2019 SPECIALTY DRUG TRENDS

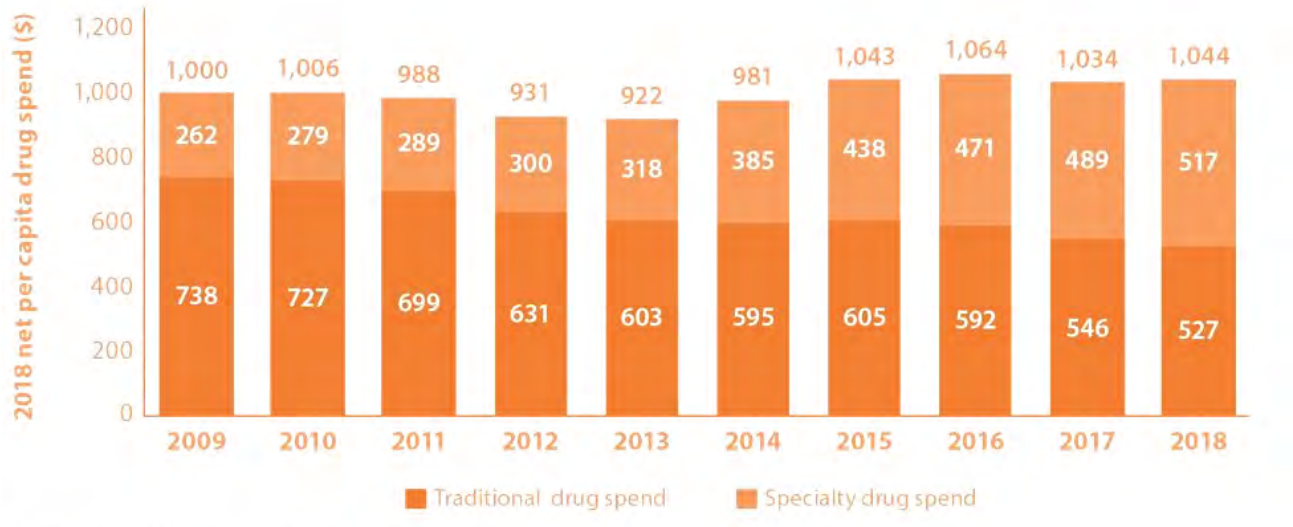
AMS
INTELLIGENT ANALYTICS

TREND HIGHLIGHTS

- 36 specialty drugs added to PredictRx
  - 13 Orphan Drugs
  - 2 Biosimilars
  - 3 Biologics
- 35 additional indications entered into PredictRx (23 unique drugs)
- 48 FDA-approved novel drugs in 2019
- Zolgensma: the most expensive drug
- Keytruda: the most viewed drug
- Feiba NF and Galafold: trending upward

DRUG SPEND

Specialty drugs are generally defined as pharmaceuticals that are classified as high-cost, high complexity, and/or high touch. Drugs that treat chronic diseases such as cancer, for instance, touch[1] upon all three criteria. In healthcare and retail pharmacy settings, the latest statistics suggest that ***specialty drugs comprise 49.5% of total spending even though they only account for about 2% of total prescription volume***. Judging from their steady increase over the years [figure 1], it would be realistic to expect that specialty pharmaceuticals would have finally surpassed traditional drugs in 2019.



Source: IQVIA, Medicine Use and Spending

[1] Medicare defines any drug for which the negotiated price is $670 per month or more as a specialty drug.

For this reason, some would argue that the moniker is a bit misleading nowadays, as a recent headline in Managed Care magazine asked: How 'Special' Are Specialty Drugs If They're Most of Drug Spending?

About 55% of specialty spend occurs under the pharmacy benefit (PBM) with the remaining 45% under the medical benefit. Whereas PBM reimbursement is easily facilitated thanks to the specific NDC codes used in billing, claims on the medical benefit side can be more challenging since they utilize HCPCS codes. Some of these "J-codes" can be problematic (i.e. the code doesn't exist or is non-specific) which can cause inaccurate billing.

On the whole, prescription drug spending is growing three times faster than inflation in the US. Americans spend about $1,200 yearly on prescriptions drugs, totaling more than $500 billion. Overall drug spend has remained flat thanks to generic drugs providing competition.

Branded drugs, on the other hand, continue to soar. According to an Express Scripts report, from Jan. 2014 through Dec. 2019 the most commonly used brand drugs experienced list price inflation of 70.5%.[2] This trend shows no signs of stopping. It is causing financial toxicity for patients who can afford to pay, and, for those who cannot, prescription rationing and avoidance.

