## US FDA approves Keytruda & Keytruda Qlex plus paclitaxel ± bevacizumab for certain adults with PD-L1+ (CPS =1) platinum-resistant ovarian carcinoma as second or third line treatment

Merck, known as MSD outside of the United States and Canada, today announced the US Food and Drug Administration (FDA) approved Keytruda (pembrolizumab) and Keytruda Qlex (pembrolizumab and berahyaluronidase alfa-pmph) plus paclitaxel, with or without bevacizumab, for the treatment of adults with PD-L1+ (Combined Positive Score [CPS] =1), as determined by an FDA-authorized test, platinum-resistant epithelial ovarian, fallopian tube or primary peritoneal carcinoma, who have received one or two prior systemic treatment regimens.

These approvals are based on data from the phase 3 KEYNOTE-B96 trial (also known as ENGOT-ov65), which were presented at the 2025 European Society for Medical Oncology (ESMO) Congress. Results from the trial showed that Keytruda plus paclitaxel, with or without bevacizumab, demonstrated a statistically significant improvement in progression-free survival (PFS), reducing the risk of disease progression or death by 28% (HR=0.72 [95% CI, 0.58-0.89]; p=0.0014) in patients with platinum-resistant recurrent ovarian cancer whose tumours express PD-L1 (CPS =1) when compared to placebo plus paclitaxel with or without bevacizumab. In this same population, the Keytruda regimen also demonstrated a statistically significant improvement in overall survival (OS), reducing the risk of death by 24% (HR=0.76 [95% CI, 0.61-0.94]; p=0.0053) compared to placebo plus paclitaxel with or without bevacizumab. The effectiveness of Keytruda Qlex for its approved indications has been established based upon evidence from the adequate and well-controlled studies conducted with Keytruda and additional data from MK-3475A-D77 comparing the pharmacokinetic, efficacy, and safety profiles of Keytruda Qlex and Keytruda.

“For many patients with ovarian cancer, the disease can become platinum-resistant, at which point recurrence is not just a setback — it’s when options can become limited, and the reality patients face can change very quickly,” said Dr. Bradley Monk, gynaecologic oncologist and medical director of the Late-Stage Clinical Research Program at Florida Cancer Specialists and Research Institute. “For patients who have been previously treated with standard platinum-based therapies, the FDA approvals of these pembrolizumab-based regimens offer the possibility of more time.”

Keytruda Qlex is contraindicated in patients with known hypersensitivity to berahyaluronidase alfa, hyaluronidase or to any of its excipients. Keytruda and Keytruda Qlex are associated with the following Warnings and Precautions: severe and fatal immune-mediated adverse reactions in any or multiple organs, which can occur during or after treatment, including pneumonitis, colitis, hepatitis, endocrinopathies, nephritis, dermatologic reactions, solid organ transplant rejection, other transplant (including corneal graft) rejection; severe and life-threatening infusion or injection-related reactions;

fatal and other serious complications in patients who receive allogeneic hematopoietic stem cell transplantation before or after beginning treatment; embryo-fetal toxicity; and increased mortality in patients with multiple myeloma when Keytruda or Keytruda Qlex is added to a thalidomide analogue plus dexamethasone, which is not recommended outside of controlled trials. Immune-mediated adverse reactions listed here may not include all such possible severe or fatal reactions.

“Historically, the prognosis has been poor for patients living with platinum-resistant recurrent ovarian cancer who have limited treatment options that may reduce the risk of disease progression or death. These approvals mark an important moment for the ovarian cancer community, reflecting years of focused investment in Keytruda,” said Dr. Gursel Aktan, vice president, global clinical development, Merck Research Laboratories. “Introducing the first PD-1 inhibitors for platinum-resistant ovarian cancer means we’re expanding what’s possible for patients facing this disease. It also reinforces our commitment to advancing innovative therapies and improved outcomes across women’s cancers, where the need is greatest.”

