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.

Summary of Investigation Results

Nivolumab (genetical recombination)
Ipilimumab (genetical recombination)

July 17, 2024

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 240 mg: November 2018
   Opdivo I.V. Infusion 120 mg: November 2020

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

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

•Unresectable, advanced or recurrent malignant pleural mesothelioma

•Malignant mesothelioma (excluding malignant pleural mesothelioma)
•Unresectable, advanced or recurrent microsatellite instability-high (MSI-High) colorectal cancer that has progressed after chemotherapy
•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, advanced or recurrent malignant epithelial tumor

b.

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

Summary of revisions

"Myelitis" 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 myelitis were evaluated. Cases for which a causal relationship between myelitis and 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 myelitis reported in Japan and overseas

a.

A total of 4 cases have been reported in Japan to date (including 1 case for which a causal

relationship between the drug and event was reasonably possible).
No patient mortalities have been reported in Japan to date.
b.
A total of 2 cases have been reported in Japan to date (including 1 case for which a causal relationship between the drug and event was reasonably possible).
No patient mortalities have been reported in Japan to date.

a.
A total of 26 cases have been reported overseas to date (including 16 cases for which a causal relationship between the drug and event was reasonably possible).
No patient mortalities have been reported overseas to date.
b.
A total of 14 cases have been reported overseas to date (including 10 cases for which a causal relationship between the drug and event was reasonably possible).
One instance of patient mortality has been reported overseas to date. (A causal relationship between the drug and death subsequent to the event could not be established for this case.)

*Cases for which information on cerebrospinal fluid tests, blood cultures, or PCR testing, in addition to information on the results of spinal MRI examinations, is available within the case report form among those collected in the PMDA's database for adverse drug reactions, etc. report

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).