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Kisplyx (*lenvatinib*)

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

What is Kisplyx and what is it used for?

Kisplyx is a cancer medicine used to treat adults with advanced renal cell carcinoma (a type of kidney cancer). It is used with another cancer medicine, pembrolizumab, when patients have not had previous treatment for their cancer. Kisplyx is also used with the cancer medicine everolimus in patients who have been previously treated with a type of cancer medicine called a vascular endothelial growth factor (VEGF) inhibitor.

Kisplyx contains the active substance lenvatinib.

How is Kisplyx used?

Kisplyx can only be obtained with a prescription and treatment should be started and supervised by a doctor who has experience in using cancer medicines.

Kisplyx is available as capsules to be taken once daily by mouth, and the recommended dose depends on whether it is given with pembrolizumab for initial treatment (20 mg) or with everolimus in previously treated patients (18 mg). The dose of Kisplyx may need to be reduced or treatment stopped temporarily if certain side effects occur. Treatment is given for as long as the patient benefits from it or until side effects become unacceptable. The dose of Kisplyx should be decreased in patients with severely reduced kidney or liver function.

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

How does Kisplyx work?

The active substance in Kisplyx, lenvatinib, is a tyrosine-kinase inhibitor. This means that it blocks the activity of enzymes known as tyrosine kinases. These enzymes can be found in certain receptors (such as VEGF, FGFR, PDGF, KIT and RET receptors) in cancer cells, where they activate several processes including cell division and the growth of new blood vessels. By blocking these enzymes, lenvatinib can block the formation of new blood vessels, cutting off the blood supply that keeps cancer cells growing, and reduce the growth of the cancer. Lenvatinib may also alter the activity of the immune system (the

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body's natural defences).

What benefits of Kisplyx have been shown in studies?

With pembrolizumab for initial treatment

Kisplyx given with pembrolizumab was shown to be of benefit in a main study involving 1,069 patients who had advanced renal cell carcinoma that had not been previously treated. The combination was compared with treatment using sunitinib, another cancer medicine. Patients given Kisplyx and pembrolizumab lived on average around 24 months without their cancer getting worse (progression-free survival), compared with around 9 months in those given sunitinib.

With everolimus in previously treated patients

Kisplyx has been investigated in one main study involving 153 adults with advanced renal cell carcinoma that had got worse despite treatment with a VEGF inhibitor. The study compared the combination of Kisplyx and everolimus with Kisplyx or everolimus alone. Patients who took the combination of Kisplyx and everolimus lived for an average of 14.6 months without their disease getting worse, compared with 7.4 months for the patients who took Kisplyx alone and 5.5 months for the patients who took everolimus alone.

What are the risks associated with Kisplyx?

The most common side effects of Kisplyx when used with pembrolizumab (which may affect more than 1 in 3 people) are diarrhoea, high blood pressure, tiredness, hypothyroidism (reduced thyroid-gland function), loss of appetite, nausea (feeling sick), stomatitis (inflammation of the lining of the mouth), proteinuria (protein in the urine, a sign of kidney problems), dysphonia (hoarse voice) and arthralgia (joint pain). When used in combination with everolimus the most common side effects reported also include weight loss, vomiting, headache, palmar-plantar erythrodysaesthesia syndrome (hand-foot syndrome, which involves rash and numbness on the palms and soles), peripheral oedema (swelling, especially of the ankles and feet) and hypercholesterolemia (high levels of cholesterol [type of fat] in the blood).

The most common serious side effects when used with pembrolizumab include high blood pressure, raised levels of the enzymes lipase and amylase (a sign of problems with the pancreas), diarrhoea, proteinuria, weight loss and tiredness; other serious effects, that led to treatment having to be stopped in some patients, included heart attacks and rash.

The most common serious side effects when used with everolimus are kidney failure and reduced kidney function; problems with the heart and circulation such as heart failure and blood clots in the arteries(which can lead to stroke or heart attack); bleeding in the brain or bleeding of a tumour within the skull; a syndrome known as 'posterior reversible encephalopathy syndrome' characterised by headache, confusion, fits and loss of vision; and liver failure.

For the full list of side effects of Kisplyx, see the package leaflet.

Kisplyx must not be taken by breastfeeding women. For the full list of restrictions, see the package leaflet.

Why is Kisplyx authorised in the EU?

For previously untreated patients with advanced renal cell carcinoma, Kisplyx combined with pembrolizumab significantly improved progression-free survival compared with standard treatment

with sunitinib. Patients also lived longer overall with the combination than with sunitinib, though more follow-up is needed to confirm this. Although the side effects of Kisplyx with pembrolizumab were greater than those of sunitinib treatment, this was considered to be outweighed by the benefits.

Previously treated patients with advanced renal cell carcinoma have poor outcomes and a high unmet medical need. Kisplyx, used in combination with everolimus, was again shown to significantly improve progression-free survival. The safety of Kisplyx used in combination with everolimus is similar to that of these medicines when used individually, and side effects are considered manageable.

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

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

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

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

Other information about Kisplyx

Kisplyx received a marketing authorisation valid throughout the EU on 25 August 2016.

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

This overview was last updated in 11-2021.