BRAND NAME: PORTRAZZA

PROPER NAME: Necitumumab

MANUFACTURER: Eli Lilly and Company

INDICATION: PORTRAZZA™ is an epidermal growth factor receptor (EGFR) antagonist indicated, in combination with gemcitabine and cisplatin, for first-line treatment of patients with metastatic squamous non-small cell lung cancer.

DESCRIPTION: Necitumumab is an anti-EGFR recombinant human monoclonal antibody of the IgG1 kappa isotype that specifically binds to the ligand binding site of the human EGFR. Necitumumab has an approximate molecular weight of 144.8 kDa. Necitumumab is produced in genetically engineered mammalian NS0 cells.

BLA NO: 125547

REGULATORY MILESTONES:

US pre-IND	December 5, 2008
US Approval	November 24, 2015
EU Approval	February 15, 2016
Health Canada Approval	March 16, 2017
Japanese Ministry of Health, Labor and Welfare (MHLW) Approval	November 22, 2019

ADVISORY COMMITTEE:

This BLA was referred to the Oncologic Drugs Advisory Committee (ODAC) for advice and presented on July 9, 2015. The majority of the committee agreed that the efficacy and safety results of SQUIRE in squamous cell NSCLC support a positive benefit: risk assessment of necitumumab in combination with gemcitabine/cisplatin in the proposed population. Most of the committee members noted that the 16% reduced risk of death and median 1.6-month survival benefit with necitumumab in the pivotal SQUIRE study is modest yet significant and noteworthy. Some committee members advised that consideration should be given to recommending against use in patient subgroups that appeared to gain little or no benefit from the anti-EGFR monoclonal antibody, such as patients over age 70 years and those whose tumors do not express EFGR proteins. Please see the transcript for details of the committee discussion.

MANUFACTURING:

PARAMETER	DATA	REFERENCE
Manufacturer	Eli Lilly and Company	
Indication	PORTRAZZA™ is an epidermal growth factor receptor (EGFR) antagonist indicated, in combination with gemcitabine and cisplatin, for first-line treatment of patients with metastatic squamous non-small cell lung cancer	1
Cell Substrate	NS0 (mouse) cell line.	3
Manufacturing platform	The upstream manufacture of each batch of necitumumab begins with the thawing of a single vial of the Working Cell Bank (WCB), derived from the Master Cell Bank (MCB), that is serially scaled-up in flasks and bioreactors. The contents of the final scale-up bioreactor are used to inoculate the production bioreactor. The culture is harvested, clarified, and then transferred for further downstream processing. The downstream manufacture of necitumumab consists of a series of	3

	chromatography, viral inactivation and nanofiltration and tangential flow filtration steps. Four manufacturing processes for necitumumab have been developed: Process A, Process B, Process C, and Process D.	
Dose in vial/final container	800 mg/50 mL (16 mg/mL) solution in a single-dose vial.	1
Dose to patient	800 mg (absolute dose) as an intravenous infusion over 60 minutes on Days 1 and 8 of each 3-week cycle.	1

1. Package insert - PORTRAZZA
2. EPAR full - PORTRAZZA
3. EPAR quality - Portrazza: EPAR - Public assessment report
4. FDA Review - PORTRAZZA (necitumumab) injection

CLINICAL TRIALS:

NCT	TRIAL PHASE	NO OF PATIENTS ENROLLED	TITLE	COUNTRIES
Randomized controlled study to support efficacy and safety				
NCT00981058	3	1093	First-line Treatment of Participants with Stage IV Squamous Non-Small Cell Lung Cancer with Necitumumab and Gemcitabine-Cisplatin	United States, Australia, Spain, Austria, Brazil, Belgium, Italy, France, Canada, Croatia, Greece, Germany, Korea, Republic of, Hungary, Philippines, Poland, Serbia, Portugal, South Africa, Taiwan, Romania, Singapore, Russian Federation, Slovakia, Thailand, United Kingdom
Randomized controlled study to support safety				
NCT00982111	3	633	First-line Treatment of Patients with Stage IV Non-squamous Non-Small Cell Lung Cancer with	United States, Australia, Austria, Belgium, Brazil, Canada, Croatia, France, Germany, Greece, Hungary, Italy, Poland,

			Necitumumab (IMC-11F8) and Pemetrexed-Cisplatin	Portugal, Romania, Spain, Russian Federation, Slovakia, South Africa, United Kingdom
Other studies to support safety and efficacy				
NCT00801177	1	60	Study of IMC-11F8 in Patients with Tumors Who Have Not Responded to Standard Therapy	Netherlands
NCT01088464	1	15	Study of IMC-11F8 in Participants with Advanced Solid Tumors	Japan
NCT01606748	2	35	A Drug-Interaction Study of necitumumab (IMC-11F8) in Combination with Gemcitabine-Cisplatin	United States
Study in other indications				
NCT00835185	2	44	Study of IMC-11F8 in Participants with Colorectal Cancer	Belgium, Spain
Ongoing studies				
NCT01624467	2	75	A Study of Necitumumab Monotherapy and the QT/QTc Interval in Patient with Advanced Solid Tumors	United States
NCT01788566	2	61	A Study of Gemcitabine-Cisplatin Chemotherapy Plus Necitumumab in the First-Line Treatment of Participants with Squamous Lung Cancer	United States, Canada, France, Mexico, Spain, Netherlands, Taiwan
NCT01769391	2	167	A Study of Necitumumab and Chemotherapy in	United States, Germany, Korea, Republic of,

			Participants with Stage IV Squamous Non-Small Cell Lung Cancer	Poland, Mexico, Russian Federation

POST APPROVAL CHANGES

DATE	TYPE OF CHANGE	DESCRIPTION	LINK