Pricing of Monoclonal Antibody Therapies: Higher If Used for Cancer?

Inmaculada Hernandez, PharmD, PhD; Samuel W. Bott, BS; Anish S. Patel, BS; Collin G. Wolf, BS; Alexa R. Hospodar, BS; Shivani Sampathkumar, BS; and William H. Shrank, MD, MSHS

ABSTRACT

OBJECTIVES: The rising prices of specialty drugs have prompted a debate about how medications are priced. With the average price of cancer drugs doubling in the last decade, the unsustainability of drug prices is especially concerning in oncology and hematology. The objective of this study was to compare the prices of monoclonal antibodies (mAbs) approved in the last 20 years by the FDA across disease states.

STUDY DESIGN: We identified all indications approved by the FDA for mAbs from 1997 to 2016 and calculated the annual price of 1-year treatment for each mAb–indication combination as the product of the US average wholesale price per milligram and the recommended dose.

METHODS: We compared the annual price of treatment with each mAb across disease states using generalized linear models with gamma distribution and log link, controlling for route of administration, chemical structure, source, and time since FDA approval.

RESULTS: The average annual price of a mAb was $96,731, exceeding $100,000 for 34 mAb–indication combinations. Oncology and hematology mAbs represented 40% of the mAb–indication combinations approved, yet they accounted for more than 85% of those priced $100,000 or higher. After adjusting for factors that can affect production costs, the annual price of oncology or hematology mAbs was $149,622 higher than those used in cardiovascular or metabolic disorders; $98,981 higher than in immunology; $128,856 higher than in infectious diseases or allergy; and $106,830 higher than in ophthalmology (all P <.001).

CONCLUSIONS: The annual price of mAb therapies is about $100,000 higher in oncology and hematology than in other disease states.

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The unsustainable rising prices of specialty drugs have prompted a debate about how medications are priced. Manufacturers contend that high prices are essential to recoup research and development costs; however, a growing societal chorus believes that manufacturers are maximizing profits at the expense of patients and the healthcare system. Concerns about drug pricing policies are amplified in oncology and hematology,[1-6] where vulnerable patients and their families often have unrealistic expectations about the value of treatment.[7] Of note, the mean price of a cancer drug has doubled in the last decade, and targeted therapies represent an important driver of this increase.[1,7,8] In this study, we compared the annual price of monoclonal antibody (mAb) therapies approved in the last 20 years by the FDA across disease states. Specifically, we evaluated whether the prices were higher for mAbs used in cancer than for those used in other disease states. We limited our analysis to mAbs to minimize the potential impact of varying production costs among different types of molecules.

