Summary of investigation results

Nivolumab (genetical recombination)

October 18, 2016

Non-proprietary name

Nivolumab (genetical recombination)

Brand name (Marketing authorization holder)

Opdivo Intravenous Infusions 20 mg, 100 mg (Ono Pharmaceutical Co., Ltd.)

Indications

Radically unresectable malignant melanoma
Unresectable, advanced, or relapsed non-small cell lung cancer
Radically unresectable or metastatic renal cell carcinoma

Summary of revision

1. Precautions related to “adverse reactions after discontinuation of treatment” should be added to the description with regard to “excessive immunoreaction” in the Important Precautions section.
2. “Immune thrombocytopenic purpura” should be newly added in the Clinically Significant Adverse Reactions section.
3. “Myocarditis, rhabdomyolysis” should be added in the Clinically Significant Adverse Reactions section with regard to “Myasthenia gravis, myositis.”

Background of the revision and investigation results

1. With regard to adverse reactions after discontinuation of treatment with the product, cases have been reported in Japan, and the company core datasheet (CCDS)* and foreign package inserts include descriptions about such adverse reactions. Following an investigation result based on the opinions of expert advisors and the available evidence, the MHLW/PMDA concluded that revision of the package insert was necessary.

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2. Cases of immune thrombocytopenic purpura have been reported in Japan. Following an investigation result based on the opinions of expert advisors and the available evidence, the MHLW/PMDA concluded that revision of the package insert was necessary.
3. Based on the accumulated data on Japanese and foreign cases of myocarditis or rhabdomyolysis, the CCDS* has been updated. Following an investigation result based on the opinions of expert advisors and the available evidence, the MHLW/PMDA concluded that revision of the package insert was necessary.

The number of reported adverse reactions and fatal cases in the last 3 fiscal years in Japan

1. A total of 50 cases associated with adverse reactions after discontinuation of treatment † has been reported (including 14 cases for which a causal relationship to the product could not be ruled out). A total of 5 fatal cases have been reported (including no cases for which a causal relationship to the product could not be ruled out).
2. A total of 5 cases associated with immune thrombocytopenic purpura has been reported (including 3 cases for which a causal relationship to the product could not be ruled out). One fatal case has been reported (including no case for which a causal relationship to the product could not be ruled out).
3. A total of 6 cases associated with myocarditis has been reported (including 3 cases for which a causal relationship to the product could not be ruled out). One fatal case has been reported (including 1 case for which a causal relationship to the product could not be ruled out).
   A total of 4 cases associated with rhabdomyolysis has been reported (including 4 cases for which a causal relationship to the product could not be ruled out). No fatality has been reported.

NOTE:

* CCDS is prepared by the marketing authorization holder and covers materials relating to safety, indications, dosing, pharmacology, and other information concerning the product.

† Reported cases of adverse reactions that occurred at least 31 days after the final dose of the product (excluding adverse reactions that were “death” or “malignant neoplasm progression” or that occurred after treatment with other antineoplastic agents in patients who received other antineoplastic agents after discontinuation of treatment with nivolumab)

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