *routine risk minimisation* measures.

II.A. List of important risks and missing information

Important risks of Cyramza are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely administered. Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of Cyramza. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (for example, on the long-term use of the medicine).

List of important risks and missing information	
Important identified risks	Arterial thromboembolic events Gastrointestinal perforation Serious haemorrhagic events Liver failure/liver injury (including hepatic encephalopathy in patients with HCC)
Important potential risks	Serious infection secondary to neutropenia Posterior reversible encephalopathy syndrome Severe clinical outcomes of venous thromboembolic events Reproductive and developmental toxicity
Missing information	Not applicable

Abbreviation: HCC = hepatocellular carcinoma.

II.B. Summary of important risks

The safety information in the proposed Product Information is aligned to the reference medicinal product.

Important identified risk: Arterial thromboembolic events (ATEs or blocking of the artery by a clot)	
Evidence for linking the risk to the medicine	Arterial thromboembolic events (ATEs) have been associated with some antiangiogenic agents (medicines that prevent the growth of new blood vessels), including ramucirumab, particularly when used in combination regimens with chemotherapy. In clinical trials, ATEs occurred more often in patients receiving ramucirumab either as a single agent or in combination with chemotherapy compared to control patients who were not treated with ramucirumab. In Phase 3 clinical trials, serious ATEs reported in patients receiving ramucirumab included heart attack, cardiac arrest (sudden stopping of the heart), stroke or reduced blood flow to the brain. ATEs have most typically occurred in patients with underlying heart disease or associated risk factors.
Risk factors and risk groups	Risk factors for ATEs in patients who receive ramucirumab are similar to patients who don't receive ramucirumab. Elderly patients, smokers, and patients with cancer and/or with cardiovascular risk factors including diabetes, abdominal obesity and high cholesterol are at increased risk of experiencing ATEs. Risk factors for developing clots in blood vessels among cancer patients include smoking, poor blood flow inside the blood vessels (for example, after surgery or immobility), activation of clotting factors in the blood, and cancer treatments such as chemotherapy, hormonal therapy, antiangiogenic agents, and medicines that stimulate the body to produce red blood cells. In patients with liver cirrhosis, alcohol-related cirrhosis and older age are independent risk factors for developing blockage in the heart arteries.
Risk minimisation measures	**Routine risk minimisation measures:** SmPC Sections 4.2, 4.4, and 4.8 PL Sections 2, 3, and 4 SmPC Section 4.2 and 4.4 advise: • Permanent discontinuation of ramucirumab in the event of severe ATEs. PL Sections 2 and 4 advise patients: • To tell their healthcare professional immediately if they experience any symptoms or signs of blockage of the artery by a blood clot either during treatment with ramucirumab or anytime thereafter, including symptoms of a heart attack or stroke.

Important identified risk: Gastrointestinal perforation (a hole in the wall of the gut)	
Evidence for linking the risk to the medicine	Gastrointestinal (GI) perforation has been associated with some antiangiogenic agents (medicines that prevent the formation of new blood vessels), including ramucirumab. In clinical trials and in all the conditions that ramucirumab can be prescribed for, GI perforation occurred more often in patients receiving ramucirumab as a single agent and in combination with chemotherapy compared to control patient not treated with ramucirumab. GI perforation usually, but not always, occurs in patients with tumours located in the abdomen or tumours that involve the lining of the abdomen. GI perforation has been observed to be associated with ramucirumab treatment in clinical studies and in the general population of people receiving ramucirumab from their doctors.
Risk factors and risk groups	Patients at increased risk include those with tumours located in the abdomen or with tumours that involve the lining of the abdomen, patients with inflammation in the abdomen, patients who have had cancer treatments known to cause GI perforation before or at the same time as receiving ramucirumab, and patient taking medicines like aspirin, non-steroidal anti-inflammatory drugs and steroids at the same time as ramucirumab. Patients with inflammatory bowel disease, diverticulitis, ischaemic bowel, peptic ulcers, obstruction and iatrogenic bowel injuries resulting from procedures such as endoscopy, colonoscopy, laparoscopy, and surgery in addition to prior radiation therapy are at higher risk of having GI perforation occur.
Risk minimisation measures	**Routine risk minimisation measures:** SmPC Sections 4.2, 4.4, and 4.8 PL Sections 2, 3, and 4 SmPC Sections 4.2 and 4.4 advise that: • Ramucirumab therapy should be permanently stopped in the event of gastrointestinal perforation. PL Sections 2 and 4 advise patients: • To tell their health care professional immediately if they develop any symptoms of a hole in the wall of their gut (‘gastrointestinal perforation’) including abdominal pain, vomiting, fever or chills during treatment with ramucirumab or anytime thereafter.

