August 25, 2026
Pharmaceuticals and Medical Devices Agency, Japan

Summary of Investigation Results

Anti-PD-1 antibody drugs, anti-PD-L1 antibody drugs, and anti-CTLA-4 antibody drugs [*1]

Non-proprietary name Brand name	Non-proprietary name	Brand name (marketing authorization holder)
	a. Tislelizumab (genetical recombination) b. Retifanlimab (genetical recombination) c. Avelumab (genetical recombination) d. Durvalumab (genetical recombination) e. Ipilimumab (genetical recombination) f. Tremelimumab (genetical recombination)	a. Tevimbra I.V. Infusion 100 mg (BeOne Medicines Japan) b. Zynyz for Intravenous Infusion 500 mg (Incyte Biosciences Japan G.K.) c. Bavencio intravenous infusion 200 mg (Merck Biopharma Co., Ltd) d. Imfinzi Injection 120 mg, 500 mg (AstraZeneca K.K.) e. Yervoy Injection 20 mg, 50 mg (Bristol-Myers Squibb K.K.) f. Imjudo Injection 25 mg, 300 mg (AstraZeneca K.K.)
Japanese market launch	See Attachment.	
Indications	See Attachment.	
Summary of revisions	"Haemophagocytic lymphohistiocytosis" should be added to the 11.1 Clinically Significant Adverse Reactions section in 11. ADVERSE REACTIONS.	
Investigation results and background of the revision	Japanese cases of haemophagocytic lymphohistiocytosis were evaluated. Cases in which a causal relationship between anti-PD-1 antibody drugs, anti-PD-L1 antibody drugs, and anti-CTLA-4 antibody drugs and haemophagocytic lymphohistiocytosis 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[*2] involving haemophagocytic lymphohistiocytosis reported in Japan	a. A total of 0 cases have been reported to date b. A total of 0 cases have been reported to date c. A total of 0 cases have been reported to date d. A total of 21 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 2 deaths have been reported to date (including 0 cases in which a causal relationship between the drug and the death following the event was reasonably possible). e. A total of 3 cases[*3] have been reported to date (including 2 cases in which a causal relationship between the drug and the event was reasonably possible). No deaths have been reported to date. f. A total of 15 cases[*4] have been reported to date (including 1 case in which a causal relationship between the drug and the event was reasonably possible). A total of 2 deaths have 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: Excluding nivolumab (genetical recombination), pembrolizumab (genetical recombination), atezolizumab (genetical recombination), and cemiplimab (genetical recombination)
*2: Cases collected in PMDA's safety database for drugs.
*3: Cases excluding those for which nivolumab (genetical recombination) was co-administered.
*4: Durvalumab (genetical recombination) was co-administered in all the cases

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).

Attachment

Brand name (Marketing authorization holder)	**Japanese market launch**	**Indications**
a. Tevimbra I.V. Infusion 100 mg (BeOne Medicines Japan)	July 2025	○ Radically unresectable, advanced or recurrent oesophageal carcinoma ○ Unresectable, advanced or recurrent gastric cancer
b. Zynyz for Intravenous Infusion 500 mg (Incyte Biosciences Japan G.K.)	March 2026	Unresectable advanced or recurrent squamous cell carcinoma of the anal canal
c. Bavencio intravenous infusion 200 mg (Merck Biopharma Co., Ltd)	November 2017	○ Radically unresectable Merkel cell carcinoma ○ Radically unresectable or metastatic renal cell carcinoma ○ Maintenance treatment of radically unresectable urothelial carcinoma following chemotherapy
d. Imfinzi Injection 120 mg, 500 mg (AstraZeneca K.K.)	August 2018	○ Maintenance treatment of locally-advanced, unresectable non-small cell lung cancer following definitive chemoradiotherapy ○ Unresectable, advanced or recurrent non-small cell lung cancer ○ Preoperative and postoperative adjuvant treatment for non-small cell lung cancer ○ Extensive stage small cell lung cancer ○ Maintenance treatment of limited-stage small cell lung cancer following definitive chemoradiation therapy ○ Unresectable hepatocellular carcinoma ○ Unresectable biliary tract cancer ○ Advanced or recurrent endometrial cancer ○ Preoperative and postoperative adjuvant treatment for bladder cancer ○ High-risk non-muscle-invasive bladder cancer ○ Preoperative and postoperative adjuvant treatment for gastric cancer
e. Yervoy Injection 20 mg Yervoy Injection 50 mg (Bristol-Myers Squibb K.K.)	November 2021 August 2015	○ 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
f. Imjudo Injection 25 mg, 300 mg (AstraZeneca K.K.)	March 2023	< Imjudo Injection 25 mg > ○ Unresectable, advanced or recurrent non-small cell lung cancer ○ Unresectable hepatocellular carcinoma < Imjudo Injection 300 mg > ○ Unresectable hepatocellular carcinoma