Abridged Pack Insert

Cyramza® (Ramucirumab), Concentrate for Solution for Infusion 10mg/ml
(100mg/10ml vial & 500mg/50 ml vial)

Indications:

Gastric cancer

- Cyramza® (Ramucirumab) in combination with paclitaxel is indicated for the treatment of adult patients with advanced gastric cancer or gastro-oesophageal junction adenocarcinoma with disease progression after prior platinum and fluoropyrimidine chemotherapy.
- Cyramza® (Ramucirumab) monotherapy is indicated for the treatment of adult patients with advanced gastric cancer or gastro-oesophageal junction adenocarcinoma with disease progression after prior platinum or fluoropyrimidine chemotherapy, for whom treatment in combination with paclitaxel is not appropriate.

Colorectal cancer

- Cyramza® (Ramucirumab), in combination with FOLFIRI (irinotecan, folinic acid, and 5-fluorouracil), is indicated for the treatment of adult patients with metastatic colorectal cancer (mCRC) with disease progression on or after prior therapy with bevacizumab, oxaliplatin and a fluoropyrimidine.

Non-small cell lung cancer

- Cyramza® (Ramucirumab) in combination with erlotinib is indicated for the first-line treatment of adult patients with metastatic non-small cell lung cancer with activating epidermal growth factor receptor (EGFR) mutations.
- Cyramza®(Ramucirumab), in combination with docetaxel, is indicated for the treatment of patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with disease progression on or after platinum-based chemotherapy.

Hepatocellular carcinoma

- Cyramza® (Ramucirumab) monotherapy is indicated for the treatment of adult patients with advanced or unresectable hepatocellular carcinoma who have a serum alpha fetoprotein (AFP) of ≥ 400 ng/ml and who have been previously treated with sorafenib.

Dosage and administration:

- Gastric cancer and gastro-oesophageal junction (GEJ) adenocarcinoma: Cyramza® in combination with Paclitaxel: The recommended dose of Ramucirumab is 8 mg/kg on days 1 and 15 of a 28 day cycle, prior to Paclitaxel infusion. The recommended dose of Paclitaxel is 80 mg/ m^2 administered by intravenous infusion over approximately 60 minutes on days 1, 8 and 15 of a 28 day cycle (Please refer Paclitaxel pack insert).
- Cyramza® as a single agent: The recommended dose of Ramucirumab as a single agent is 8 mg/kg every 2 weeks.
- Colorectal cancer: The recommended dose of Ramucirumab is 8 mg/kg every 2 weeks administered by intravenous infusion, prior to FOLFIRI administration.
- Non-small cell lung cancer (NSCLC):
    - Cyramza® in combination with erlotinib for the treatment of NSCLC with activating EGFR mutations. The recommended dose of ramucirumab in combination with erlotinib is 10 mg/kg every two weeks. EGFR mutation status should be determined prior to initiation of treatment with ramucirumab and erlotinib using a validated test method. See erlotinib prescribing information for the posology and method of administration of erlotinib.
    - Cyramza® in combination with docetaxel for the treatment of NSCLC after platinum-based chemotherapy: The recommended dose of Ramucirumab is 10 mg/kg on day 1 of a 21 day cycle, prior to docetaxel infusion. The recommended dose of docetaxel is 75 mg/ m^2 administered by intravenous infusion over approximately 60 minutes on day 1 of a 21 day cycle.
- Hepatocellular carcinoma (HCC): The recommended dose of ramucirumab as a single agent is 8 mg/kg every 2 weeks

Method of administration:

After dilution, Cyramza® is administered as an intravenous infusion over approximately 60 minutes. It should not be administered as an intravenous bolus or push.

Special warnings and precautions for use:

Arterial thromboembolic events; Gastrointestinal perforations; Severe bleeding; Pulmonary haemorrhage in NSCLC; Infusion-related reactions; Hypertension; Posterior Reversible Encephalopathy Syndrome (PRES), Aneurysms and artery dissections, Impaired wound healing; Hepatic impairment; Fistula; Proteinuria; Stomatitis; Renal impairment; Sodium restricted diet; Elderly patients with NSCLC.

Contraindications:

Hypersensitivity to the active substance or to any of the excipients (L-Histidine, L-Histidine monohydrochloride, Glycine, Sodium chloride, Polysorbate 80). For patients with NSCLC, Ramucirumab is contraindicated where there is tumour cavitation or tumour involvement of major vessels.

Undesirable effects:

The most serious adverse reactions associated with Ramucirumab treatment (as a single agent or in combination with cytotoxic chemotherapy) were: Gastrointestinal perforation, Severe gastrointestinal haemorrhage, Arterial thromboembolic events, Posterior reversible encephalopathy syndrome. The most common adverse reactions observed in patients treated with Ramucirumab as monotherapy are: Peripheral Oedema, hypertension, diarrhoea, abdominal pain, headache, proteinuria and thrombocytopenia.

The most common adverse reactions observed in patients treated with ramucirumab in combination with chemotherapy are: fatigue/asthenia, neutropenia, diarrhoea, epistaxis and stomatitis.

The most common adverse reactions observed in patients treated with ramucirumab in combination with erlotinib are: infections, diarrhoea, hypertension, stomatitis, proteinuria, alopecia and epistaxis.

Summary of use in specific populations:

Elderly

In the pivotal studies there is limited evidence that patients 65 years of age or older are at increased risk of adverse events compared to patients younger than 65 years old. No dose reductions are recommended.

Renal impairment

There have been no formal studies with Cyramza® in patients with renal impairment. Clinical data suggest that no dose adjustments are required in patients with mild, moderate. or severe renal impairment. No dose reductions are recommended.

Hepatic impairment

There have been no formal studies with Cyramza® in patients with hepatic impairment. Clinical data suggest that no dose adjustments are required in patients with mild or moderate hepatic impairment. There are no data regarding Ramucirumab administration in patients with severe hepatic impairment. No dose reductions are recommended.

Paediatric population

The safety and efficacy of Cyramza® in children and adolescents (<18 years) has not been established.

There is no relevant use of Ramucirumab in the paediatric population for the indications of advanced gastric cancer or gastro-oesophageal adenocarcinoma, adenocarcinoma of the colon, lung carcinoma, and hepatocellular carcinoma.

Overdose:

There is no data on overdose in humans. Cyramza® has been administered in a Phase 1 study up to 10 mg/kg every two weeks without reaching a maximum tolerated dose. In case of overdose, supportive therapy should be used.

PLEASE SEE FULL PRESCRIBING INFORMATION

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