



Summary of Investigation Results

Nivolumab (genetical recombination)

Ipilimumab (genetical recombination)

June 13, 2023

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

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.

- Unresectable, advanced or recurrent 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

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

“Meningitis” should be added to the Clinically Significant Adverse Reactions section.

Investigation results and background of the revision

Cases involving meningitis reported in Japan were evaluated. Cases for which a causal relationship between nivolumab (genetical recombination) or ipilimumab (genetical recombination) and meningitis 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 meningitis reported in Japan

- a. A total of 27 cases have been reported to date (including 21 cases for which a causal relationship between the drug and event was reasonably possible).
No patient mortalities have been reported to date.



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b. A total of 21 cases have been reported to date (including 16 cases for which a causal relationship between the drug and event was reasonably possible).

No patient mortalities have been reported to date.

*: Cases collected in the PMDA's database for adverse drug reactions, etc. reports

†: Cases retrieved by the following conditions

- Retrieved by MedDRA ver. 25.1 PT “meningitis” and “aseptic meningitis”
- Cases in which a spinal fluid test has been performed and the results of the test are referred to.

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).