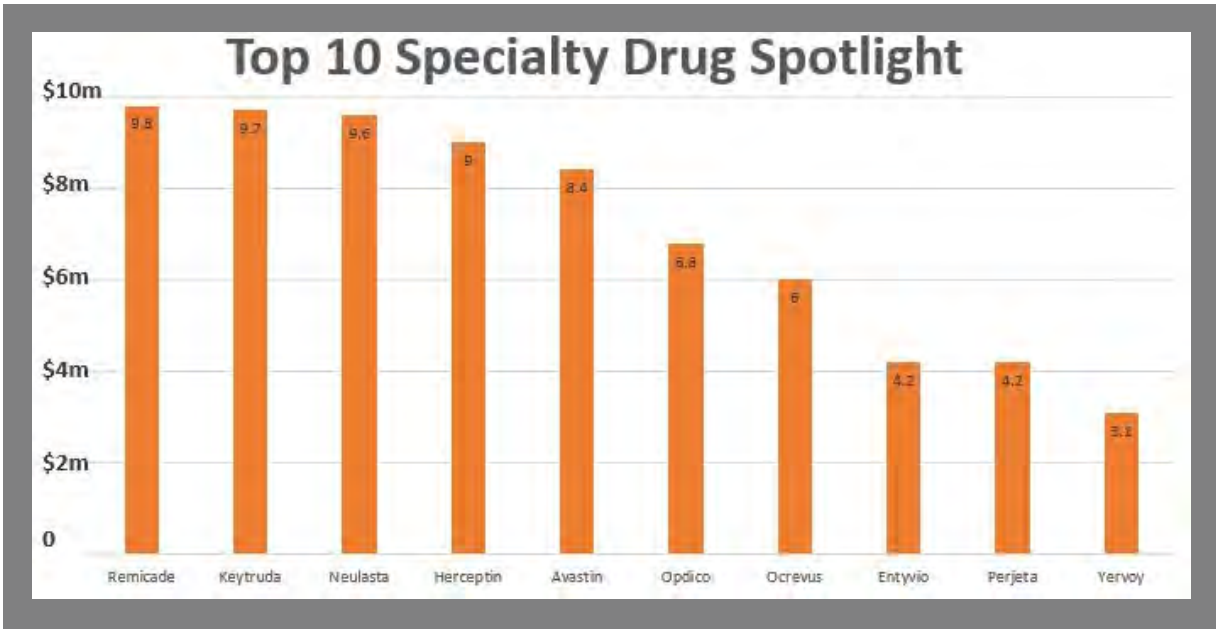
Meanwhile, despite all the tough rhetoric on Capitol Hill about lowering prescription drug prices and the bipartisan legislation meant to achieve those goals, the momentum to agree upon and pass new drug reforms eventually ground to a halt. 2019 ended in gridlock.

This situation certainly hurts consumers who are looking to their elected representatives in government to "fix healthcare." Payers, too, face issues with price transparency and costs.

Patients who use specialty medications comprise roughly ***5% of commercially insured member populations yet they account for 50% of health plan payments***. This egregious low-in-percentage[3] but high-in-dollar issue is perhaps the biggest concern that payers face. It goes straight to the heart of their payment integrity problems.

[2]https://www.express-scripts.com/corporate/drug-trend-report#2019-by-the-numbers
[3]https://www.psgconsults.com/blog/highlights-from-the-2019-pbmi-trends-in-specialty-drug-benefits-report-specialty-drug-benefits-by-the-numbers

Based on total claims data of $25 billion in allowed charges from Aug. through Dec. 2019, Advanced Medical Strategies' FACS platform[4] spotlighted [figure 2] the Top 10 specialty drugs causing the most cost concerns for payers.



Not only should payers be aware of those high-cost pharmaceuticals, they should also be particularly mindful of drug price overspend. During that same timeframe FACS flagged [figure 3] the specialty drugs that exceeded multiple cost benchmarks (which help payers determine whether the billed prices fall within reasonable ranges and/or predict spend much more accurately for members taking those drugs).

