BRAND NAME: Yervoy

PROPER NAME: Ipilimumab

MANUFACTURER: Bristol-Myers Squibb Company

INDICATION: YERVOY is a human cytotoxic T-lymphocyte antigen 4 (CTLA-4)-blocking antibody indicated for the treatment of unresectable or metastatic melanoma.

DESCRIPTION: YERVOY (ipilimumab) is a recombinant, human monoclonal antibody that binds to the cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4). Ipilimumab is an IgG1 kappa immunoglobulin with an approximate molecular weight of 148 kDa.

BLA NO: 125377

REGULATORY MILESTONES:

US pre-IND	April 25, 2008
US Approval	March 25, 2011
EU Approval	July 12, 2011
Health Canada Approval	February 1, 2012
TGA	June 27, 2011

ADVISORY COMMITTEE:

Advice regarding the approvability of this application was not sought from the Oncologic Drugs Advisory Committee Since demonstration of overall survival in two controlled, clinical trials provided sufficient evidence of clinical benefit, particularly in this malignancy where there

is currently no highly effective treatment. evidence of improved survival also provides assurance that the benefits generally outweigh the risk.

MANUFACTURING:

PARAMETER	DATA	REFERENCE
Manufacturer	Bristol-Myers Squibb Company	
Indication	YERVOY is a human cytotoxic T-lymphocyte antigen 4 (CTLA-4)-blocking antibody indicated for the treatment of unresectable or metastatic melanoma.	1
Cell Substrate	CHO cell line	3
Manufacturing platform	Ipilimumab is produced as a secreted protein in large-scale cell culture employing a CHO cell line that was transfected with an expression vector containing the coding sequences for both heavy and light chains of ipilimumab. This cell line is maintained with a Master Cell Bank and a Working Cell Bank (WCB) both of which have been tested consistent with ICH guidance documents.	3
Dose in vial/final container	50 mg/10 mL (5 mg/mL). 200 mg/40 mL (5 mg/mL)	1
Dose to patient	3 mg/kg administered intravenously over 90 minutes every 3 weeks for a total of four doses.	1

1. Package insert - Yervoy
2. EPAR full - Yervoy
3. EPAR quality - Yervoy: EPAR - Public assessment report
4. FDA Review - YERVOY (ipilimumab) Injection

CLINICAL TRIALS:

NCT	TRIAL PHASE	NO OF PATIENTS ENROLLED	TITLE	COUNTRIES
Primary efficacy and safety study				

NCT00094653	3	1783	MDX-010 Antibody, MDX-1379 Melanoma Vaccine, or MDX-010/MDX-1379 Combination Treatment for Patients with Unresectable or Metastatic Melanoma	United States, Chile, Belgium, Brazil, Canada, France, Germany, Hungary, Argentina, Netherlands, South Africa, Switzerland, United Kingdom
Other efficacy study of interest				
NCT00324155	3	681	Dacarbazine and Ipilimumab vs. Dacarbazine With Placebo in Untreated Unresectable Stage III or IV Melanoma	United States, Argentina, Australia, Austria, Belgium, Brazil, Canada, Spain, Chile, France, Israel, Germany, Italy, Hungary, Ireland, Czech Republic, Poland, Norway, Portugal, Netherlands, Russian Federation, South Africa, Switzerland, Ukraine, United Kingdom
Other studies				
NCT00289640	2	210	Study of Ipilimumab (MDX-010) Monotherapy in Patients with Previously Treated Unresectable Stage III or IV Melanoma	United States, Australia, Belgium, Brazil, Canada, Czech Republic, France, Germany, Hungary, South Africa
NCT00289627	2	155	A Single Arm Study of Ipilimumab Monotherapy in Patients with Previously Treated Unresectable Stage III or IV Melanoma	United States, Italy, Austria, Finland, Norway, Poland, Russian Federation, Spain, Sweden, Ukraine
NCT00135408	2	115	A Study of MDX-010 (BMS-734016) Administered with or Without Prophylactic Oral Budesonide	United States, Peru, Canada, Israel, Italy, United Kingdom

NCT00261365	1, 2	80	Phase II Study to Determine Predictive Markers of Response to BMS-734016 (MDX-010)	United States, Peru, Denmark, Israel, Italy, Norway, Sweden
NCT00050102	2		Comparison Study of MDX-010 (CTLA-4) Alone and Combined with DTIC in the Treatment of Metastatic Melanoma	United States
NCT00623766	2	99	Evaluation of Tumor Response to Ipilimumab in the Treatment of Melanoma with Brain Metastases	United States
NCT00928031		160	Long-term Data Collection for Subjects in MDX-010 Studies	United States

POST APPROVAL CHANGES

DATE	TYPE OF CHANGE	DESCRIPTION	LINK