METHODS

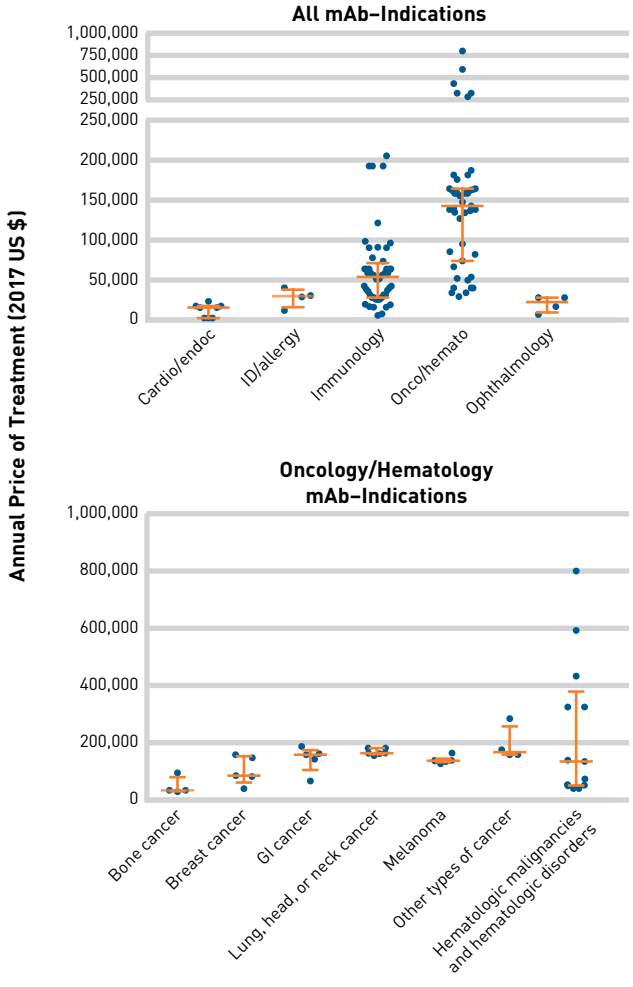
Study Design

We identified all indications approved by the FDA for mAbs from 1997 to 2016 using the FDA website.[9] After excluding radioactive mAb–indication combinations (n = 1), antidotes (n = 1), and those approved for diagnostic purposes (n = 3), withdrawn from the market by 2016 (n = 2), or not available to the public for other reasons (n = 2), our sample included 107 unique mAb–indication combinations (**eAppendix Table 1** [eAppendices available at **ajmc.com**]). From the FDA-approved label of each mAb, we extracted the recommended dose for each indication, chemical structure (whole mAb, antigen-binding fragment antibody, or other), source (human, humanized, chimeric, or murine), and route of administration (subcutaneous, intravenous, intramuscular, or intraocular). We categorized indications into 5 disease states: oncology or hematology, cardiology

TAKEAWAY POINTS

- The average price of a cancer drug has doubled in the last decade, and targeted therapies represent an important driver of that increase.
- We identified all monoclonal antibody (mAb) therapies approved by the FDA in the last 20 years and compared their annual price across disease states.
- Oncology and hematology mAbs represented 40% of the mAb–indication combinations approved, yet they accounted for more than 85% of those priced $100,000 or higher. With a median annual price of $142,833, the annual price of mAbs used in oncology or hematology was about $100,000 higher than those used in other disease states.

FIGURE. Annual Price of Treatment for mAb–Indications Approved by the FDA in 1997-2016, by Disease State[a]



Cardio/endoc indicates cardiology or endocrinology; ID, infectious diseases; GI, gastrointestinal; mAb, monoclonal antibody; onco/hemato, oncology or hematology.

[a]Cardiology and endocrinology included mAbs approved for the treatment of atherosclerotic cardiovascular disease, hypercholesterolemia, and metabolic bone disease; immunology included mAbs approved for autoimmune disorders and prevention of organ transplant rejection; and hematology included mAbs approved for hematologic malignancies and other hematologic disorders, including paroxysmal nocturnal hemoglobinuria and atypical hemolytic uremic syndrome. Overlapped bars show the median and interquartile range of the annual price of treatment.

or endocrinology, immunology, infectious diseases or allergy, and ophthalmology. We further classified oncology and hematology indications into 7 categories: bone cancer; breast cancer; gastrointestinal cancer; lung, head, or neck cancer; melanoma; hematologic malignancies and hematologic disorders; and other types of cancer, which included glioblastoma, metastatic renal cell carcinoma, urothelial carcinoma, and neuroblastoma (details in **Figure**).

Endpoints

We extracted the US average wholesale price per milligram as of January 2017 from UpToDate[10] and calculated the annual price of treatment for a standard patient—a 70-kg/1.80-m adult, a 40-kg patient in the case of mAb–indication combinations approved for juvenile conditions (ie, with childhood onset), or a 4.5-kg infant for mAb–indication combinations used in pediatrics (ie, for diseases that occur in the first weeks of life)—for each mAb–indication combination as the product of the recommended dose for 1 year of treatment and the price per milligram. We used lower-bound values for the weight of a standard patient because dosing is based on weight only for some mAbs, so using a higher value would increase the probability of type I error when comparing prices of mAbs that require dose adjustment with those that do not.

Statistical Analysis

We constructed generalized linear models with gamma distribution and log link to evaluate how the annual price of treatment differed across disease states. We controlled for route of administration, chemical structure, time since FDA approval, and source, all of which can affect production costs.[11] We followed the same methodology to examine how pricing of oncology and hematology mAb–indication combinations differed by type of cancer or hematologic disorder. All analyses were conducted at the mAb–indication combination level, meaning that for mAbs approved for more than 1 indication, each indication counted as a separate observation (details in **Table**).

