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), pembrolizumab (genetical recombination)

June 14, 2022

Non-proprietary name

a. Nivolumab (genetical recombination)

b. 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. 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

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b.
·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
·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
·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)

Summary of revisions
“Severe gastritis” should be added to the Clinically Significant Adverse Reactions section.

Investigation results and background of the revision
Cases of severe gastritis reported in Japan were evaluated. Cases for which a causal relationship of severe gastritis to nivolumab (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. Also, since it is considered that gastritis observed this time is caused by immune reactions, as a result of consultation with expert advisors, MHLW/PMDA

concluded that making a precautionary statement regarding the treatment after the onset of gastritis was necessary as well.

Number of cases and patient mortalities of severe gastritis reported in Japan during the previous 3 fiscal years

a.

A total of 11 cases involving severe gastritis have been reported to date (including 3 cases for which a causal relationship between the drug and the event was reasonably possible).
1 instance of patient mortality has been reported to date (A causal relationship between the drug and the event could not be established for this case).

b.

A total of 12 cases involving severe gastritis have been reported to date (including 3 cases for which a causal relationship between the drug and the 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).