Important identified risk: Serious haemorrhagic events (bleeding events)	
Evidence for linking the risk to the medicine	Bleeding/haemorrhage is associated with the use of some antiangiogenic agents (medicines that prevent the formation of new blood vessels), including ramucirumab. In clinical trials across all indications, bleeding/haemorrhagic events occurred more often in patients receiving ramucirumab in combination with chemotherapy compared to those who received chemotherapy alone. Severe gastrointestinal haemorrhage, bleeding from swollen veins in the oesophagus (oesophageal varices), lung and nervous system haemorrhages (for example, brain haemorrhages), including fatal events, have been reported in patients with advanced cancer treated with ramucirumab. Haemorrhagic events have been observed to be associated with ramucirumab treatment in clinical studies and/or in the general population of people receiving ramucirumab from their doctors.
Risk factors and risk groups	Patients at higher risk of bleeding events include those with a bleeding tendency, such as patients who develop blood clotting problems due to another disease, prior history of bleeding (including variceal bleeding), liver insufficiency/failure, or any condition that carries a high risk of bleeding (for example, a tumour involving major blood vessels or fragile blood vessels in the oesophagus). Also, patients who are taking blood thinners or non-steroidal anti-inflammatory drugs have a greater tendency to bleed. Severe gastrointestinal bleeding usually, but not always, occurs in patients with tumours located in the abdomen or that involve the lining of the abdomen. In lung cancer, patients with a previous history of bleeding from the lung, or who have tumours in the more central parts of the lung, squamous-type of lung cancer, tumour cavitation (hollow tumours), or those with tumours that have spread to, invaded or encased the large blood vessels of the heart/lung are at increased risk of lung bleeding. Patients with brain metastases may be at higher risk of bleeding in the brain; however, no clear evidence has been shown for an increased risk of intracranial bleeding in cancer patients with brain metastases treated with antiangiogenic agents (medicines that prevent the growth of new blood vessels), including ramucirumab. In patients with liver cirrhosis and oesophageal varices, the size of varices and the degree of decreased liver function are associated with a greater risk of bleeding from oesophageal varices.

Risk minimisation measures	**Routine risk minimisation measures:** SmPC Sections 4.2, 4.3, 4.4, and 4.8 PL Sections 2, 3, and 4 SmPC Sections 4.2 and 4.4 advise that: • Ramucirumab should be permanently stopped in the event of severe bleeding. SmPC Section 4.3 states that: • For patients with NSCLC, ramucirumab is contraindicated where there is tumour cavitation or tumour involvement of major vessels. SmPC Section 4.4 advises that: • Blood counts and blood clotting tests should be monitored in patients with conditions that make them more at risk of bleeding, and in those being treated with blood thinners or other medicines that increase the risk of bleeding. • For HCC patients with evidence of portal hypertension or prior history of oesophageal variceal bleeding, screening for and treatment of oesophageal varices should be performed as per standard of care before starting ramucirumab treatment. PL Section 2 advises patients before they receive ramucirumab: • To talk to their doctor or nurse if they have any condition that increases the risk of bleeding. • To tell their doctor if they are taking any medicines that may increase the risk of bleeding or that affect blood clotting ability. • To talk to their doctor or nurse if they have lung cancer and have had recent bleeding in the lung (coughing up bright red blood) or are regularly taking non-steroidal anti-inflammatory medicines, or medicines that affect blood clotting ability. • To talk to their doctor or nurse if they have liver cancer and have had previous bleeding from enlarged veins in the food pipe (oesophagus) or have high blood pressure in the portal vein, which carries the blood from the bowel and spleen to the liver. PL Sections 2 and 4 advise patients: • To tell their health care professional immediately if they experience symptoms of severe bleeding or severe bleeding in the gut, including extreme tiredness, weakness, dizziness or changes in the colour of stools, either during treatment with ramucirumab or any time thereafter. PL Section 4 advises patients: • To tell their doctor if they experience bleeding in their lungs.