Drug Price Overspend

HCPCS Code	Drug Name	Flagged Amount	Amount >ART	Amount > ACP	Amount > PBM
J9355	Herceptin	$38,105,928	$7,432,235	$14,379,260	$14,946,364
J2505	Neulasta	$36,136,233	$7,269,412	$12,713,986	$14,467,780
J1745	Remicade	$33,494,406	$8,082,369	$14,649,797	$18,138,743
J9299	Opdivo	$27,646,989	$5,960,542	$10,811,852	$12,752,376
J9306	Perjeta	$25,915,043	$3,650,578	$6,113,608	$6,934,618
J9035	Avastin	$25,489,974	$3,962,381	$9,738,915	$12,069,797
J9271	Keytruda	$24,279,579	$5,023,210	$10,689,466	$12,955,968
J1453	Emend Injectable	$23,108,433	$787,799	$1,338,247	$1,613,471
J2350	Ocrevus	$20,407,161	$5,545,681	$9,602,641	$11,225,425
J9045	Carboplatin	$13,474,857	$534,585	$583,298	$619,832
Total		**$256,199,704**	**$62,430,853**	**$127,843,049**	**$151,241,454**

[4] FACS (Financial and Clinical Surveillance) is a payment accuracy and clinical integrity platform that provides AI-driven insights into the costliest and most complex healthcare claims.

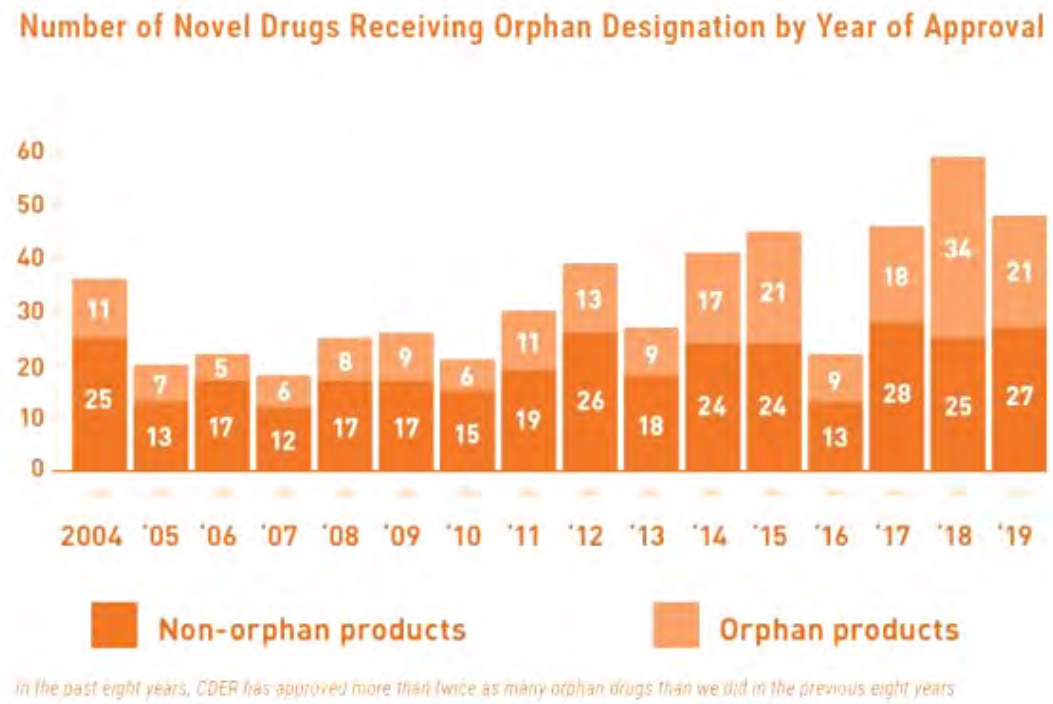
FACS data on total drug overspend revealed there is over $104 million in flagged claims. In just five months Herceptin, Neulasta, Remicade, and Keytruda respectively all topped $10 million in suspect charges pertaining to, among other issues, medical appropriateness, dosage regimens, and specialty drug coding inconsistencies.

The amount over AMS Cost Projection (ACP)[5], a benchmark of the reasonable and expected costs of a drug, surpassed $60 million. "Worse yet is the amount above ART. ART[6] is the absolute highest tolerable benchmark pertaining to allowed charges, and as a general reference point, represents close to 400% of Medicare. Even that exceedingly high threshold was exceeded by 36 million dollars!"

The impact of inappropriate drug spend, as well as drug overspend, cannot be understated. A Gartner analyst summed up it up best, writing “the combination of [predictive and prescriptive] software tools, use of data, and professional expertise provides the strongest protection against improper payments.”

