News Release

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Precision medicine helping to change the prognosis of a rare subtype of bowel cancer

Immuno-oncology therapy KEYTRUDA® (pembrolizumab) registered for bowel cancer patients with a specific genetic biomarker

Australians with a specific type of bowel cancer are no longer subject to a 'one-size fits all' treatment approach, with immuno-oncology therapy KEYTRUDA now available as a treatment option.

MSD announced today that its cancer treatment KEYTRUDA has been listed for use on the Australian Register of Therapeutic Goods (AUST R 263932 and AUST R 226597) for the first-line treatment of patients with unresectable or metastatic colorectal cancer that have a specific alteration (known as a biomarker) called microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR), as determined by a validated test[1].

KEYTRUDA is a cancer immunotherapy that works to reactivate the immune system to attack tumour cells by blocking a cancer cell protein (known as programmed death receptor 1 or PD-1) which left unchecked allows cancer cells to pass undetected by the body's natural defences[1].

MSD has made a submission to the Pharmaceutical Benefits Advisory Committee (PBAC) for reimbursement of the treatment, for mismatch repair deficient (dMMR) metastatic colorectal cancer (a specific type of bowel cancer), which will be considered by the PBAC at the upcoming meeting in March 2021[2]. Australian patients, carers and the community can currently submit a 'consumer comment' to the PBAC by 10 February with their views regarding the availability and access of this treatment for eligible patients.

This latest indication for metastatic bowel cancer provides another option for Australian patients. An estimated 15,000 Australian patients will be diagnosed with bowel cancer each year[3] - the fourth most commonly diagnosed cancer in Australia[3]; and in 2020, there were an estimated 5300 deaths from bowel cancer in Australia[3] - making bowel cancer the second leading cause of cancer death in Australia[3]. Risk factors can include older age (over 50), diet, obesity, family history, smoking, alcohol, inflammatory bowel disease and polyps[4].

Julien Wiggins, CEO Bowel Cancer Australia, welcomed KEYTRUDA as a treatment option for this for this subset of bowel cancer patients: “While there is a lot of important discussion regarding bowel cancer screening, treatment options remain vital. Up to half of the 15,000 Australians diagnosed with bowel cancer each year already have metastatic disease or will go on to develop it[567].”

“While bowel cancer is considered a common cancer, rare subtypes exist. Eligible patients with certain types of cancer, including melanoma and non-small cell lung cancer, already have reimbursed PBS access to immuno-oncology medicines.”

A small number of bowel cancers have a biomarker (mismatch repair deficiency – dMMR or Microsatellite Instability-High - MSI-H) which helps in identifying patients that may respond to immuno-oncology therapies such as KEYTRUDA[8]. This biomarker may also provide information on the likely course of disease in an untreated patient with bowel cancer. Testing for this biomarker in bowel cancer is already standard practice in Australia but there were previously no alternative treatment options, or treatment options that matched this specific biomarker for Metastatic colorectal cancer patients, until now[9].

Professor Peter Gibbs, from Western Health in Melbourne, specialises in treating patients with bowel cancer and was a co-author for the publication of the MSD-sponsored clinical trial in this indication in the December 2020 edition of the New England Journal of Medicine[10]: “Australians with bowel cancer are tested for this rare biomarker called mismatch-repair deficiency (dMMR) or Microsatellite Instability-High (MSI-H), and approximately 6.9 percent of patients at the metastatic stage will have this marker[11]. Knowing this information helps us to appropriately guide their treatment journey and provide the right options for the right patients.

“This treatment is a form of personalised medicine for the treatment of bowel cancer for eligible patients and enables us to finally move away from a ‘one-size fits all’ approach to treating these patients. It gives these seriously ill patients more hope,” continued Professor Gibbs.

“It’s availability in Australia has been eagerly anticipated across the medical community and bring us one step closer to ensuring this treatment is soon available for patients on the PBS.”

MSD Managing Director for Australia and New Zealand, Mr Michael Azrak, said this latest registration for KEYTRUDA is the therapy’s 17th indication on the ARTG[1] and cements the place of KEYTRUDA as a treatment option for eligible Australian bowel cancer patients.

“This indication is a new oncology milestone for Australian patients and clinicians. Health Technology Assessment reform, however, is needed in Australia to improve alignment between Therapeutic Goods Administration (TGA) and PBAC processes so that eligible Australian patients can access these medicines as quickly as possible.

“The TGA registered this indication in six months, three months earlier than expected, via their priority pathway and in collaboration with international regulatory agencies (US, Switzerland and Canada) through Project Orbis. However, registration is only the first step. Timely and affordable access, through reimbursement on the Pharmaceutical Benefits Scheme, is our goal for these patients. We believe that this indication provides a high-added therapeutic value to Australian patients, and we hope that the PBAC also recognises the value of this treatment for eligible bowel cancer patients,” said Mr Azrak.

KEYTRUDA Minimum Product Information (v35)

Please review the Product Information before prescribing. Product Information is available at www.msdinfo.com.au/keytrudapi.

▼ This medicinal product is subject to additional monitoring in Australia due to provisional approval of an extension of indication. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse events at www.tga.gov.au/reporting-problems.

