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)

September 15, 2015

Non-proprietary name

Nivolumab (genetical recombination)

Brand name (Marketing authorization holder)

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

Indications

Radically unresectable malignant melanoma

Summary of revision

1. Precautions regarding occurrence of adverse reaction due to the excessive immunoreaction after administration of nivolumab should be newly added in the Important Precautions section.
2. “Myasthenia gravis and myositis” should be newly added in the Clinically significant adverse reactions section.
3. “Colitis and severe diarrhoea” should be newly added in the Clinically significant adverse reactions section.

Background of the revision and investigation results

- Myasthenia gravis and myositis

  Cases of myasthenia gravis and myositis have been reported in patients treated with nivolumab in Japan. In addition, (1) cases of complications with myasthenia gravis and myositis have been reported, and (2) cases of rapid progression of respiratory failure due to myasthenia gravis crisis have been reported. 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.

Pharmaceuticals and Medical Devices Agency
Office of Safety I
3-3-2 Kasumigaseki, Chiyoda-ku, Tokyo 100-0013 Japan
E-mail: safety.info@pmda.go.jp

- Colitis and severe diarrhoea

  Cases of colitis and severe diarrhoea have been reported in patients treated with nivolumab 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.

- Adverse reaction due to excessive immunoreaction

  (1) Due to the T cell activation effect of this drug, various diseases or conditions caused by excessive immunoreaction are expected to occur, (2) cases of adverse reaction due to the excessive immunoreaction have been reported in patients treated with nivolumab in Japan, and (3) the company core datasheet (CCDS)* and package inserts overseas include precautions regarding adverse reaction due to the immunological mechanism of this drug. 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 and 2.

A total of 6 cases associated with myasthenia gravis or myositis have been reported (including 6 cases for which a causal relationship to the product could not be ruled out). Of the 6 cases, 1 fatal case has been reported (a causal relationship between the product and the fatal outcome could not be ruled out for this patient).

1 and 3.

A total of 5 cases associated with colitis or severe diarrhoea have been reported (including 4 cases for which a causal relationship to the product could not be ruled out). Of the 5 cases, 1 fatal case has been reported (a causal relationship between the product and the fatal outcome could not be established for this patient).

NOTE:

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