THE FDA

In 2019 the FDA’s Center for Drug Evaluation and Research (CDER) approved 48 new drug therapies, 21 of which were Orphan Drugs (defined as treatments for rare diseases that affect 200,000 or fewer Americans). “Patients with rare diseases frequently have few or no drugs available to treat their condition—and for them, approvals of so-called ‘orphan’ drugs can mean new hope for an enhanced quality of life, and in some cases, survival,” CDER Director Janet Woodcock said.



[5] This AMS Proprietary benchmark is calculated using federally contracted rates for government agencies, incorporating amounts paid by any private-sector purchaser for the pharmaceutical. Discounts, rebates, chargebacks, and other fiscal adjustments are all factored into the price. Simply put, ACP is the expected cost for a particular drug dosage amount.
[6] ART represents a fiscal red line of cost tolerance. ART is the absolute maximum specialists should tolerate as allowed on a claim. Anything approaching—and certainly beyond—this price threshold should be reviewed for additional cost containment.

Analysis from a 2019 EvaluatePharma[7] report stated that "Mean orphan drug cost per patient in the US is almost 4.5 times greater than non-orphan drug cost." As we noted last year, there's a good news/bad news situation with Orphan Drugs. It is excellent news that drug companies are making investments in these rare disease therapies. However, loopholes in the Orphan Drug Act have been exploited by Big Pharma to gain lucrative exclusivity rights. Moreover, because of the huge profit margins of drugs for niche diseases, there's less incentive for pharmaceutical companies to create innovation for less profitable drugs that treat common conditions.

The FDA has also touted its efficiency to expedite the development and approval of novel drugs through various regulatory pathways. Their statistics show that 29 of the 48 novel drugs approved (60%) were designated in one or more expedited categories of Fast Track, Breakthrough, Priority Review, and/or Accelerated Approval. CDER approved 90% on the first cycle of review.

This too is a double-edged sword. Though the FDA is adamant that "safety remains our top priority," there are real concerns that safety and efficacy issues could be overlooked in their haste to quickly bring the drugs to market.

This past January an article in Chemical & Engineering News (C&EN)[8] addressed the controversy, pointing to one study showing "that just 20% of the cancer drugs that received accelerated approval between 1992 and 2017 actually prolonged survival in trials conducted after the drugs were marketed," and yet another study stating:

… the FDA often approves 80% more drugs in December than in any other month, a "desk-clearing" process that the authors say could have serious consequences for patients. 'Drugs approved in December and at month-ends are associated with significantly more adverse effects, including more hospitalizations, life-threatening incidents, and deaths,' the researchers write.

For the record, August was the busiest month in 2019 with nine approvals—there were seven in December. Month-end approvals totaled 15.

Perhaps the biggest news from the FDA this year wasn't even about one of the 48 CDER-approved drugs, but rather a Biological License Application (BLA) approval. Indicated for treatment of spinal muscular atrophy (SMA), the orphan drug—biologic, technically—Zolgensma gained immediate infamy for its staggering Wholesale Acquisition Cost (WAC) of $2.1 million per dose.

Additionally, Zolgensma joined Benlysta and Ruzurgi as notable FDA-approvals for pediatric populations. Payers should be aware that "approvals of drugs for the pediatric population have been primarily in three categories: specialty drugs, gene therapy, and chimeric antigen receptor T-cell (CAR-T) treatments. All of these treatments raise budgetary and revenue capture obstacles."[9]

[7] https://www.evaluate.com/thought-leadership/pharma/evaluatepharma-orphan-drug-report-2019
[8] https://cen.acs.org/pharmaceuticals/drug-development/new-drugs-2019/98/i3
[9] https://www.vizientinc.com/our-solutions/pharmacy-solutions/drug-price-forecast-public

COSTS

Specialty drugs are continually monitored by Advanced Medical Strategies (AMS) in their PredictRx drug database. This subscriber-based software system evaluates drug costs and dosing regimens. As of this writing, ***PredictRx is comprised of 500+ specialty pharmaceuticals with an associated 2,300 drug indications***—approximately 1,200 FDA-approved; another 1,100 are Notable Off-Label (NOL) uses.

PER DOSE - ALL: There emerged a new leader in 2019 among the Top 5 Most Expensive Specialty Drugs (Per Dose). The gene therapy ***Zolgensma is a whopping $2.4 million*** per infusion based on ACP. Though Zolgensma is only given once, payers are struggling with coverage/reimbursement decisions on the hefty one-time sum. The problem isn't going away soon. There are already drugs in the pipeline that pose similar dosing/price challenges.