Important identified risk: Liver failure/liver injury (including hepatic encephalopathy in patients with HCC)	
Evidence for linking the risk to the medicine	Lilly considers liver failure/liver injury to be an important potential risk for ramucirumab. Lilly does not consider hepatic encephalopathy in patients with liver cancer (hepatocellular carcinoma [HCC]) to be an important identified risk, since there is insufficient evidence to support a causal relationship between ramucirumab and hepatic failure with secondary hepatic encephalopathy. However, liver failure/liver injury (including hepatic encephalopathy in patients with HCC) is considered as an important identified risk by the Pharmacovigilance Risk Assessment Committee (PRAC), the European Medicines Agency (EMA) committee that is responsible for assessing and monitoring the safety of human medicines. Across all Phase 3 trials (except in liver cancer), the incidence of clinical liver events was low in ramucirumab arm and similar to the control arm. Most of the liver events observed in the NSCLC study when ramucirumab was used in combination with erlotinib were due to abnormalities in liver blood tests (increased liver enzymes) of low severity only without any evidence of liver failure, and there were no events of hepatic encephalopathy. A higher incidence of increased liver enzymes in ramucirumab-treated patients compared to control patients has not been observed across other Phase 3 clinical trials in other indications. Therefore, based on the review of safety data from completed non-liver cancer Phase 3 trials and lack of data from medical literature showing that medicines in the same family as ramucirumab are associated with developing liver failure, Lilly considered there is insufficient evidence to prove that ramucirumab causes liver failure. Patients with liver cancer and underlying chronic liver disease are expected to have a higher rate of liver failure/injury events as part of the natural history of their disease, no matter what type of anti-cancer treatment they may receive. Liver injury events of ascites (accumulation of fluid in the belly) and hepatic encephalopathy (build-up of toxins in the brain) have been reported at a higher rate in the ramucirumab arm in the combined patient population from 2 liver cancer studies REACH-2 and REACH. In REACH-2, the incidence of all events and severe clinical liver events (including fatal events) was higher in patients who received ramucirumab. Hepatic encephalopathy events (including hepatic coma) were reported only in the patients who received ramucirumab in the REACH-2 study. Due to the higher number of hepatic encephalopathy events in ramucirumab-treated patients versus placebo patients in liver cancer trials, hepatic encephalopathy is considered an adverse drug reaction (ADR) for ramucirumab given as a single therapy for the treatment of liver cancer and not in any other indications. However, based on a review of cases of hepatic encephalopathy from the combined patient population in HCC studies (REACH-2 and REACH), Lilly considers that there is insufficient evidence to show that use of ramucirumab causes liver failure and subsequent hepatic encephalopathy. This is because a worsening of liver function tests, which would be expected to occur in liver failure with hepatic encephalopathy, was not consistently observed in all cases. Across Phase 3 clinical trials in non-HCC indications, only 1 case of hepatic encephalopathy was reported in ramucirumab-treated patients, and therefore hepatic encephalopathy is not considered an ADR or a risk in non-HCC indications.

