This English version is intended to be a reference material to provide convenience for 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)
Pembrolizumab (genetical recombination)

October 12, 2022

Non-proprietary name

a. Nivolumab (genetical recombination)

b. Ipilimumab (genetical recombination)

c. Pembrolizumab (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.)

c. Keytruda Injection 100 mg (MSD K.K.)

Indications

a.

·Malignant melanoma

·Unresectable, advanced or recurrent 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

·Unresectable, advanced or recurrent microsatellite instability-high (MSI-High) colorectal cancer that has progressed after chemotherapy

·Radically unresectable, advanced or recurrent esophageal cancer

·Postoperative adjuvant therapy for esophageal cancer

·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 esophageal cancer
c.
·Malignant melanoma
·Unresectable, advanced or recurrent non-small cell lung cancer
·Relapsed or refractory classical Hodgkin lymphoma
·Radically unresectable urothelial carcinoma that has progressed after cancer chemotherapy
·Advanced or recurrent microsatellite instability-high (MSI-High) solid tumours that have progressed after cancer chemotherapy (limited to patients who are refractory or intolerant to standard treatments)
·Radically unresectable or metastatic renal cell carcinoma
·Postoperative adjuvant therapy for renal cell carcinoma
·Recurrent or metastatic head and neck cancer
·Radically unresectable advanced or recurrent esophageal cancer
·Unresectable, advanced or recurrent microsatellite instability-high (MSI-High) colorectal cancer
·PD-L1-positive, hormone receptor-negative and HER2-negative inoperable or recurrent breast cancer
·Pre- and postoperative adjuvant therapy for hormone receptor-negative and HER2-negative breast cancer at high risk of recurrence
·Unresectable, advanced or recurrent endometrial carcinoma that has progressed after cancer chemotherapy

·Advanced or recurrent, tumour mutational burden-high (TMB-High) solid tumours that have progressed after cancer chemotherapy (limited to patients who are refractory or intolerant to standard treatments)
·Advanced or recurrent cervical cancer

Summary of revisions

1. a., b. A statement should be added to the IMPORTANT PRECAUTIONS section as follows: "Uveitis may occur. Whether ocular abnormalities have occurred should be examined periodically. In addition, patients should be instructed to immediately seek medical attention if any ocular abnormalities are observed."
2. a., b., c. “Uveitis” should be added to the Clinically Significant Adverse Reactions section.

Investigation results and background of the revision

Cases involving uveitis of grade 3 or higher by Common Terminology Criteria for Adverse Events (CTCAE) reported in Japan were evaluated. Cases for which a causal relationship between uveitis and nivolumab (genetical recombination), ipilimumab (genetical recombination), or pembrolizumab (genetical recombination) was reasonably possible have been reported in Japan. As a result of consultation with expert advisors, MHLW/PMDA concluded that revision of Precautions was necessary.

Number of cases and patient mortalities involving uveitis reported in Japan during the previous 3 fiscal years

a.

A total of 19 cases have been reported to date (including 11 cases for which a causal relationship between the drug and event was reasonably possible).
No patient mortalities have been reported to date.

b.

A total of 10 cases have been reported to date (including 7 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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c.

A total of 4 cases have been reported to date (including 1 case for which a causal relationship between the drug and event was reasonably possible).

No patient mortalities have been reported to date.

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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