News Release

For Immediate Release

First 'tumour agnostic' indication announced[1,2]*

KEYTRUDA® (pembrolizumab) indicated* to treat tumours based on biomarker[2]

Australians who have a cancer which displays a specific biomarker may be eligible for treatment with a medicine that activates the immune system to fight cancer cells.[3]

A medicine to treat cancer based on the genetic profile of the tumour, rather than tumour type or location, has now been registered on the Australian Register of Therapeutic Goods < 263932>.[2] This marks the first 'tumour agnostic' approach to cancer treatment in Australia.[1,2,4]

MSD confirmed that KEYTRUDA can now be used to treat eligible patients whose cancer has a specific genetic alteration (known medically as a biomarker) called deficient DNA-mismatch repair (dMMR) or microsatellite instability-high (MSI-H). These patients must have advanced cancer (where the cancer has spread to other organs) that has progressed following prior treatment and have no satisfactory alternative treatment options.[2]

Colorectal (colon or rectum) cancer is one form of cancer that can display the dMMR and/or MSI-H biomarker, and the new indication specifically identifies advanced colorectal cancer patients with this biomarker, whose disease has progressed following treatment with multiple therapies, as eligible for treatment.[2] This indication was approved under the provisional approval pathway, which provides a six-year window to collect further data to support KEYTRUDA's use in microsatellite instability-high cancer and to transition to a full registration.[2,5]

It is estimated that there are more than 20 different tumours types that may display MSI-H and/or dMMR, which can be identified through laboratory tests.[2,6] These tumours include: Colorectal, Endometrial, Gastric, Small intestinal, Pancreatic, Cholangiocarcinoma, Adrenocortical, Mesothelioma, Small-cell lung, Cervical, Neuroendocrine, Thyroid, Urothelial, Brain, Ovarian, Prostate, Retroperitoneal, Salivary, Sarcoma, Testicular and Tonsillar cancers.[2,6]

"This is the first tumour agnostic indication made available in Australia. It marks a shift in treating cancer according to the genetic type of the tumour as opposed to the tumour location," said Michael Azrak, Managing Director of MSD Australia.

"It represents a new way in which some cancers will be treated in Australia and is an important step in Precision Medicine," he said.

"MSD is proud of our leadership and commitment to cancer research and innovation," Mr Azrak said.

About MSI-H and/or dMMR and KEYTRUDA:
KEYTRUDA is a PD-1 inhibitor and works to reactivate the immune system to attack cancer cells by blocking a specific protein (known as PD-1 or programmed cell death protein 1); which left unchecked allows cancer cells to pass undetected by the body's natural defences.[2]

KEYTRUDA is used to treat[3]:
• a kind of skin cancer called melanoma in adults.
• a kind of lung cancer called non-small cell lung cancer in adults.
• a kind of head and neck cancer called head and neck squamous cell carcinoma in adults.
• a kind of cancer called classical Hodgkin Lymphoma in adults.
• a kind of cancer called primary mediastinal B-cell lymphoma in adults and children.
• a kind of cancer called urothelial carcinoma, including bladder cancer in adults.
• a kind of cancer in adults and children that can occur in any part of the body and is shown by laboratory tests to be microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR).

KEYTRUDA is currently only PBS listed for eligible Australians with unresectable or malignant melanoma, refractory or relapsed classical Hodgkin Lymphoma, previously untreated metastatic non-small cell lung cancer and locally advanced or metastatic urothelial cancer.[7]

** KEYTRUDA was assessed under a provisional pathway that provides a six-year window to collect further data to support its use in microsatellite instability-high cancer. This includes the following indications:[2]*

The MSI-H/dMMR indications are as follows:
Colorectal: *KEYTRUDA is indicated in adult and paediatric patients for the treatment of unresectable or metastatic, microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) colorectal cancer that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan. This indication was approved via the provisional-approval pathway, based on objective response rate and response duration in single-arm trials. Continued approval for this indication depends on verification and description of clinical benefit in the confirmatory trials.*

Non-colorectal: *KEYTRUDA is indicated in adult and paediatric patients for the treatment of unresectable or metastatic, microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) tumours that have progressed following prior treatment and when there are no satisfactory alternative treatment options. This indication was approved via the provisional-approval pathway, based on the pooling of data on objective response rate and response duration across multiple different tissue types in a single-arm trial. Sample sizes for individual tissue types were too small to provide data on clinical utility of the MSI-H/dMMR tests for each of the tissue types, individually. The assumption that MSI-H/dMMR-status is predictive of the treatment effect of Keytruda for every tissue type has not been verified. Continued approval for this indication depends on verification and description of clinical benefit in the confirmatory trials.*

The safety and effectiveness of KEYTRUDA in paediatric patients with MSI-H central nervous system cancers have not been established.

