BRAND NAME: Keytruda

PROPER NAME: Pembrolizumab

MANUFACTURER: MERCK SHARP DOHME

INDICATION: KEYTRUDA is a human programmed death receptor-1 (PD-1)-blocking antibody indicated for the treatment of patients with unresectable or metastatic melanoma and disease progression following ipilimumab and, if BRAF V600 mutation positive, a BRAF inhibitor.

DESCRIPTION: Pembrolizumab is a humanized monoclonal antibody that blocks the interaction between PD-1 and its ligands, PD-L1 and PD-L2. Pembrolizumab is an IgG4 kappa immunoglobulin with an approximate molecular weight of 149 kDa.

BLA NO: 125514

REGULATORY MILESTONES:

US pre-BLA	October 25, 2013
US Approval	September 4, 2014
EU Approval	July 17, 2015
Health Canada Approval	May 19, 2015
Japanese Ministry of Health, Labor and Welfare (MHLW) Approval	December 20, 2016
TGA	September 17, 2019

ADVISORY COMMITTEE:

The BLA for pembrolizumab was not referred to an advisory committee although it is for a new molecular entity. The application did not raise significant public health questions on the role of the pembrolizumab for this indication and outside expertise was not necessary as there were no controversial issues that would benefit from an advisory committee discussion.

MANUFACTURING:

PARAMETER	DATA	REFERENCE
Manufacturer	MERCK SHARP DOHME	
Indication	KEYTRUDA is a human programmed death receptor-1 (PD-1)-blocking antibody indicated for the treatment of patients with unresectable or metastatic melanoma and disease progression following ipilimumab and, if BRAF V600 mutation positive, a BRAF inhibitor.	1
Cell Substrate	IgG4/ /kappa isotype monoclonal antibody	3
Manufacturing platform	MK-3475 is a humanized monoclonal antibody that is expressed as a secreted product from a suspension Chinese Hamster Ovary (CHO) cell line. Cells from the WCB are expanded in shake flasks, disposable rocker bags, and a seed bioreactor to generate the inoculum for a production bioreactor to produce the antibody product. The downstream processing includes three chromatography steps, two orthogonal viral clearance steps, ultrafiltration/diafiltration, and a final 0.2 µm filtration step. All raw materials used in upstream/downstream manufacturing processes are animal component free. Upstream and downstream processing is considered as state of the art for production of monoclonal antibodies.	3
Dose in vial/final container	50 mg, lyophilized powder in single-use vial for reconstitution	1
Dose to patient	2 mg/kg as an intravenous infusion over 30 minutes every 3 weeks.	1

1. Package insert – Keytruda
2. EPAR full - Keytruda
3. EPAR quality - Keytruda: EPAR - Public assessment report
4. FDA Review - Keytruda (pembrolizumab) Powder for Injection

CLINICAL TRIALS:

NCT	TRIAL PHASE	NO OF PATIENTS ENROLLED	TITLE	COUNTRIES
Single arm/safety and response rate				
NCT01295827	1	1260	Study of Pembrolizumab (MK-3475) in Participants with Progressive Locally Advanced or Metastatic Carcinoma, Melanoma, or Non-small Cell Lung Carcinoma (P07990/MK-3475-001/KEYNOTE-001)	
NCT01704287	2	540	Study of Pembrolizumab (MK-3475) Versus Chemotherapy in Participants with Advanced Melanoma (MK-3475-002/P08719/KEYNOTE-002)	
NCT01866319	3	834	Study to Evaluate the Safety and Efficacy of Two Different Dosing Schedules of Pembrolizumab (MK-3475) Compared to Ipilimumab in Participants With Advanced Melanoma (MK-3475-006/KEYNOTE-006)	
NCT01905657	2, 3	1061	Study of Two Doses of Pembrolizumab (MK-3475) Versus Docetaxel in Previously Treated Participants with Non-Small Cell Lung Cancer (MK-3475-010/KEYNOTE-010)	
Safety and efficacy				
NCT01848834	1	297	Study of Pembrolizumab (MK-3475) in Participants with Advanced Solid Tumors (MK-3475-012/KEYNOTE-012)	

POST APPROVAL CHANGES

DATE	TYPE OF CHANGE	DESCRIPTION	LINK