Risk factors and risk groups	Risk factors for the development of liver failure/liver injury in patients receiving ramucirumab include a history of severe liver injury, liver cancer including liver cancer that has spread to the lymph nodes, and liver cirrhosis. Risk factors also include acute viral hepatitis A, B, or C; use of a drug that is toxic to the liver or exposure to liver toxins at the same time as receiving ramucirumab; autoimmune or alcoholic hepatitis; biliary tract disease; and circulatory problems of low blood pressure or right heart congestive failure that may cause low blood flow and lack of oxygen to the liver. Erlotinib and other drugs in the same class known as epidermal growth factor receptor tyrosine kinase inhibitors (EGFR TKIs) are known to be associated with liver toxicity, most commonly abnormal liver blood tests such as increases in transaminase (liver enzyme) levels. Patients with advanced cancer frequently already have liver problems before receiving ramucirumab, such as having tumour that has spread to the liver, cirrhosis, hepatitis C, a primary diagnosis of liver cancer or liver problems that are not related to alcohol use. Hepatic encephalopathy is a neuropsychiatric complication of both acute (sudden) liver disease and acute worsening of chronic (long-term) liver disease which affects the brain. Patients who have cirrhosis of the liver are at risk of developing hepatic encephalopathy. Evidence from an HCC study (REACH) suggests that a greater severity of the underlying chronic liver disease (severity based on Child-Pugh classification or score at start of treatment) was associated with a higher risk of developing hepatic encephalopathy. Hepatic encephalopathy is not uncommonly seen in patients with HCC at the time their liver cancer is diagnosed, and the rate of occurrence increases with disease severity. Risk factors for developing hepatic encephalopathy in cirrhosis include infections, bleeding in the gut, constipation, changes in the levels of chemicals in the blood (sodium and potassium), drugs (sedatives, water tablets), low blood sugar levels, low blood oxygen levels, and changes in the liver circulation (such as portal hypertension). In patients with cirrhosis, a previous history of hepatic encephalopathy is a risk factor for having further episodes of hepatic encephalopathy.

Risk minimisation measures	**Routine risk minimisation measures:** SmPC Sections 4.2, 4.4, 4.8, and 5.2 PL Sections 2, 3, and 4 SmPC Section 4.2: • Provides advice to check blood chemistry prior to each paclitaxel infusion, and includes liver function test criteria to be met prior to each paclitaxel administration. • Ramucirumab should be permanently discontinued in the event of hepatic encephalopathy or hepatorenal syndrome. SmPC Section 4.4 advises that: • Ramucirumab should be used with caution in patients with severe liver cirrhosis (Child-Pugh B or C), cirrhosis with hepatic encephalopathy, clinically significant ascites due to cirrhosis, or hepatorenal syndrome. Ramucirumab should only be used in these patients if the potential benefits of treatment are judged to outweigh the potential risk of progressive hepatic failure. • Patients should be monitored for clinical signs and symptoms of hepatic encephalopathy. • Ramucirumab should be permanently discontinued in the event of hepatic encephalopathy or hepatorenal syndrome. PL Section 2 advises patients: • To talk to their doctor or nurse prior to being given ramucirumab if they have severe liver disease (‘cirrhosis’) and associated conditions, such as excessive accumulation of fluid in the abdomen (‘ascites’). PL Section 4 advises patients with chronic liver problems: • To tell their doctor if they experience common side effects of confusion and/or disorientation.