KEYTRUDA Minimum Production Information (v24.1) Indications: As monotherapy for unresectable or metastatic melanoma in adults. As monotherapy for adjuvant treatment of melanoma with lymph node involvement following complete resection. As monotherapy for first-line treatment of patients with metastatic NSCLC whose tumours express PD-L1 ≥50% tumour proportion score (TPS) on a validated test, with no EGFR or ALK genomic tumour aberrations. As monotherapy for advanced NSCLC patients with a PD-L1 TPS level≥1% and who have received platinum-containing chemotherapy. Patients with EGFR or ALK genomic tumour aberrations should have received prior therapy for these aberrations before receiving KEYTRUDA. In combination with pemetrexed and platinum chemotherapy for first-line treatment of metastatic non-squamous NSCLC in patients with no EGFR or ALK genomic tumour aberrations. In combination with carboplatin and either paclitaxel or nab-paclitaxel for the first-line treatment of patients with metastatic squamous NSCLC. As monotherapy for recurrent or metastatic Head and Neck Squamous Cell Carcinoma with disease progression on or after platinum-containing chemotherapy. As monotherapy for relapsedor refractory classical Hodgkin Lymphoma following ASCT or at least two or more prior therapies when ASCT or multi-agent chemotherapy is not a treatment option. As monotherapy for refractory, or following two prior therapies for relapsed, primary mediastinal B-cell lymphoma (PMBCL) in adults and children. As monotherapy for patients with locally advanced or metastatic urothelial carcinoma (UC) who are not eligible for cisplatin- containing therapy and whose tumours express PD-L1 [Combined Positive Score (CPS) ≥10], or in patients who are not eligible for, or have received priorplatinum-containing chemotherapy regardless of PD-L1 status. As monotherapy for MSI-H/dMMR colorectal cancer that has progressed following standard prior treatment in adults and children (provisional approval). As monotherapy for MSI-H/dMMR non-colorectal tumours that have progressed following prior treatment and with no satisfactory alternatives in adults and children (provisional approval). See full PI. **Contraindications**: None. **Precautions**: Immune-mediated adverse reactions, including pneumonitis, colitis(including gastrointestinal perforation), hepatitis, nephritis, hypophysitis, type 1 diabetes mellitus, hyperthyroidism, hypothyroidism, thyroiditis, uveitis, myositis, Guillain-Barre syndrome, myasthenic syndrome/ myasthenia gravis (incl. exacerbation), pancreatitis, sarcoidosis, encephalitis, myocarditis, pericarditis and pericardial effusion, peripheral neuropathy, solid organ transplant rejection, severe skin reactions (including Stevens-Johnson syndrome, toxic epidermal necrolysis, and bullous pemphigoid), severe infusion reactions (hypersensitivity, anaphylaxis), and complications of allogeneic HSCT including fatal graft-versus-host-disease and hepatic veno-occlusive disease. Severe and fatal cases of immune-mediated adverse reactions have occurred. Increased mortality when in combination with dexamethasone and a thalidomide analogue in multiple myeloma (not indicated). Immune-mediated adverse reactions affecting more than one body system can occur simultaneously. For management of immune-mediated adverse events, see full PI. Limited information in patients with active infection and patients with on-going adverse reaction to ipilimumab – use caution. Increased deaths observed in previously-treated UC patients in first two months of treatment compared to chemotherapy. See full PI for further information **Pregnancy**. : Category D.**Interactions**:None expected. Avoid corticosteroids or immunosuppressants prior to treatment. **Adverse events**: hypothyroidism, nausea, asthenia, fatigue, hyperthyroidism, pneumonitis, colitis, hepatitis, hypophysitis, nephritis, type 1 diabetes mellitus, arthralgia, cough, back pain, vitiligo, abdominal pain, pruritus, rash, hyponatremia, anaemia, diarrhoea, pyrexia, adrenal insufficiency, autoimmune hepatitis, upper respiratory tract infection, constipation, vomiting, urinary tract infection, decreased appetite, musculoskeletal pain, haematuria, dyspnoea, diarrhoea, alopecia, headache, neutropenia. Post-marketing: arthritis, Vogt-Koyanagi-Harada syndrome, haemophagocytic lymphohistiocytosis. **Dosage**:200 mgadministered as an intravenous infusion over 30 minutes every 3weeks. Paediatric PMBCL or MSI-H/dMMR cancer: 2mg/kg up to 200mg. Treat with KEYTRUDA until disease progression or unacceptable toxicity, or up to two yearsor 35 cycles for UC, NSCLC, PMBCL or MSI-H/dMMR cancer. KEYTRUDA should be administered first when used in combination. Atypical responses (i.e. an initial transient increase in tumour size or small new lesions followed by shrinkage) have been observed. Clinically stable patients (i.e. asymptomatic and not requiring urgent intervention) with initial evidence of progression can remain on treatment until confirmed. Treat with KEYTRUDA for up to one year or until disease recurrence or unacceptable toxicity for adjuvant melanoma. See full PI for further information

KEYTRUDA Consumer Medical Information available here

PBS Information: Authority required (STREAMLINED) or Authority required. Refer to PBS Schedule for full authority information. This product is not listed on the PBS for treatment of HNSCC, PMBCL, first-line UC patients who are ineligible for cisplatin- or platinum-containing therapy, MSI-H/dMMR tumours, NSCL after platinum-containing chemotherapy or in combination, or for the adjuvant treatment of patients with melanoma.

Issued by Ethical Strategies on behalf of MSD Australia.

MSD Media Contact: Ben Gommers (0408 669 740)

Agency Contact: John Morton (0416 184 044) or Fiona Beveridge (0405 902 826)

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About MSD

For more than a century, MSD, a leading global biopharmaceutical company, has been inventing for life, bringing forward medicines and vaccines for the world's most challenging diseases. MSD is a trade name of Merck & Co., Inc., with headquarters in Kenilworth, N.J., U.S.A. Through our prescription medicines, vaccines, biologic therapies and animal health products, we work with customers and operate in more than 140 countries to deliver innovative health solutions. We also demonstrate our commitment to increasing access to health care through far-reaching policies, programs and partnerships. Today, MSD continues to be at the forefront of research to advance the prevention and treatment of diseases that threaten people and communities around the world - including cancer, cardio-metabolic diseases, emerging animal diseases, Alzheimer's disease and infectious diseases including HIV and Ebola. For more information, visit www.msdaustralia.com.au and connect with us on Twitter and LinkedIn.

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