In patients whose tumors express PD-L1 (CPS =1), the median PFS was 8.3 months (95% CI, 7.0-9.4) for those receiving Keytruda plus paclitaxel, with or without bevacizumab, versus 7.2 months (95% CI, 6.2-8.1) for those receiving placebo plus paclitaxel with or without bevacizumab. The median OS for these patients receiving the Keytruda regimen was 18.2 months (95% CI, 15.3-21.0) versus 14.0 months (95% CI, 12.5-16.1) for those receiving the placebo regimen.

Of the 643 enrolled patients, 72% of patients had tumours expressing PD-L1 (CPS =1), 73% received bevacizumab in the study, and 46% received prior bevacizumab. A total of 47% had a platinum-free interval of less than 3 months. Patients were enrolled regardless of PD-L1 tumour expression status.

The safety of Keytruda in combination with paclitaxel with or without bevacizumab was evaluated in 463 patients with epithelial ovarian, fallopian tube, or primary peritoneal carcinoma whose tumours express PD-L1 (CPS =1) enrolled in KEYNOTE-B96. The median duration of exposure to Keytruda was 7.4 months (range 1 day to 35.9 months).

Serious adverse reactions occurred in 54% of patients receiving Keytruda and paclitaxel with or without bevacizumab. Serious adverse reactions in =2% of patients were pneumonia (4.3%), urinary tract infection (3.9%), adrenal insufficiency (3%), hyponatremia (3%), COVID-19 (2.6%), decreased neutrophil count (2.6%), pulmonary embolism (2.6%), abdominal pain (2.1%), anaemia (2.1%), colitis (2.1%), diarrhoea (2.1%), febrile neutropenia (2.1%), pyrexia (2.1%) and vomiting (2.1%).

Fatal adverse reactions occurred in 3.9% of patients receiving Keytruda and paclitaxel with or without bevacizumab, including assisted suicide (0.9%), death (0.4%), intestinal

perforation (0.4%), sepsis (0.4%), Covid-19 (0.4%), cardio-respiratory arrest (0.4%), colitis (0.4%), and embolic stroke (0.4%).

Keytruda was permanently discontinued for adverse reactions in 16% of patients. The most common adverse reactions resulting in permanent discontinuation of Keytruda (=1%) were, colitis (1.3%), and increased alanine aminotransferase (1.3%). Adverse reactions leading to the interruption of Keytruda occurred in 44% of patients. The most common adverse events leading to interruption of Keytruda in =2% were urinary tract infection (3.9%), adrenal insufficiency (2.6%), pyrexia (2.6%), pneumonitis (2.6%), upper respiratory tract infection (2.6%), neutropenia (2.1%), diarrhoea (2.1%) and Covid-19 (2.1%).

The most common (=20%) adverse reactions for patients treated with Keytruda in combination with paclitaxel with or without bevacizumab were: diarrhoea (45%), fatigue (43%), nausea (41%), alopecia (38%), peripheral neuropathy (38%), epistaxis (31%), urinary tract infection (27%), constipation (25%), abdominal pain (24%), decreased appetite (24%), vomiting (24%), hypothyroidism (21%), cough (20%), hypertension (20%), and rash (20%). The most common (=20%) laboratory abnormalities worsening from baseline were: anaemia (85%), leukopenia (82%), decreased neutrophil count (71%), lymphopenia (60%), hypoalbuminemia (50%), hyponatremia (53%), hypomagnesemia (45%), increased aspartate aminotransferase (43%), increased alanine aminotransferase (40%), hypocalcemia (40%), increased alkaline phosphatase (31%), increased creatinine (29%), hypokalemia (27%) and neutropenia (21%).

For patients treated with Keytruda in combination with paclitaxel and bevacizumab (N=169), decreased white blood cell count (27%), stomatitis (22%) and pyrexia (21%) were also reported as adverse reactions.