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 NSCLC whose tumours express PD-L1 tumour proportion score (TPS) ≥1% on a validated test, with no EGFR or ALK genomic tumour aberrations and are either; metastatic, or stage III where patients are not candidates for surgical resection or definitive chemoradiation. 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 or in combination with platinum and 5-fluorouracil (5-FU) chemotherapy for the first-line treatment of patients with metastatic or unresectable recurrent head and neck squamous cell carcinoma (HNSCC), and whose tumours express PD-L1 [Combined Positive Score (CPS) ≥1] as determined by a validated test. As monotherapy for metastatic or unresectable recurrent HNSCC with disease progression on or after platinum-containing chemotherapy and whose tumours express PD-L1 [Combined Positive Score (CPS) ≥1] as determined by a validated test. As monotherapy for relapsed or 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 prior platinum-containing chemotherapy regardless of PD-L1 status. As monotherapy for the first-line treatment of unresectable or metastatic MSI-H/dMMR colorectal cancer as determined by a validated test. As monotherapy for MSI-H/dMMR colorectal cancer, as determined by a validated test, that has progressed following standard prior treatment in adults and children (provisional approval). As monotherapy for MSI-H/dMMR non-colorectal solid tumours, as determined by a validated test, that have progressed following prior treatment and with no satisfactory alternatives in adults and children (provisional approval). In combination with lenvatinib for patients with advanced endometrial carcinoma (EC) that is not MSI-H/dMMR, as determined by a validated test, who have disease progression following prior

systemic therapy, and are not candidates for curative surgery or radiation (provisional approval). In combination with axitinib for the first-line treatment of patients with advanced renal cell carcinoma (RCC). See full PI. **Contraindications:** None. **Precautions:** Immune-mediated adverse reactions, including pneumonitis, colitis (including gastrointestinal perforation), hepatitis, hepatotoxicity (in combination with axitinib), nephritis, adrenal insufficiency, hypophysitis, type 1 diabetes mellitus, hyperthyroidism, hypothyroidism, thyroiditis, uveitis, myositis, Guillain-Barre syndrome, myasthenic syndrome/myasthenia gravis (incl. exacerbation), myelitis, 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. Limited experience in paediatrics (only indicated in PMBCL and MSI-H/dMMR cancers). Monitor thyroid and liver function. Limited data in combination with axitinib and in combination with chemotherapy in patients ≥75 years. 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. Pregnancy (Category D). See full PI for further information. **Interactions:** None expected. Avoid corticosteroids or immunosuppressants prior to treatment (except as premedication in combination with chemotherapy). **Adverse events:** Monotherapy: fatigue, pruritus, rash, diarrhoea, nausea, hypothyroidism, hyperthyroidism, pneumonitis, colitis, arthralgia, cough, back pain, vitiligo, abdominal pain, hyponatremia, asthenia, neutropenia, dyspnoea, upper respiratory tract infection, pyrexia, febrile neutropenia, musculoskeletal pain, decreased appetite, constipation, elevated LFTs, urinary tract infection, acute kidney injury, haematuria, sepsis, urosepsis, anaemia, vomiting, increased creatinine, peripheral oedema, pneumonia, decreased weight, other laboratory abnormalities, mucosal inflammation, dysphagia, stomatitis, headache, dizziness, peripheral sensory neuropathy, myalgia, neck pain, insomnia, thrombocytopenia (see full PI). Combination (where not already listed under Monotherapy) *with chemotherapy*: nephritis, alopecia; *with lenvatinib*: gastrointestinal perforation, reversible posterior leukoencephalopathy syndrome with intraventricular haemorrhage, intracranial haemorrhage, haemorrhage, confusional state, pleural effusion, adrenal insufficiency, pancreatitis, muscular weakness, renal impairment, increased lipase, increased blood alkaline phosphatase, headache, skin ulcer, increased amylase, hypocalcaemia, syncope, hypertension, haemorrhagic events, stomatitis, hypomagnesemia, dysphonia, palmar-plantar erythrodysesthesia syndrome; *with axitinib:* hypertension, hepatotoxicity, palmar-plantar erythrodysesthesia syndrome, stomatitis/mucosal inflammation, dysphonia. **Dosage:** Adults: 200 mg every 3 weeks, or, 400 mg every 6 weeks (melanoma/NSCLC monotherapy). Paediatric PMBCL or MSI-H/dMMR cancer: 2 mg/kg up to 200 mg. Administered as an intravenous infusion over 30 minutes. Treat with KEYTRUDA until disease progression or unacceptable toxicity, or up to 24 months or the equivalent number of treatment cycles for UC, NSCLC, HNSCC, PMBCL, EC, or MSI-H/dMMR cancers. KEYTRUDA should be administered first when used in combination with intravenous chemotherapy. 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.

Based on PI approved December 2020.

Refer to the Consumer Medical Information leaflet, available at
http://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2015-CMI-01640-1
or your doctor or pharmacist for further information about KEYTRUDA.

PBS Information: Authority required (STREAMLINED) or Authority required. This product is not listed on the PBS for certain indications. Refer to PBS Schedule for full authority information.

Note to Editor: Professor Peter Gibbs has been involved in clinical trials sponsored by MSD. He has received honoraria as a member of advisory boards for MSD. In relation to this media announcement,

no compensation was provided to Professor Peter Gibbs and the opinions expressed is his own. Professor Peter Gibbs has been briefed by MSD on the approved use of this product.

-ENDS-

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About MSD

For more than 125 years, MSD has been inventing for life, bringing forward medicines and vaccines for many of the world's most challenging diseases in pursuit of our mission to save and improve lives. MSD is a trade name of Merck & Co., Inc., Kenilworth, N.J., U.S.A. We demonstrate our commitment to patients and population health by increasing access to health care through far-reaching policies, programs and partnerships. Today, MSD continues to be at the forefront of research to prevent and treat diseases that threaten people and animals – including cancer, infectious diseases such as HIV and Ebola, and emerging animal diseases – as we aspire to be the premier research-intensive biopharmaceutical company in the world. For more information, visit www.msd-australia.com.au and connect with us on Twitter and LinkedIn.

References

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