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Rybrevant (*amivantamab*)

An overview of Rybrevant and why it is authorised in the EU

What is Rybrevant and what is it used for?

Rybrevant is a cancer medicine used to treat adults with advanced non-small cell lung cancer (NSCLC) whose cancer cells have certain genetic changes in the epidermal growth factor receptor (EGFR) gene.

When the cancer has activating EGFR exon 20 insertion mutations, Rybrevant is used:

- in combination with other cancer medicines, carboplatin and pemetrexed, in patients who have not been treated before;
- on its own in patients for whom previous treatment with platinum-based cancer medicines has not worked well enough.

When the cancer has EGFR exon 19 deletions or exon 21 L858R substitution mutations, Rybrevant is used:

- in combination with the cancer medicine lazertinib in patients who have not been treated before;
- in combination with carboplatin and pemetrexed in patients for whom previous treatments, including an EGFR tyrosine kinase inhibitor, have not worked well enough.

Rybrevant contains the active substance amivantamab.

How is Rybrevant used?

The medicine can only be obtained with a prescription. Treatment with Rybrevant should be started and supervised by a doctor who is experienced in using cancer medicines and given in a setting where any infusion-related side effects can be managed. Before starting treatment, patients must be tested to confirm that the tumour cells have changes to the EGFR gene.

Rybrevant is given as an infusion (drip) into a vein. The first week's dose is split over two successive days, and the medicine is then given once weekly for the next three weeks. After that, the medicine is given once every three weeks when used in combination with carboplatin and pemetrexed, and once every two weeks when used on its own or in combination with lazertinib.

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

Treatment is continued until the disease gets worse or side effects become too severe. Treatment should be stopped temporarily or permanently, or subsequent doses may be reduced, if the patient experiences certain side effects.

Patients taking Rybrevant in combination with lazertinib should be given anticoagulants (substances that prevent the blood from clotting) at the initiation of treatment to reduce risks of venous thromboembolic events (VTE, problems due to the formation of blood clots in veins).

Patients should be given antihistamines (allergy medicines), antipyretics (fever-reducing medicines) and corticosteroids before the first two treatment sessions with Rybrevant, to reduce infusion-related reactions. In the following treatment sessions, patients should be given antihistamines and antipyretics.

For more information about using Rybrevant, see the package leaflet or contact your doctor or pharmacist.

How does Rybrevant work?

In NSCLC cells with activating EGFR exon 20 insertion mutations, exon 21 L858R substitution mutations or exon 19 deletions, the EGFR protein is overactive, causing uncontrolled growth of cancer cells.

The active substance in Rybrevant, amivantamab, is a monoclonal antibody (a type of protein) designed to recognise and attach to two receptors (targets) on the surface of the NSCLC cells at the same time. One part of the antibody attaches to EGFR. The other part attaches to MET, a receptor important for cancer growth and metastasis (cancer that has spread from another part of the body). By attaching to the two receptors, amivantamab blocks them from receiving the messages the cancer cells need for growing and spreading. The attached antibody also attracts and activates immune cells to kill the targeted cancer cells.

What benefits of Rybrevant have been shown in studies?

The benefits of Rybrevant were investigated in four main studies in patients with NSCLC with specific EGFR gene mutations.

In the first main study, Rybrevant was effective at reducing the size of the cancer in patients who had previously been treated with platinum-based cancer medicines. Rybrevant was not compared with any other treatment or placebo (a dummy treatment). The response to treatment (shrinkage in size of the cancer) was assessed using body imaging. In around 37% (42 out of 114) of the patients, the cancer shrank after treatment with Rybrevant. On average, responses lasted for just over 12 months.

The second main study, involving over 300 patients, compared the effect of Rybrevant in combination with platinum-based medicines with that of platinum-based medicines alone in patients who had not been treated before. On average, patients given Rybrevant with platinum-based medicines lived 11.4 months without their disease getting worse, compared with 6.7 months for patients given only platinum-based medicines.

The third main study involved 394 patients with NSCLC whose cancer has EGFR exon 21 L858R substitution mutation or exon 19 deletion and for whom osimertinib (an EGFR tyrosine kinase inhibitor) had not worked well enough. Carboplatin and pemetrexed were given with or without Rybrevant. On average, patients given Rybrevant with carboplatin and pemetrexed lived around 6.3 months without the disease getting worse, compared with around 4.2 months for patients given only carboplatin and pemetrexed.