RESULTS

Our sample included 107 mAb–indication combinations, with a mean (median) annual price of $96,731 ($58,968). The annual price of treatment exceeded $100,000 for 34 (32%) mAb–indication combinations and was highest for 2 indications of eculizumab ($800,280 for atypical hemolytic uremic syndrome and $592,654 for paroxysmal nocturnal hemoglobinuria) and lowest for denosumab, which is indicated for fracture prevention ($2465) (eAppendix Table 1). The annual price of treatment was highest for mAbs

used in oncology or hematology (median, $142,833; interquartile range [IQR], $73,920-$164,291], followed by immunology (median, $53,969; IQR, $28,056-$68,770) (Figure and **eAppendix Table 2**). Of 43 oncology and hematology mAb–indication combinations, 29 (67%) were priced higher than $100,000 per year of treatment. Although oncology and hematology mAb–indication combinations represented only 40% of all mAb–indication combinations approved in the last 20 years (43 of 107), they accounted for more than 85% of those priced $100,000 or higher (29 of 34). Within oncology and hematology indications, the annual price of treatment was highest for mAbs indicated for types of cancer delineated as "other," which included glioblastoma, metastatic renal cell carcinoma, urothelial carcinoma, and neuroblastoma (median, $167,152; IQR, $158,456-$230,225), followed by lung, head, or neck cancer (median, $163,746; IQR, $162,086-$181,417).

After adjusting for route of administration, source, chemical structure, and time since FDA approval, the annual price of oncology or hematology mAbs was $149,622 higher than those used in cardiovascular or metabolic disorders; $98,981 higher than in immunology; $128,856 higher than in infectious diseases or allergy; and $106,830 higher than in ophthalmology (all P <.001) (Table). Other than disease state, the chemical structure of a mAb was the only factor significantly associated with pricing. In subgroup analysis, we found no significant differences in prices of mAbs by type of cancer or hematologic disorder, which was probably due to the small sample size of each group, as well as the large price variability of hematology mAbs.

TABLE. Adjusted Differences in the Annual Price of Treatment of Drug Indications Approved by the FDA for mAbs in 1997-2016[a]

	Annual Price of Treatment ($)	
All Drug Indications	**Difference in Means**	***P***
Indication: disease state		
Oncology/hematology[b]	Ref	
Cardiology/endocrinology[c]	**–149,622**	**<.001**
Immunology[d]	**–98,981**	**<.001**
Infectious diseases/allergy	**–128,856**	**<.001**
Ophthalmology	**–106,830**	**<.001**
Route of administration		
Intravenous	Ref	
Subcutaneous	26,688	.536
Structure		
Whole mAb	Ref	
Antigen-binding fragment	–25,610	.324
Other[e]	**363,636**	**.006**
Source		
Human	Ref	
Humanized	4621	.879
Chimeric or murine	–55,363	.065
Time since FDA approval, per year[f]	–2914	.178

(continued)

DISCUSSION

Our analysis is the first to compare the price of mAbs approved by the FDA in the last 20 years across disease states. Our results document the high prices of this type of medication; with an average price of $96,731, the annual price of treatment exceeded $100,000 for 32% of 107 mAb–indication combinations approved by the FDA between 1997 and 2016. Oncology and hematology mAbs represented 40% of the combinations approved, yet they accounted for more than 85% of those priced $100,000 or higher. After adjusting for factors that can affect production costs, we found that mAb therapies approved for the treatment of cancer and hematologic disorders are around $100,000 per year of treatment more expensive than mAbs used in other disease states.

Higher prices for mAbs used in oncology and hematology may be explained by multiple factors. First, in order to recover development costs, manufacturers set higher prices for drugs used for a short period of time or for drugs indicated in rare conditions. This likely explains why the 2 most expensive mAb–indication combinations were those with eculizumab, originally approved for paroxysmal nocturnal hemoglobinuria, which affects only 5000 patients in the United States.[12] In addition, duration of treatment is usually shorter in cancer, where drugs are commonly used for weeks or months, than in other disease states where drugs may be used for years. Second, the therapeutic arsenal available for the treatment of some types of cancer and hematologic disorders is narrower than in other disease states, which makes patients and providers less responsive to the prices of these medications. Third, payers have limited levers to restrict access to, and hence lower prices for, cancer drugs.[6,13] This is because Medicare Part D plans are required to include all cancer drugs in their formularies and some states also mandate the coverage of cancer drugs by private insurers.[6,14]

Limitations

This study was designed to describe patterns in pricing and did not aim to assess the process manufacturers apply when determining the asking price for their medications. Moreover, our study did not attempt to assess the value of the agents studied in terms of cost-effectiveness or clinical outcomes. In addition, our study did not evaluate the pricing of targeted therapies other than mAbs, and we used average wholesale prices, which do not account for manufacturers' rebates. Nevertheless, this does not invalidate our results because the objective of our study was not to estimate net drug prices after discounts but to compare prices across disease states, and rebates should not differ across disease states.

