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

Anti-PD-1 antibody drugs

July 9, 2019

Non-proprietary name

a. Nivolumab (genetical recombination)

b. Pembrolizumab (genetical recombination)

Branded name (Marketing authorization holder)

a. Opdivo Intravenous Infusion 20 mg, 100 mg, 240 mg (Ono Pharmaceutical Co.,Ltd.)

b. Keytruda Injection 20 mg, 100 mg (MSD K.K.)

Indications

a.

Malignant melanoma

Unresectable advanced or recurrent non-small cell lung cancer

Unresectable or metastatic renal cell carcinoma

Relapsed or refractory classical Hodgkin lymphoma

Relapsed or metastatic head and neck cancer

Unresectable, advanced or recurrent gastric cancer that has progressed after cancer chemotherapy

Unresectable, advanced or recurrent malignant pleural mesothelioma that has progressed after cancer chemotherapy

b.

Malignant melanoma

Unresectable advanced or recurrent non-small cell lung cancer

Relapsed or refractory classical Hodgkin lymphoma

Unresectable urothelial carcinoma exhibiting progression after chemotherapy

Advanced or recurrent, microsatellite instability-high (MSI-H) solid tumours exhibiting

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progression after chemotherapy (only when management cannot be achieved with standard therapies)

Summary of revisions

"Colitis, severe diarrhea" in the Clinically Significant Adverse Reactions section should be replaced with "colitis, enteritis, severe diarrhea" and language concerning reported cases of enterocolitis that resulted in perforation or ileus should be added.

Investigation results and background of the revision

Cases of enterocolitis that resulted in perforation or ileus, and cases of enteritis have been reported in patients treated with anti PD-1 antibody drugs in Japan. MHLW/PMDA concluded that revision of the package insert was necessary based on the results of their investigation of the currently available evidence and in consultation with expert advisors.

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

Enteritis

a. A total of 7 cases have been reported to date (including 5 cases for which a causal relationship between the drug and event could not be ruled out). 2 instances of patient mortalities have been reported to date (including 1 instance for which a causal relationship between the drug and the death subsequent to event could not be ruled out).
b. A total of 3 cases have been reported to date (including 2 cases for which a causal relationship between the drug and event could not be ruled out). No patient mortalities have been reported to date.

Intestinal perforation

a. A total of 18 cases have been reported to date (including 4 cases for which a causal relationship between the drug and event could not be ruled out). 3 instances of patient mortality have been reported to date (a causal relationship between the drug and the death subsequent to event could not be established in any of these instances.)
b. A total of 17 cases have been reported to date (including 4 cases for which a causal relationship between the drug and event could not be ruled out). 4 instances of patient mortality have been reported to date (a causal relationship between the drug and the death subsequent to event could not be established in any of these instances).

Ileus

a. A total of 21 cases have been reported to date (including 1 case for which a causal relationship between the drug and event could not be ruled out). No patient mortalities have been reported to date.
b. A total of 14 cases have been reported to date (including 1 case for which a causal relationship between the drug and event could not be ruled out). No patient mortalities have been reported to date.

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