Important potential risk: Serious infection secondary to neutropenia (serious infection due to low white blood cell count)	
Evidence for linking the risk to the medicine	Neutropenia (low white blood cell count which help fight infection) makes a patient more susceptible to developing serious infection, which is a known and major cause of sickness and death in neutropenic patients. Phase 3 studies showed a higher incidence of febrile neutropenia (fever accompanied by neutropenia) in patients who received ramucirumab together with chemotherapy compared to patients who received chemotherapy alone, although the difference frequency in 3 studies was very small. The incidence of infections due to neutropenia in patients who received ramucirumab compared to those who didn't was similar in 2 of the 3 studies. In the 3rd study (REVEL), patients who received ramucirumab had a higher rate of infection due to neutropenia. In a study using ramucirumab in combination with erlotinib (RELAY study), neutropenia occurred in a similar proportion of ramucirumab-treated patients and control patients, and the incidence of infection due to neutropenia was low and infections were not associated with neutropenia. Since ramucirumab has been marketed, the reporting of serious infections due to neutropenia is low and the majority of cases occur in patients taking ramucirumab in combination with chemotherapy that suppressed the bone marrow. There is not enough evidence to definitively say that ramucirumab given by itself causes serious infection due to neutropenia. Therefore, serious infections due to neutropenia are considered to be an important potential risk for ramucirumab.
Risk factors and risk groups	Neutropenia places patients at a higher risk of life-threatening complications, including infections, and remains a prevalent problem associated with substantial sickness and death. Identified risk factors for neutropenia can be categorised as patient-specific (for example, patient age, other medical conditions, and level of ability to complete daily activities) or regimen-specific (chemotherapy that suppresses the bone marrow is one of the primary risk factors). The duration of neutropenia and how severe it is are two factors that impact the risk of developing subsequent serious infection complications. Several other factors appear to affect the risk of neutropenic complications or infections in patients with cancer, such as advanced age, other medical conditions, exposure to additional germs due to being hospitalised or receiving cancer treatment. Prior treatment with cytotoxic chemotherapy regimens, such as anthracycline-based chemotherapy, may increase the risk of severe neutropenia or febrile neutropenia (fever associated with neutropenia).
Risk minimisation measures	**Routine risk minimisation measures:** SmPC Sections 4.2, 4.8, and 5.2 PL Sections 2 and 4 SmPC Section 4.2 includes: Advice to check complete blood count prior to each paclitaxel infusion, and provides white blood cell count criteria to be met before giving paclitaxel each time. Paclitaxel dose reduction guidance for severe blood/bone marrow toxicity. FOLFIRI dose reduction guidance for moderate to severe low white blood count and fever accompanied by low white blood cell count. Docetaxel dose adjustments for low white blood count and fever accompanied by low white blood cell count. PL Section 2 advises patients:

	To tell their doctor or nurse immediately if they experience fever and infection or symptoms of infection such as sweating, headache, pain in the limbs, or decreased appetite either during treatment with ramucirumab or any time thereafter. PL Section 4 advises patients: To tell their doctor if they experience low white blood cell counts (may increase the risk of infection), fever accompanied by low white blood cell counts, infections, or serious infection (sepsis).

Important potential risk: Posterior reversible encephalopathy syndrome (PRES; neurological syndrome including symptoms of headache, confusion, seizures and loss of vision)	
Evidence for linking the risk to the medicine	PRES has been reported very rarely in patients who received ramucirumab in completed Phase 3 clinical trials. A small number of cases of PRES have also been reported since ramucirumab has been marketed, and not all cases contained radiological confirmation of the diagnosis. Based on the clinical trial data and data collected since ramucirumab has been marketed, there is no clear evidence to indicate that ramucirumab causes PRES. However, PRES is considered to be an important potential risk because it is a serious condition and is known to be caused by other medicines in the same family as ramucirumab.
Risk factors and risk groups	Known risk factors for PRES in ramucirumab-treated patients include infection / sepsis / septic shock, pre-eclampsia/eclampsia, autoimmune diseases, chronic kidney failure, and chronic high blood pressure. Patients who receive other chemotherapy drugs agents that are associated with PRES, such as bevacizumab, platinums or antimetabolites, could be at increased risk of developing PRES.
Risk minimisation measures	**Routine risk minimisation measures:** None