TABLE. *(continued)* Adjusted Differences in the Annual Price of Treatment of Drug Indications Approved by the FDA for mAbs in 1997-2016[a]

Oncology/Hematology mAb–Indication Combinations	Annual Price of Treatment ($)	
	Difference in Means	*P*
Indication: type of cancer		
Hematology[g]	Ref	
Bone	−140,705	.055
Breast	−102,707	.196
Gastrointestinal	−49,022	.532
Lung, head, or neck	−28,544	.704
Melanoma	−51,267	.499
Other[h]	12,146	.890
Route of administration		
Intravenous	Ref	
Subcutaneous	−79,419	.069
Structure		
Whole mAb	Ref	
Other[e]	**279,088**	**.022**
Source		
Human	Ref	
Humanized	3935	.923
Chimeric or murine	−52,042	.210
Time since FDA approval, per year	−414	.930

mAb indicates monoclonal antibody; ref, reference group.
[a]Results show marginal effects of each covariate at the median level and were obtained from generalized linear models with gamma distribution and log link, which included all covariates listed here. All analyses were conducted at the mAb–indication combination level because the outcome variable (the annual price of treatment) was calculated as the product of the price per milligram and the standard dose for a 1-year treatment for each indication, which varies across indications (eAppendix Table 1). For this reason, the units of observation (mAb–indication combinations) were independent data. **Bold** denotes statistically significant results at $P < .05$.
[b]Oncology and hematology indications included solid tumors, hematologic malignancies, and other hematologic disorders, including paroxysmal nocturnal hemoglobinuria and atypical hemolytic uremic syndrome.
[c]Cardiology and endocrinology indications included atherosclerotic cardiovascular disease, hypercholesterolemia, and metabolic bone disease.
[d]Immunology indications included autoimmune disorders and prevention of organ transplant rejection.
[e]Other structures included bi-specific T-cell engagers and antibody–drug conjugates.
[f]Time since FDA approval was calculated as the difference between the date of first approval of each molecule and December 31, 2016.
[g]Hematology indications included hematologic malignancies and other hematologic disorders, including paroxysmal nocturnal hemoglobinuria and atypical hemolytic uremic syndrome.
[h]Other types of cancer included glioblastoma, metastatic renal cell carcinoma, urothelial carcinoma, and neuroblastoma.

CONCLUSIONS

Despite these limitations, our study has important implications. At a time when healthcare resources are constrained and threaten state and federal budgets, the rapidly rising costs of prescription drugs, specialty drugs in particular, will continue to garner media and policy attention.[7] In the absence of some type of value framework where prices are justified by the value they bring to specific patients or the population, attention to drug pricing is likely to grow. There may be a unique opportunity for clinical experts and manufacturers to collaborate and redefine how the value of pharmaceuticals is measured and fundamentally shift the way manufacturers are reimbursed for high-cost medications like mAbs.[5,15-17] ■

Author Affiliations: Department of Pharmacy and Therapeutics, School of Pharmacy, University of Pittsburgh (IH, SWB, ASP, CGW, ARH, SS), Pittsburgh, PA; Insurance Division, University of Pittsburgh Medical Center (WHS), Pittsburgh, PA.

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Address Correspondence to: Inmaculada Hernandez, PharmD, PhD, Department of Pharmacy and Therapeutics, School of Pharmacy, University of Pittsburgh, 3501 Terrace St, Pittsburgh, PA 15261. Email: inh3@pitt.edu.

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eAppendix Table 1. Drug–Indications Approved by the FDA for Monoclonal Antibodies in 1997-2016[a]