KEYNOTE-B96, also known as ENGOT-ov65, is a multicenter, randomized, double-blind placebo-controlled phase 3 trial (ClinicalTrials.gov, NCT05116189) sponsored by Merck and conducted in collaboration with the European Network for Gynecologic Oncology Trial (ENGOT) groups investigating Keytruda, Merck’s anti-PD-1 therapy, in combination with chemotherapy (paclitaxel), with or without bevacizumab, compared to placebo plus paclitaxel, with or without bevacizumab, for the treatment of platinum-resistant recurrent ovarian cancer. The primary endpoint is PFS, as assessed by investigator according to Response Evaluation Criteria in Solid Tumours version 1.1 (RECIST v1.1), and OS is a key secondary endpoint. The trial enrolled 643 patients with epithelial ovarian, fallopian tube or primary peritoneal carcinoma who received one or two prior lines of systemic therapy for ovarian carcinoma, including at least one line of platinum-based chemotherapy.

All study medications were administered as an intravenous infusion. Keytruda 400 mg or placebo were administered on Day 1 of each 6-week treatment cycle and paclitaxel 80 mg/m2 was administered on Days 1, 8, and 15 of each 3-week treatment cycle. The

option to use bevacizumab was by investigator choice prior to randomization. Bevacizumab 10 mg/kg was administered on Day 1 of a 2-week treatment cycle. Treatment with Keytruda continued until RECIST v1.1-defined progression of disease, unacceptable toxicity or a maximum of 24 months. Administration of Keytruda was permitted beyond RECIST-defined disease progression if the patient was clinically stable and considered to be deriving clinical benefit by the investigator. Assessment of tumour status was performed every 9 weeks for the first year, followed by every 12 weeks thereafter.

Ovarian cancer often begins in the fallopian tubes or the ovaries. As of 2022, it is the eighth most commonly diagnosed cancer and the eighth leading cause of cancer death among women worldwide. In the US, it is estimated there will be approximately 21,010 patients diagnosed with ovarian cancer and about 12,450 deaths from the disease in 2026. Over 80% of patients diagnosed with ovarian cancer will experience disease progression following standard treatment with platinum-based chemotherapy regimens. Approximately 25% of these patients develop resistance within six months of completing first-line platinum-based chemotherapy – defined as primary platinum-resistant ovarian cancer. Prognosis is particularly poor for these patients and approved treatment options are limited.

Keytruda is an anti-programmed death receptor-1 (PD-1) therapy that works by increasing the ability of the body’s immune system to help detect and fight tumour cells. Keytruda is a humanized monoclonal antibody that blocks the interaction between PD-1 and its ligands, PD-L1 and PD-L2, thereby activating T lymphocytes which may affect both tumour cells and healthy cells.

Merck has the industry’s largest immuno-oncology clinical research programme. There are currently more than 1,600 trials studying Keytruda across a wide variety of cancers and treatment settings. The Keytruda clinical programme seeks to understand the role of Keytruda across cancers and the factors that may predict a patient's likelihood of benefitting from treatment with Keytruda, including exploring several different biomarkers.

Keytruda Qlex is a fixed-combination drug product of pembrolizumab and berahyaluronidase alfa. Pembrolizumab is a programmed death receptor-1 (PD-1) blocking antibody and berahyaluronidase alfa enhances dispersion and permeability to enable subcutaneous administration of pembrolizumab. Keytruda Qlex is administered as a subcutaneous injection into the thigh or abdomen, avoiding the 5 cm area around the navel, over one minute every three weeks (2.4 mL) or over two minutes every six weeks (4.8 mL).

Merck committed to supporting accessibility to its cancer medicines. Merck provides multiple programmes to help appropriate patients who are prescribed Keytruda have access to our anti-PD-1 therapy. The Merck Access Program provides reimbursement

support for patients receiving Keytruda, including information to help with out-of-pocket costs and co-pay assistance for eligible patients.

Merck is committed to helping provide patients and their caregivers support throughout their treatment with Keytruda. The KEY+YOU Patient Support Programme provides a range of resources and support.

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