August 25, 2026
Pharmaceuticals and Medical Devices Agency, Japan

Summary of Investigation Results

Nivolumab (genetical recombination) and Ipilimumab (genetical recombination)

Non-proprietary name Brand name	Non-proprietary name	Brand name (marketing authorization holder)
	a. Nivolumab (genetical recombination) b. Ipilimumab (genetical recombination)	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.)
Japanese market launch	a. Opdivo I.V. Infusion 20 mg, 100 mg: September 2014 Opdivo I.V. Infusion 120 mg: November 2020 Opdivo I.V. Infusion 240 mg: November 2018 b. Yervoy Injection 20 mg: November 2021 Yervoy Injection 50 mg: August 2015	
Indications	a. ○ Malignant melanoma ○ Unresectable, advanced or recurrent non-small cell lung cancer ○ Neoadjuvant therapy for 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 ○ Malignant mesothelioma (excluding malignant pleural mesothelioma) ○ Unresectable, advanced or recurrent microsatellite instability-high (MSI-High) colorectal cancer ○ Radically unresectable, advanced or recurrent oesophageal carcinoma ○ Postoperative adjuvant therapy for oesophageal carcinoma ○ Carcinoma of unknown primary ○ Postoperative adjuvant therapy for urothelial carcinoma ○ Radically unresectable urothelial carcinoma ○ Radically unresectable, advanced or recurrent epithelial skin malignancies ○ Unresectable hepatocellular carcinoma b.	

	○ Radically unresectable malignant melanoma ○ Radically unresectable or metastatic renal cell carcinoma ○ Unresectable, advanced or recurrent microsatellite instability-high (MSI-High) colorectal cancer ○ Unresectable, advanced or recurrent non-small cell lung cancer ○ Unresectable, advanced or recurrent malignant pleural mesothelioma ○ Radically unresectable, advanced or recurrent oesophageal carcinoma ○ Unresectable hepatocellular carcinoma
Summary of revisions	"Severe oesophagitis" should be added to the 11.1 Clinically Significant Adverse Reactions section in 11. ADVERSE REACTIONS.
Investigation results and background of the revision	Cases involving oesophagitis were evaluated. Cases in which a causal relationship between nivolumab (genetical recombination) or ipilimumab (genetical recombination) and severe oesophagitis was reasonably possible have been reported. As a result of consultation with expert advisors regarding the causality assessment of the cases and the necessity of revision of PRECAUTIONS, the MHLW/PMDA concluded that revision of PRECAUTIONS was necessary.
Reference: Number of cases*1 involving oesophagitis*2 reported in Japan	a. A total of 15 cases have been reported to date (including 6 cases in which a causal relationship between the drug and the event was reasonably possible). A total of 1 death has been reported to date (including 0 cases in which a causal relationship between the drug and the death following the event was reasonably possible). b. A total of 8 cases have been reported to date (including 3 cases in which a causal relationship between the drug and the event was reasonably possible). A total of 1 death has been reported to date (including 0 cases in which a causal relationship between the drug and the death following the event was reasonably possible).

*1: Cases collected in PMDA's safety database for drugs.
*2: Among cases that fell under MedDRA ver. 28.1 PTs "Oesophagitis," "Oesophageal disorder," "Oesophageal ulcer," "Immune-mediated oesophagitis," "Oesophagitis ulcerative," and "Necrotising oesophagitis", cases assessed as Grade 3 or higher according to CTCAE ver. 6.0 were retrieved.

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).