Generic Name	Brand Name	Type	Source	Target	Indication	Disease State	Route of Administration	FDA Approval Date	Price per mg ($)	Annual Price Treatment ($)
Rituximab	Rituxan	mab	Chimeric	CD20	Non-Hodgkin lymphoma	Oncology/ Hematology	IV	11/26/1997	9.64	52,056
Rituximab	Rituxan	mab	Chimeric	CD20	Chronic lymphocytic leukemia	Oncology/ Hematology	IV	11/26/1997	9.64	49,887
Rituximab	Rituxan	mab	Chimeric	CD20	Rheumatoid arthritis	Immunology	IV	11/26/1997	9.64	38,560
Rituximab	Rituxan	mab	Chimeric	CD20	Granulomatosis with polyangiitis and microscopic polyangiitis	Immunology	IV	11/26/1997	9.64	26,028
Basiliximab	Simulect	mab	Chimeric	CD25	Prevention of organ transplant rejections in renal transplantation	Immunology	IV	5/12/1998	194.00	7760
Palivizumab	Synagis	mab	Humanized	Respiratory syncytial virus	Prevention) of respiratory syncytial virus disease	ID/Allergy	Intramuscular	6/19/1998	35.25	11,897
Infliximab	Remicade	mab	Chimeric	TNF-α	Ankylosing Spondylitis	Immunology	IV	8/24/1998	13.36	37,408
Infliximab	Remicade	mab	Chimeric	TNF-α	Crohn's disease	Immunology	IV	8/24/1998	13.36	28,056
Infliximab	Remicade	mab	Chimeric	TNF-α	Pediatric Crohn's disease	Immunology	IV	8/24/1998	13.36	16,032
Infliximab	Remicade	mab	Chimeric	TNF-α	Psoriatic arthritis	Immunology	IV	8/24/1998	13.36	28,056
Infliximab	Remicade	mab	Chimeric	TNF-α	Rheumatoid arthritis	Immunology	IV	8/24/1998	13.36	16,834
Infliximab	Remicade	mab	Chimeric	TNF-α	Ulcerative colitis	Immunology	IV	8/24/1998	13.36	28,056
Infliximab	Remicade	mab	Chimeric	TNF-α	Pediatric ulcerative colitis	Immunology	IV	8/24/1998	13.36	16,032
Trastuzumab	Herceptin	mab	Humanized	HER2/neu	HER2 overexpressing breast cancer	Oncology/ Hematology	IV	9/25/1998	11.07	82,139
Trastuzumab	Herceptin	mab	Humanized	HER2/neu	HER2 overexpressing gastric cancer	Oncology/ Hematology	IV	9/25/1998	11.07	66,641
Daclizumab	Zenapax	mab	Humanized	CD25	Prevention of organ transplant rejections	Immunology	SQ	12/10/1998	54.67	19,135
Adalimumab	Humira	mab	Human	TNF-α	Rheumatoid arthritis	Immunology	SQ	12/31/2002	61.46	63,914
Adalimumab	Humira	mab	Human	TNF-α	Crohn's disease	Immunology	SQ	12/31/2002	61.46	63,914
Adalimumab	Humira	mab	Human	TNF-α	Plaque psoriasis	Immunology	SQ	12/31/2002	61.46	63,914
Adalimumab	Humira	mab	Human	TNF-α	Psoriatic arthritis	Immunology	SQ	12/31/2002	61.46	63,914
Adalimumab	Humira	mab	Human	TNF-α	Ankylosing spondylitis	Immunology	SQ	12/31/2002	61.46	63,914
Adalimumab	Humira	mab	Human	TNF-α	Juvenile idiopathic arthritis	Immunology	SQ	12/31/2002	61.46	63,914
Omalizumab	Xolair	mab	Humanized	IgE Fc region	Allergic asthma	ID/Allergy	SQ	6/20/2003	7.87	28,922
Omalizumab	Xolair	mab	Humanized	IgE Fc region	Chronic idiopathic urticaria	ID/Allergy	SQ	6/20/2003	7.87	30,693
eAppendix Table 1 continued										

