Summary of Investigation Results

Dabrafenib mesilate
Trametinib dimethyl sulfoxide

March 5, 2025

Non-proprietary name

a. Dabrafenib mesilate

b. Trametinib dimethyl sulfoxide

Brand name (marketing authorization holder)

a. Tafinlar Capsules 50 mg, 75 mg, Tafinlar Dispersible tablets for Pediatric 10 mg (Novartis Pharma K.K.)

b. Mekinist Tablets 0.5 mg, 2 mg, Mekinist Dry syrup for Pediatric 4.7mg (Novartis Pharma K.K.)

Japanese market launch

See attachment.

Indications

See attachment.

Summary of revisions

1. Precautions for neutropenia and leukopenia should be added to 8. IMPORTANT PRECAUTIONS.
2. “Neutropenia” and “leukopenia” should be added to the 11.1 Clinically Significant Adverse Reactions section in 11. ADVERSE REACTIONS.

Investigation results and background of the revision

While neutropenia and leukopenia are currently included in the 11.2 Other Adverse Reactions section in 11. ADVERSE REACTIONS, cases involving neutropenia and/or leukopenia were

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reevaluated. Serious cases for which a causal relationship of neutropenia and/or leukopenia to dabrafenib mesilate or trametinib dimethyl sulfoxide was reasonably possible have been reported. As a result of consultation with expert advisors regarding the causality assessment of the cases and the necessity of revision of PRECAUTIONS, the MHLW/PMDA concluded that revision of PRECAUTIONS was necessary.

Reference: Number of cases* and patient mortalities involving neutropenia reported in Japan

a.

A total of 24 cases have been reported to date (including 17 cases for which a causal relationship between the drug and the event was reasonably possible).

No patient mortalities have been reported to date.

b.

A total of 25 cases have been reported to date. (A causal relationship between the drug and the event was reasonably possible for 18 cases, including 1 case in which the drug was administered outside the approved indications.)

No patient mortalities have been reported to date.

Reference: Number of cases* and patient mortalities involving leukopenia reported in Japan

a.

A total of 8 cases have been reported to date (including 4 cases for which a causal relationship between the drug and the event was reasonably possible).

No patient mortalities have been reported to date.

b.

A total of 8 cases have been reported to date (including 4 cases for which a causal relationship between the drug and the event was reasonably possible).

No patient mortalities have been reported to date.

* Cases classified as grade 3 or higher according to Common Terminology Criteria for Adverse Events (CTCAE) version 5.0, among those collected in the PMDA's database for adverse drug reactions, etc. reports

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.

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

No.	Non-proprietary name	Brand name	Japanese market launch	Indications
a.	Dabrafenib mesilate	Tafinlar Capsules 50 mg Tafinlar Capsules 75 mg	June 2016	•BRAF mutation-positive malignant melanoma •Unresectable, advanced or recurrent BRAF mutation-positive non-small-cell lung cancer •Advanced or recurrent BRAF mutation-positive solid tumour (excluding colon/rectal cancer) that is refractory or intolerant to standard therapies •Relapsed or refractory BRAF mutation-positive hairy cell leukaemia •BRAF mutation-positive low-grade glioma
		Tafinlar Dispersible tablets for Pediatric 10 mg	November, 2024	•Advanced or recurrent BRAF mutation-positive solid tumour (excluding colon/rectal cancer) that is refractory or intolerant to standard therapies •BRAF mutation-positive low-grade glioma
b.	Trametinib dimethyl sulfoxide	Mekinist Tablets 0.5 mg Mekinist Tablets 2 mg	June 2016	•BRAF mutation-positive malignant melanoma •Unresectable, advanced or recurrent BRAF mutation-positive non-small-cell lung cancer. •Advanced or recurrent BRAF mutation-positive solid tumour (excluding colon/rectal cancer) that is refractory or intolerant to standard therapies •Relapsed or refractory BRAF mutation-positive hairy cell leukaemia •BRAF mutation-positive low-grade glioma
		Mekinist Dry syrup for Pediatric 4.7mg	November, 2024	•Advanced or recurrent BRAF mutation-positive solid tumour (excluding colon/rectal cancer) that is refractory or intolerant to standard therapies •BRAF mutation-positive low-grade glioma

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