独立行政法人 医薬品医療機器総合機構
Pharmaceuticals and Medical Devices Agency

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Summary of Investigation Results

Nivolumab (genetical recombination)
Ipilimumab (genetical recombination)

September 9, 2025

Non-proprietary name

a. Nivolumab (genetical recombination)

b. Ipilimumab (genetical recombination)

Brand name (marketing authorization holder)

a. Opdivo I.V. Infusion 20 mg, 100 mg, 120 mg, 240 mg (Ono Pharmaceutical Co., Ltd.)

b. Yervoy Injection 20 mg, 50 mg (Bristol-Myers Squibb K.K.)

Japanese market launch

a. Opdivo I.V. Infusion 20 mg, 100 mg: September 2014
   Opdivo I.V. Infusion 120 mg: November 2020
   Opdivo I.V. Infusion 240 mg: November 2018

b. Yervoy Injection 20 mg: November 2021
   Yervoy Injection 50 mg: August 2015

Indications

a.

•Malignant melanoma

•Unresectable, advanced or recurrent non-small cell lung cancer

•Neoadjuvant therapy for non-small cell lung cancer

•Radically unresectable or metastatic renal cell carcinoma

•Relapsed or refractory classical Hodgkin lymphoma

•Recurrent or metastatic head and neck cancer

•Unresectable, advanced or recurrent gastric cancer

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•Unresectable, advanced or recurrent malignant pleural mesothelioma
•Malignant mesothelioma (excluding malignant pleural mesothelioma)
•Unresectable, advanced or recurrent microsatellite instability-high (MSI-High) colorectal cancer
•Radically unresectable, advanced or recurrent oesophageal carcinoma
•Postoperative adjuvant therapy for oesophageal carcinoma
•Carcinoma of unknown primary
•Postoperative adjuvant therapy for urothelial carcinoma
•Radically unresectable urothelial carcinoma
•Radically unresectable, advanced or recurrent epithelial skin malignancies
•Unresectable hepatocellular carcinoma

b.

•Radically unresectable malignant melanoma
•Radically unresectable or metastatic renal cell carcinoma
•Unresectable, advanced or recurrent microsatellite instability high (MSI-High) colorectal cancer
•Unresectable, advanced or recurrent non-small cell lung cancer
•Unresectable, advanced or recurrent malignant pleural mesothelioma
•Radically unresectable advanced or recurrent oesophageal carcinoma
•Unresectable hepatocellular carcinoma

Summary of revisions

1. A statement regarding tumour lysis syndrome should be added to 8. IMPORTANT PRECAUTIONS.
2. “Tumour lysis syndrome” should be added to the 11.1 Clinically Significant Adverse Reactions section in 11. ADVERSE REACTIONS.

Investigation results and background of the revision

Cases involving tumour lysis syndrome were evaluated. Cases in which a causal relationship of tumour lysis syndrome to nivolumab (genetical recombination) or Ipilimumab (genetical recombination) 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 tumour lysis syndrome reported in Japan and overseas

a.

A total of 14 cases have been reported in Japan to date (including 4 cases in which a causal relationship between the drug and the event was reasonably possible).

A total of 4 patient mortalities have been reported in Japan to date. (A causal relationship between the drug and the death following the event could not be established for any of these cases.)

A total of 11 cases have been reported overseas to date. (A causal relationship between the drug and the event was reasonably possible for 4 cases, in which the drug was administered outside the approved indications.)

A total of 2 patient mortalities have been reported overseas to date. (A causal relationship between the drug and the death following the event could not be established for any of these cases.)

b.

A total of 10 cases have been reported in Japan to date (including 3 cases in which a causal relationship between the drug and the event was reasonably possible).

One instance of patient mortality has been reported in Japan to date. (A causal relationship between the drug and the death following the event could not be established for this case.)

A total of 5 cases have been reported overseas to date. (A causal relationship between the drug and the event was reasonably possible for 2 cases, including 1 case in which the drug was administered outside the approved indications.)

A total of 3 patient mortalities have been reported overseas to date. (A causal relationship between the drug and the death following the event could not be established for any of these cases.)

*Among the cases collected in the PMDA's safety database for drugs, those for which blood test results for 2 or more of the following items (uric acid, potassium, phosphorus, and

calcium) were documented in the case report forms were retrieved.

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).