



Summary of Investigation Results

Drugs With an Inhibitory Effect on Vascular Endothelial Growth Factor (VEGF) Pathway*

February 15, 2024

Non-proprietary name

- a. Axitinib
- b. Aflibercept beta (genetical recombination)
- c. Sunitinib malate
- d. Sorafenib tosilate
- e. Pazopanib hydrochloride
- f. Vandetanib
- g. Ramucirumab (genetical recombination)
- h. Regorafenib hydrate
- i. Lenvatinib mesilate
- j. Cabozantinib malate
- k. Ponatinib hydrochloride
- l. Nintedanib ethanesulfonate

Brand name (marketing authorization holder)

- a. Inlyta Tablets 1 mg, 5 mg (Pfizer Japan Inc.)
- b. Zaltrap 100 mg I.V. Infusion, 200 mg I.V. Infusion (Sanofi K.K.)
- c. Sutent Capsule 12.5 mg (Pfizer Japan Inc.)
- d. Nexavar tablets 200 mg (Bayer Yakuhin, Ltd.)
- e. Votrient Tablets 200 mg (Novartis Pharma K.K.)
- f. Caprelsa Tablets 100 mg (Sanofi K.K.)
- g. Cyramza Intravenous Injection 100 mg, 500 mg (Eli Lilly Japan K.K.)
- h. Stivarga tablets 40 mg (Bayer Yakuhin, Ltd.)

Pharmaceuticals and Medical Devices Agency

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This English version is intended to be a reference material for the convenience of users. In the event of inconsistency between the Japanese original and this English translation, the former shall prevail.

- i. Lenvima Capsules 4 mg, 10 mg (Eisai Co., Ltd.)
- j. Cabometyx tablets 20 mg, 60 mg (Takeda Pharmaceutical Company Limited)
- k. Iclusig tablets 15 mg (Otsuka Pharmaceutical Co., Ltd.)
- l. Ofev Capsules 100 mg, 150 mg (Nippon Boehringer Ingelheim Co., Ltd.)

Japanese market launch

See attachment.

Indications

See attachment.

Summary of revisions

“Artery dissection” should be added to the Clinically Significant Adverse Reactions section in ADVERSE REACTIONS.

Investigation results and background of the revision

Based on the summary of the evaluation of the risk of artery dissection due to systemic exposure to vascular endothelial growth factor (VEGF) or its receptor (VEGFR) inhibitors (hereinafter referred as VEGF/VEGFR inhibitors) (appendix), the pharmacological mechanism of VEGF/VEGFR inhibitors, etc., the PMDA considered that the risk of artery dissection is common to VEGF/VEGFR inhibitors.

As a result of consultation with expert advisors regarding the appropriateness of the above-mentioned PMDA’s opinion and the necessity of taking safety measures for artery dissection, the MHLW/PMDA concluded that revision of PRECAUTIONS was necessary for VEGF/VEGFR inhibitors.

* VEGF or VEGFR inhibitors administered orally or intravenously excluding bevacizumab (genetical recombination)

The expert advisors present at the Expert Discussion regarding the current investigation were nominated based on their conflict of interest declarations concerning the relevant products, pursuant to the “Rules for Convening Expert Discussions, etc.” by the Pharmaceuticals and Medical Devices Agency” (PMDA Administrative Rule No. 20-8, dated December 25, 2008).

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Attachment

Brand name (Marketing authorization holder)	Japanese market launch	Indications
a. Inlyta Tablets 1 mg, 5 mg (Pfizer Japan Inc.)	August 2012	Radically unresectable or metastatic renal cell carcinoma
b. Zaltrap 100 mg I.V. Infusion, 200 mg I.V. Infusion (Sanofi K.K.)	May 2017	Unresectable, advanced or recurrent colorectal cancer
c. Sutent Capsule 12.5 mg (Pfizer Japan Inc.)	June 2008	Imatinib-resistant gastrointestinal stromal tumour Radically unresectable or metastatic renal cell carcinoma Pancreatic neuroendocrine tumour
d. Nexavar tablets 200 mg (Bayer Yakuhin, Ltd.)	April 2008	Radically unresectable or metastatic renal cell carcinoma Unresectable hepatocellular carcinoma Radically unresectable thyroid cancer
e. Votrient Tablets 200 mg (Novartis Pharma K.K.)	November 2012	Malignant soft tissue tumour Radically unresectable or metastatic renal cell carcinoma
f. Caprelsa Tablets 100 mg (Sanofi K.K.)	December 2015	Radically unresectable medullary thyroid cancer
g. Cyramza Intravenous Injection 100 mg, 500 mg (Eli Lilly Japan K.K.)	June 2015	Unresectable, advanced or recurrent gastric cancer Unresectable, advanced or recurrent colorectal cancer Unresectable, advanced or recurrent non-small cell lung cancer Unresectable hepatocellular carcinoma with serum AFP greater than 400 ng/mL that has progressed after cancer chemotherapy
h. Stivarga tablets 40 mg (Bayer Yakuhin, Ltd.)	May 2013	Unresectable, advanced or recurrent colorectal cancer Gastrointestinal stromal tumour that has progressed after cancer chemotherapy Unresectable hepatocellular carcinoma that has progressed after cancer chemotherapy.
i. Lenvima Capsules 4 mg, 10 mg (Eisai Co., Ltd.)	May 2015	<Lenvima Capsules 4 mg> Radically unresectable thyroid cancer, unresectable hepatocellular carcinoma, unresectable thymic carcinoma, unresectable, advanced or recurrent endometrial cancer that has progressed after cancer chemotherapy, radically unresectable or metastatic renal cell carcinoma <Lenvima Capsules 10 mg> Radically unresectable thyroid cancer, unresectable thymic carcinoma, unresectable, advanced or recurrent endometrial cancer that has progressed after cancer chemotherapy, radically unresectable or metastatic renal cell carcinoma
j. Cabometyx tablets 20 mg, 60 mg (Takeda Pharmaceutical Company Limited)	May 2020	Radically unresectable or metastatic renal cell carcinoma Unresectable hepatocellular carcinoma that has progressed after cancer chemotherapy
k. Iclusig tablets 15 mg (Otsuka Pharmaceutical Co., Ltd.)	November 2016	Chronic myeloid leukaemia with resistance or intolerance to prior drug therapies Relapsed or refractory Philadelphia positive acute lymphocytic leukaemia

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I. Ofev Capsules 100 mg, 150 mg (Nippon Boehringer Ingelheim Co., Ltd.)	August 2015	Idiopathic pulmonary fibrosis Systemic scleroderma-associated interstitial lung disease Progressive fibrosing interstitial lung disease
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