Generic Name	Brand Name	Type	Source	Target	Indication	Therapeutic Area of Indication	Route of Administration	FDA Approval Date	Price per mg ($)	Price Annual Treatment ($)
Bevacizumab	Avastin	mab	Humanized	VEGF-A	Metastatic colorectal cancer	Oncology/ Hematology	IV	2/26/2004	8.71	158,456
Bevacizumab	Avastin	mab	Humanized	VEGF-A	Non-small cell lung cancer	Oncology/ Hematology	IV	2/26/2004	8.71	155,408
Bevacizumab	Avastin	mab	Humanized	VEGF-A	Metastatic breast cancer	Oncology/ Hematology	IV	2/26/2004	8.71	158,456
Bevacizumab	Avastin	mab	Humanized	VEGF-A	Glioblastoma	Oncology/ Hematology	IV	2/26/2004	8.71	158,456
Bevacizumab	Avastin	mab	Humanized	VEGF-A	Metastatic renal cell carcinoma	Oncology/ Hematology	IV	2/26/2004	8.71	158,456
Ranibizumab	Lucentis	Fab	Humanized	VEGF-A	Age-related macular degeneration	Ophthalmology	Intraocular	6/30/2006	4680.00	28,080
Ranibizumab	Lucentis	Fab	Humanized	VEGF-A	Macular edema following retinal vein occlusion	Ophthalmology	Intraocular	6/30/2006	4680.00	28,080
Ranibizumab	Lucentis	Fab	Humanized	VEGF-A	Diabetic macular edema	Ophthalmology	Intraocular	6/30/2006	4680.00	16,848
Ranibizumab	Lucentis	Fab	Humanized	VEGF-A	Myopic choroidal neovascularization	Ophthalmology	Intraocular	6/30/2006	4680.00	7020
Panitumumab	Vectibix	mab	Human	EGFR	Metastatic colorectal cancer	Oncology/ Hematology	IV	9/27/2006	13.08	142,834
Eculizumab	Soliris	mab	Humanized	C-5	Paroxysmal nocturnal hemoglobinuria	Oncology/ Hematology	IV	3/16/2007	25.65	592,654
Eculizumab	Soliris	mab	Humanized	C-5	Atypical hemolytic uremic syndrome	Oncology/ Hematology	IV	3/16/2007	25.65	800,280
Certolizumab pegol	Cimzia	Fab	Humanized	TNF-α	Crohn's disease	Immunology	SQ	4/22/2008	10.53	58,968
Certolizumab pegol	Cimzia	Fab	Humanized	TNF-α	Psoriatic arthritis	Immunology	SQ	4/22/2008	10.53	58,968
Certolizumab pegol	Cimzia	Fab	Humanized	TNF-α	Ankylosing spondylitis	Immunology	SQ	4/22/2008	10.53	58,968
Golimumab	Simponi	mab	Human	TNF-α	Psoriatic arthritis	Immunology	SQ	4/24/2009	52.59	31,554
Golimumab	Simponi	mab	Human	TNF-α	Rheumatoid arthritis	Immunology	SQ	4/24/2009	52.59	31,554
Golimumab	Simponi	mab	Human	TNF-α	Ulcerative colitis	Immunology	SQ	4/24/2009	52.59	73,626
Canakinumab	Ilaris	mab	Human	IL-1	Cryopyrin-associated periodic syndromes	Immunology	SQ	6/17/2009	107.03	96,327
Canakinumab	Ilaris	mab	Human	IL-1	Tumor necrosis factor receptor associated periodic syndrome	Immunology	SQ	6/17/2009	107.03	192,654
Canakinumab	Ilaris	mab	Human	IL-1	Familial Mediterranean fever	Immunology	SQ	6/17/2009	107.03	192,654
Canakinumab	Ilaris	mab	Human	IL-1	Systemic juvenile idiopathic arthritis	Immunology	SQ	6/17/2009	107.03	205,498
eAppendix Table 1 continued										