Important potential risk: Severe clinical outcomes of venous thromboembolic events (blood clots forming in the veins)	
Evidence for linking the risk to the medicine	In completed Phase 3 randomised trials of ramucirumab, severe venous thromboembolic events (VTEs) occurred about as often in patients who received ramucirumab as patients who did not. Therefore, clinical trial evidence does not support a causal relationship between ramucirumab as a single agent or in combination with chemotherapeutic agents and the development of VTEs. VTE is therefore not considered an ADR for ramucirumab. Since ramucirumab has been marketed, the rate of serious VTEs events has been low. However, VTEs can result in significant human health problems and fatal events have been reported. VTEs are associated with cancer itself, although the risk depends on the type of cancer, stage of cancer, and the ability to find a clot in the veins with an imaging machine. VTEs have been associated with some antiangiogenic agents (medicines that prevent the formation of new blood vessels), although the incidence varies depending on the type of therapy, the use of other chemotherapy agents at the same time, and the specific type of cancer.
Risk factors and risk groups	Risk factors for VTEs in patients who receive ramucirumab are the same as known risk factors for developing VTEs in all individuals and include advanced age, surgery, hospitalisation, immobility, post-operative status, trauma, pregnancy, oral birth control use and hormone use for menopause, cancer, obesity, and inherited and acquired blood clotting diseases. Cytotoxic chemotherapy given at the same time as ramucirumab is considered to be an additional risk factor. Patients with cirrhosis are at an increased risk of VTEs compared with the general population. Patients with both cirrhosis and primary liver cancer have a greater risk of thrombosis in the portal vein (vein that brings blood from the stomach/intestines to the liver), with approximately 3.5-times higher risk than in cancer-free cirrhosis patients.
Risk minimisation measures	**Routine risk minimisation measures:** None

Important potential risk: Reproductive and developmental toxicity (side effects on pregnancy and risks to the unborn baby)	
Evidence for linking the risk to the medicine	In animal models, VEGF receptor interaction and angiogenesis (the ability of the body to form new blood vessels) are considered essential for female reproduction, normal embryo-foetal development in the womb, and post-natal development. Therefore, since ramucirumab blocks angiogenesis, ramucirumab treatment may adversely affect female fertility (ovulation) and is highly likely to cause negative effects on the placenta and the development of the foetus during pregnancy. Therefore, reproductive and developmental toxicity is considered to be an important potential risk for ramucirumab. No human data are available.
Risk factors and risk groups	Women who have not gone through menopause are at risk of developing reproductive toxicity. Ramucirumab may result in negative effects during pregnancy and after a baby has been born.
Risk minimisation measures	**Routine risk minimisation measures:** SmPC Sections 4.6 and 5.3 PL Section 2 SmPC Section 4.6 states that: • Women should be advised to avoid becoming pregnant while on ramucirumab. • Women of child-bearing potential should use effective birth control during and up to 3 months after the last dose of ramucirumab treatment. • Ramucirumab is not recommended during pregnancy and in women of child-bearing potential not using birth control. Ramucirumab should only be used if the potential benefit to the mother justifies the potential risk during pregnancy. • Breast-feeding should be discontinued during treatment with ramucirumab and for at least 3 months after the last dose. PL Section 2 advises patients: • To tell their doctor if they are pregnant or breast-feeding, suspect they may be pregnant, or are planning to become pregnant before starting treatment. • To avoid getting pregnant while receiving this medicine and for at least 3 months after the last dose. • If planning to have a baby, to talk to their doctor about the best birth control method for them. • That ramucirumab should not be used during pregnancy. • That breast-feeding should be avoided during treatment and for at least 3 months after the last dose.

II.C. Post-authorisation development plan

II.C.1. Studies that are conditions of the marketing authorisation

Not applicable.

II.C.2. Other studies in post-authorisation development plan

Study short name: Study I4T-MC-JVDD: Safety and Effectiveness of Ramucirumab in Patients with Advanced Gastric Cancer in the European Union and North America: A Prospective Observational Registry

Purpose of the study: To describe the safety profile of ramucirumab administered as monotherapy or in combination therapy for second-line treatment of adult patients with advanced gastric cancer under real-world disease conditions in the EU and North America, and to describe the effectiveness of ramucirumab administered as monotherapy or in combination therapy for second-line treatment of adult patients with advanced gastric cancer under real-world disease conditions in the EU and North America.