The fourth study involved 1,074 patients with advanced NSCLC with EGFR gene exon 19 deletion or exon 21 L858R substitution mutation who had not been treated before. Patients either took Rybrevant plus lazertinib, lazertinib alone or another medicine targeting mutated EGFR, osimertinib. Those given Rybrevant plus lazertinib lived 23.7 months without their disease getting worse compared with 16.6 months for patients given osimertinib alone.

What are the risks associated with Rybrevant?

For the full list of side effects and restrictions with Rybrevant, see the package leaflet.

When used on its own, the most common side effects with Rybrevant (which may affect more than 1 in 5 people) include rash, infusion-related reactions, nail toxicity (nail abnormalities with pain or discomfort), hypoalbuminaemia (low blood levels of the protein albumin), oedema (fluid retention), tiredness, stomatitis (inflammation of the lining of the mouth), nausea (feeling sick), and constipation. The most common serious side effects (which may affect more than 1 in 100 people) include interstitial lung disease (disorders causing scarring in the lungs), infusion-related reactions and rash.

When used in combination with carboplatin and pemetrexed, the most common side effects with Rybrevant (which may affect more than 1 in 5 people) include rash, neutropenia (low levels of neutrophils, a type of white blood cell), nail toxicity, stomatitis, infusion-related reactions, thrombocytopenia (low levels of blood platelets, components that help the blood to clot), hypoalbuminaemia, oedema, constipation, nausea, decreased appetite, tiredness, an increase in the level of liver enzymes in the blood, vomiting and hypokalaemia (low blood levels of potassium). The most common serious side effects (which may affect more than 1 in 50 people) include rash, venous thromboembolism (problems due to the formation of blood clots in veins), thrombocytopenia and interstitial lung disease.

When used in combination with lazertinib, the most common side effects with Rybrevant (which may affect more than 1 in 5 people) include rash, nail toxicities, infusion-related reaction, hypoalbuminaemia, hepatotoxicity (liver damage), oedema, stomatitis, venous thromboembolism, paraesthesia (sensations like numbness, tingling, pins and needles), tiredness, constipation, diarrhoea, dry skin, decreased appetite, itching, hypocalcaemia (low blood calcium levels), eye problems and nausea. The most common serious side effects (which may affect more than 1 in 10 people) is venous thromboembolism. Other serious side effects (which may affect up to 1 in 10 people) include pneumonia (infection of the lungs), rash, interstitial lung disease, pneumonitis (inflammation of the lungs), hepatotoxicity, COVID-19, infusion-related reactions and pleural effusion (fluid around the lungs).

Why is Rybrevant authorised in the EU?

Studies showed that Rybrevant can be of benefit to patients with NSCLC who have certain EGFR mutations. Rybrevant represents an additional treatment option for these patients.

Regarding safety, there is a risk of venous thromboembolism with Rybrevant when given with lazertinib, which should be minimised by giving anticoagulants to patients. Other side effects were considered manageable with appropriate measures, such as changing the dose or, for infusion-related reactions, modifying the infusion and treating the symptoms.

The European Medicines Agency therefore decided that Rybrevant's benefits are greater than its risks and it can be authorised for use in the EU.

Rybrevant was originally given 'conditional authorisation'. The authorisation has now been switched to a standard authorisation as the company has provided additional data requested by the Agency.

What measures are being taken to ensure the safe and effective use of Rybrevant?

Recommendations and precautions to be followed by healthcare professionals and patients for the safe and effective use of Rybrevant have been included in the summary of product characteristics and the package leaflet.

As for all medicines, data on the use of Rybrevant are continuously monitored. Suspected side effects reported with Rybrevant are carefully evaluated and any necessary action taken to protect patients.

Other information about Rybrevant

Rybrevant received a conditional marketing authorisation valid throughout the EU on 9 December 2021. The conditional marketing authorisation was switched to a standard marketing authorisation on 27 June 2024.

Further information on Rybrevant can be found on the Agency's website: ema.europa.eu/medicines/human/EPAR/rybrevant.

This overview was last updated in 12-2024.