Generic Name	Brand Name	Type	Source	Target	Indication	Therapeutic Area of Indication	Route of Administration	FDA Approval Date	Price per mg ($)	Price Annual Treatment ($)
Ustekinumab	Stelara	mab	Human	IL-12, IL-23	Psoriatic arthritis	Immunology	SQ	9/25/2009	235.74	42,433
Ofatumumab	Arzerra	mab	Human	CD20	Chronic lymphocytic leukemia	Oncology/ Hematology	IV	10/26/2009	6.25	139,375
Tocilizumab	Actemra	mab	Humanized	IL-6 receptor	Rheumatoid arthritis	Immunology	IV	1/8/2010	5.43	19,765
Denosumab	Prolia	mab	Human	RANKL	Post-menopausal osteoporosis	Cardiology/ Endocrinology	SQ	6/1/2010	20.54	2465
Denosumab	Prolia	mab	Human	RANKL	Fracture prevention in men receiving androgen deprivation therapy for prostate cancer	Cardiology/ Endocrinology	SQ	6/1/2010	20.54	2465
Denosumab	Prolia	mab	Human	RANKL	Fracture prevention in women receiving aromatase inhibitor therapy for breast cancer	Cardiology/ Endocrinology	SQ	6/1/2010	20.54	2465
Denosumab	Xgeva	mab	Human	RANKL	Bone metastases from solid tumors	Oncology/ Hematology	SQ	6/1/2010	20.35	29,303
Denosumab	Xgeva	mab	Human	RANKL	Giant cell tumor of bone	Oncology/ Hematology	SQ	6/1/2010	20.35	34,187
Denosumab	Xgeva	mab	Human	RANKL	Hypercalcemia of malignancy	Oncology/ Hematology	SQ	6/1/2010	20.35	34,187
Belimumab	Benlysta	mab	Human	BAFF	Systemic lupus erythematosus	Immunology	IV	3/9/2011	4.92	51,645
Ipilimumab	Yervoy	mab	Human	CTLA-4	Melanoma	Oncology/ Hematology	IV	3/25/2011	164.64	138,304
Brentuximab	Adcetris	ADC	Chimeric	CD-30	Hodgkin lymphoma	Oncology/ Hematology	IV	8/19/2011	151.87	325,310
Brentuximab	Adcetris	ADC	Chimeric	CD-30	Systemic anaplastic large cell lymphoma	Oncology/ Hematology	IV	8/19/2011	151.87	325,310
Pertuzumab	Perjeta	mab	Humanized	HER2/neu	HER2+ metastatic breast cancer	Oncology/ Hematology	IV	6/8/2012	12.72	85,478
Pertuzumab	Perjeta	mab	Humanized	HER2/neu	HER2+ early stage breast cancer	Oncology/ Hematology	IV	6/8/2012	12.72	40,068
Trastuzumab	Kadcyla	mab	Humanized	HER2/neu	HER+ metastatic breast cancer	Oncology/ Hematology	IV	2/22/2013	33.78	147,551
Tocilizumab	Actemra	mab	Humanized	IL-6 receptor	Rheumatoid arthritis	Immunology	SQ	10/21/2013	6.16	25,946
Tocilizumab	Actemra	mab	Humanized	IL-6 receptor	Systemic juvenile idiopathic arthritis	Immunology	SQ	10/21/2013	6.16	51,251
Obinutuzumab	Gazyva	mab	Humanized	CD20	Chronic lymphocytic leukemia	Oncology/ Hematology	IV	11/1/2013	6.72	53,760
Obinutuzumab	Gazyva	mab	Humanized	CD20	Follicular lymphoma	Oncology/ Hematology	IV	11/1/2013	6.72	73,920
eAppendix Table 1 continued										

Generic Name	Brand Name	Type	Source	Target	Indication	Therapeutic Area of Indication	Route of Administration	FDA Approval Date	Price per mg ($)	Price Annual Treatment ($)
Siltuximab	Sylvant	mab	Chimeric	IL-6	Multicentric Castleman's disease	Oncology/ Hematology	IV	4/23/2014	10.29	134,773
Vedolizumab	Entyvio	mab	Humanized	Integrin receptor	Ulcerative colitis	Immunology	IV	5/20/2014	20.84	56,292
Vedolizumab	Entyvio	mab	Humanized	Integrin receptor	Crohn's disease	Immunology	IV	5/20/2014	20.84	56,292
Pembrolizumab	Keytruda	mab	Humanized	PD-1	Melanoma	Oncology/ Hematology	IV	9/4/2014	53.36	126,992
Pembrolizumab	Keytruda	mab	Humanized	PD-1	Non-small cell lung cancer	Oncology/ Hematology	IV	9/4/2014	53.36	181,417
Pembrolizumab	Keytruda	mab	Humanized	PD-1	Head and neck cancer	Oncology/ Hematology	IV	9/4/2014	53.36	181,417
Alemtuzumab	Lemtrada	mab	Humanized	CD52	Multiple sclerosis	Immunology	IV	11/14/2014	2,024.38	121,463
Blinatumomab	Blincyto	BiTE	Murine	CD-19 and CD3	B-cell acute lymphoblastic leukemia	Oncology/ Hematology	IV	12/3/2014	114,318.85	432,925
Nivolumab	Opdivo	mab	Human	PD-1	Melanoma	Oncology/ Hematology	IV	12/22/2014	30.09	164,291
Secukinumab	Cosentyx	mab	Human	IL-17A	Plaque psoriasis	Immunology	SQ	1/21/2015	16.26	78,038
Dinutuximab	Unituxin	mab	Chimeric	GD-2	Pediatric patients at high risk of neuroblastoma	Oncology/ Hematology	IV	3/10/2015	564.68	284,602
Alirocumab	Praluent	mab	Human	PCSK9	Heterozygous familial hypercholesterolemia	Cardiology/ Endocrinology	SQ	7/24/2015	8.96	17,472
Alirocumab	Praluent	mab	Human	PCSK9	Clinical atherosclerotic cardiovascular disease	Cardiology/ Endocrinology	SQ	7/24/2015	8.96	17,472
Evolocumab	Repatha	mab	Human	PCSK9	Heterozygous familial hypercholesterolemia	Cardiology/ Endocrinology	SQ	8/27/2015	4.65	15,624
Evolocumab	Repatha	mab	Human	PCSK9	Clinical atherosclerotic cardiovascular disease	Cardiology/ Endocrinology	SQ	8/27/2015	4.65	15,624
Evolocumab	Repatha	mab	Human	PCSK9	Homozygous familial hypercholesterolemia	Cardiology/ Endocrinology	SQ	8/27/2015	4.65	23,436
Mepolizumab	Nucala	mab	Humanized	IL-5	Severe asthma	Immunology	SQ	11/4/2015	30.90	40,170
Daratumumab	Darzalex	mab	Human	CD-38	Multiple myeloma	Oncology/ Hematology	IV	11/16/2015	5.55	136,752
Necitumumab	Portrazza	mab	Human	EGFR	Non-small cell lung cancer	Oncology/ Hematology	IV	11/24/2015	6.00	163,200
Elotuzumab	Empliciti	mab	Humanized	SLAMF7	Multiple myeloma	Oncology/ Hematology	IV	11/30/2015	7.10	134,266
Ixekizumab	Talz	mab	Humanized	IL-17A	Plaque psoriasis	Immunology	SQ	3/22/2016	67.03	91,168
Reslizumab	Conqair	mab	Humanized	IL-5	Severe asthma	ID/Allergy	IV	3/23/2016	10.02	40,381
Atezolizumab	Tecentriq	mab	Humanized	PD-L1	Urothelial carcinoma	Oncology/ Hematology	IV	5/18/2016	8.62	175,848
eAppendix Table 1 continued										

