BRAND NAME: SYLVANT

PROPER NAME: Siltuximab

MANUFACTURER: Janssen Biotech, Inc.

INDICATION: SYLVANT is an interleukin-6 (IL-6) antagonist indicated for the treatment of patients with multicentric Castleman's disease (MCD) who are human immunodeficiency virus (HIV) negative and human herpesvirus-8 (HHV-8) negative.

DESCRIPTION: SYLVANT (siltuximab) is a human-mouse chimeric monoclonal antibody that binds human interleukin-6 (IL-6). SYLVANT is produced by Chinese hamster ovary cells.

BLA NO: 125496

REGULATORY MILESTONES:

US pre-BLA	July 24, 2013
US Approval	April 22, 2014
EU Approval	May 22, 2014
Health Canada Approval	December 4, 2014
TGA	August 31, 2015

ADVISORY COMMITTEE:

MANUFACTURING:

PARAMETER	DATA	REFERENCE
Manufacturer	Janssen Biotech, Inc.	

Indication	SYLVANT is an interleukin-6 (IL-6) antagonist indicated for the treatment of patients with multicentric Castleman's disease (MCD) who are human immunodeficiency virus (HIV) negative and human herpesvirus-8 (HHV-8) negative.	1
Cell Substrate	Human/murine chimeric immunoglobulin G1κ (IgG1κ) monoclonal antibody against human interleukin-6 (hIL-6) produced in a Chinese Hamster Ovary (CHO) cell line.	3
Manufacturing platform	Siltuximab active substance Final Bulk (FB) is manufactured in a 9-stage process. Briefly, the active substance is obtained by several purification steps (protein A, cation exchange and anion exchange chromatography) from the harvests of one or more CHO cell line bioreactor culture(s). The FB is stored frozen at -40 °C until further processing into the final lyophilized product.	3
Dose in vial/final container	• 100 mg of lyophilized powder in a single-use vial. • 400 mg of lyophilized powder in a single-use vial	1
Dose to patient	Administer as an 11 mg/kg dose given over 1 hour by intravenous infusion every 3 weeks.	1

1. Package insert - SYLVANT
2. EPAR full - SYLVANT
3. EPAR quality - Sylvant: EPAR - Public assessment report
4. FDA Review - SYLVANT (siltuximab)

CLINICAL TRIALS:

NCT	TRIAL PHASE	NO OF PATIENTS ENROLLED	TITLE	COUNTRIES
Summary of clinical studies in patients with Castleman's Disease				
NCT01024036	2	79	A Study to Evaluate the Efficacy and Safety of CNTO328 Plus Best Supportive Care in	United States, Australia, China, Belgium, Brazil, Canada, Egypt, France, Hong Kong, Germany,

			Multicentric Castleman's Disease	Hungary, India, Israel, Korea, Republic of, Norway, Malaysia, Spain, Netherlands, New Zealand, Russian Federation, Taiwan, Singapore, United Kingdom
NCT00412321	1	67	A Safety and Efficacy Study of CNTO 328 in Patients with B-Cell Non-Hodgkin's Lymphoma, Multiple Myeloma, or Castleman's Disease	United States
NCT01400503	2	60	A Study to Evaluate the Safety of Long-term Treatment with Siltuximab in Patients with Multicentric Castleman's Disease	United States, Belgium, Brazil, Canada, China, Egypt, France, Hong Kong, Germany, Israel, Korea, Republic of, Norway, New Zealand, Taiwan, Singapore, United Kingdom, Spain
Summary of clinical studies in Healthy Volunteers				
NCT02074800	1	145	A Study to Assess the Safety and Pharmacokinetics of a Single Intravenous Administration of CNTO 328 Derived From 2 Different Cell Lines in Healthy Participants	United States
Summary of clinical studies in patients with Hematologic Malignancies other than Castleman's Disease				
NCT00402181	2	53	An Efficacy and Safety Study of Siltuximab in Participants with Relapsed or Refractory Multiple Myeloma	United States, Netherlands
NCT00401843	2	307	A Study of the Safety and Efficacy of CNTO 328 and Bortezomib to Bortezomib	United States, Belgium, Brazil, Bulgaria, Spain, Canada, Czechia,

			Alone in Patients with Relapsed or Refractory Multiple Myeloma	France, Germany, Greece, Hungary, Netherlands, Poland, Portugal, Romania, Russian Federation, Slovakia, United Kingdom
NCT00911859	2	118	A Study to Compare CNTO 328 (Anti-IL-6 Monoclonal Antibody) and VELCADE-Melphalan-Prednisone (VMP) with VMP Alone in Previously Untreated Multiple Myeloma Patients	United States, France, Australia, India, Israel, Korea, Republic of, Poland, Romania, Russian Federation, Singapore, Spain
NCT01219010	1	30	A Study Evaluating the Effects of Siltuximab on the Heart in Patients with Monoclonal Gammopathy of Undetermined Significance, Smoldering Multiple Myeloma, or Indolent Multiple Myeloma	United States, Belgium, Russian Federation
NCT01513317	2	76	A Study Comparing Siltuximab Plus Best Supportive Care to Placebo Plus Best Supportive Care in Anemic Patients with International Prognostic Scoring System Low- or Intermediate-1-Risk Myelodysplastic Syndrome	United States, Belgium, Australia, Russian Federation, Spain, Netherlands, Sweden
NCT01309412	1	9	A Phase 1 Study of CNTO 328 (Siltuximab) in Relapsed or Refractory Multiple Myeloma	Japan
Summary of clinical studies in patients with Solid Tumors				
NCT00265135	1, 2	68	A Study of CNTO 328 in Subjects with Metastatic Renal Cell Carcinoma	Czech Republic, France, Netherlands, United Kingdom
NCT00401765	1	40	A Study of CNTO 328 in Patients with Metastatic	United States

			Hormone-Refractory Prostate Cancer	
NCT00841191	1, 2	84	A Safety, Efficacy and Pharmacokinetic Study of Siltuximab (CNTO 328) in Participants with Solid Tumors	United States, Belgium, France, Spain, United Kingdom
NCT00385827	2	106	A Safety and Efficacy Study of Siltuximab (CNTO 328) in Male Subjects with Metastatic Hormone-Refractory Prostate Cancer (HRPC)	United States, Belgium, Austria, France, Spain, Germany, United Kingdom

POST APPROVAL CHANGES

DATE	TYPE OF CHANGE	DESCRIPTION	LINK