Generic Name	Brand Name	Type	Source	Target	Indication	Therapeutic Area of Indication	Route of Administration	FDA Approval Date	Price per mg ($)	Price Annual Treatment ($)
Ustekinumab	Stelara	mab	Human	IL-12, IL-23	Crohn's disease	Immunology	IV	9/23/2016	14.77	5,760
Olaratumab	Lartruvo	mab	Human	PDGFR-α	Soft tissue sarcoma	Oncology/ Hematology	IV	10/29/2016	5.66	95,088

ADC indicates antibody-drug conjugates; BiTE, bi-specific T-cell engagers; Fab, antigen-binding fragment antibody; ID, infectious diseases; IV, intravenous; mab, monoclonal antibody; SQ, subcutaneous.

[a]Data are sorted by FDA approval date.

eAppendix Table 2. Summary Statistics for the Annual Price of Treatment for Drug–Indications Approved by the FDA for Monoclonal Antibodies in 1997-2016

	Annual Price of Treatment ($)			
Indication	**Median**	**IQR**	**Minimum**	**Maximum**
Oncology/Hematology[a] (n = 43)	142,833	73,920-164,291	29,303	800,280
Hematology[b] (n = 13)	134,773	52,056-325,310	40,302	800,280
Bone (n = 4)	34,187	34,745-64,638	29,303	95,088
Breast (n = 5)	85,478	82,139-147,551	40,068	158,456
GI (n = 5)	158,456	142,834-162,086	66,641	187,242
Lung, head, or neck (n = 6)	163,746	162,086-181,417	155,408	181,417
Melanoma (n = 6)	137,528	134,266-138,306	126,992	164,291
Other[c] (n = 4)	167,152	158,456-230,225	158,456	284,602
Cardiology/Endocrinology[d] (n = 8)	15,624	2465-17,472	2465	23,436
Immunology[e] (n = 48)	53,969	28,056-68,770	5760	205,498
ID/Allergy (n = 4)	29,808	20,410-35,537	11,897	40,381
Ophthalmology (n = 4)	22,464	11,934-28,080	7020	28,080

GI indicates gastrointestinal; ID, infectious diseases; IQR, interquartile range.

[a]Oncology and hematology indications include solid tumors, hematologic malignancies, and other hematologic disorders, including paroxysmal nocturnal hemoglobinuria and atypical hemolytic uremic syndrome.

[b]Hematology indications include hematologic malignancies, and other hematologic disorders, including paroxysmal nocturnal hemoglobinuria and atypical hemolytic uremic syndrome.

[c]Other types of cancer included glioblastoma, metastatic renal cell carcinoma, urothelial carcinoma, and neuroblastoma.

[d]Cardiology and endocrinology indications included atherosclerotic cardiovascular disease, hypercholesterolemia, and metabolic bone disease.

[e]Immunology indications included autoimmune disorders, and prevention of organ transplant rejection.