Trade Name	Usage	Drug Category	Orphan Drug	ACP Dose
Zolgensma	Spinal Muscular Atrophy (SMA)	Gene Therapy	Y	$2,448,000
Kymriah	Acute Lymphoblastic Leukemia (ALL)	Antineoplastic Agent	Y	$661,063
Luxturna	Inherited Retinal Dystrophy	Adeno-associated Virus Vector-based Gene Therapy	Y	$565,906
Yescarta	Non-Hodgkin Lymphomas (NHL)	Antineoplastic Agent	Y	$519,216
Kymriah	Non-Hodgkin Lymphoma (NHL)	Antineoplastic Agent	Y	$519,108

PER DOSE - NON-ORPHAN: Since every one of the drugs above happen to be Orphan-designated here is a list of the most expensive non-Orphans per dose.

Trade Name	Usage	Drug Category	Orphan Drug	ACP Dose
Provenge	Prostate Cancer	Antineoplastic Agent	N	$78,641
Acthar (HP Acthar Gel)	Multiple Indications	Corticosteroid	N	$52,495
Yervoy	Small Cell Lung Cancer (SCLC)	Antineoplastic Agent	N	$40,908
Targretin (1% Gel)	Cutaneous T-cell Lymphoma	Antineoplastic Agent	N	$38,164
Lemtrada	Multiple Sclerosis (MS)	Disease Modifying Agent	N	$31,887

YEARLY ADULT: While the two grids above deal with drug costs on a per dose basis, the following lists pertain to ACP prices per year.

For adults, Revcovi leads the Top 5 by a wide margin, more than double the cost of the 2nd place finisher.

Trade Name	Usage	Drug Category	Orphan Drug	ACP Adult Yearly
Revcovi	Severe Combined Immune Deficiency (SCID)	Enzyme	Y	$8,265,792
Feiba NF	Routine Prophylaxis in Hemophilia A and B	Hemostatic Agent	Y	$3,353,122
Carbaglu	NAGS (N-acetylglutamate synthase) Enzyme Deficiency (Urea Cycle Disorder)	UCD (Urea Cycle Disorder) Agent	Y	$3,163,878
Exondys 51	Duchenne Muscular Dystrophy	Neurologic Agent	Y	$2,892,851
Elzonris	Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN)	Antineoplastic Agent	Y	$2,880,499

YEARLY PEDIATRIC: Payers cannot afford to overlook pediatric populations. According to a recent Sun Life report: "In 2019, members under two years old made up only about 6% of total stop-loss claims. However, they made up 26% of claims over $1M and 43% over $3M." Even though Zolgensma is the most expensive drug per dose, three other drugs eclipse even its staggering cost on a per year basis.

Trade Name	Usage	Drug Category	Orphan Drug	ACP Pediatric Yearly
Revcovi	Severe Combined Immune Deficiency (SCID)	Enzyme	Y	$3,542,482
Elzonris	Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN)	Antineoplastic Agent	Y	$2,880,499
Demser	Management of Pheochromocytoma	Cardiovascular Agent (Miscellaneous)	N	$2,569,637
Zolgensma	Spinal Muscular Atrophy (SMA)	Gene Therapy	Y	$2,448,000
Feiba NF	Routine Prophylaxis in Hemophilia A and B	Hemostatic Agent	Y	$1,788,332

COST TRENDS

Gene therapies, CAR-T therapies, and specialty drugs all continue to trend upwards in price and volume. Within PredictRx is a Drug Trend graph that tracks (and projects) quarterly pricing data based on ACP as well as ART amounts.

DOLLAR INCREASE: End of year analysis reveals Feiba NF was the biggest gainer with an ACP increase of nearly $190k during the calendar year.

Rx Drug	*Rx Drug Indication*	Adult/Pediatric	2019 $ DIFF
Feiba NF	*Routine Prophylaxis in Hemophilia A and B*	*Adult*	$189,353
Korlym	*Treatment of Cushing Syndrome*	*Adult*	$147,655
Demser	*Management of Pheochromocytoma*	*Adult/Pediatric*	$132,367
Procysbi	*Treatment of Nephropathic Cystinosis*	*Adult*	$131,317
Carbaglu	*Treatment in N-acetylglutamate synthase (NAGS) Enzyme Deficiency*	*Adult*	$119,664

PERCENTAGE INCREASE: As for which drug rose the most on a percentage basis, Galafold led the field.

Rx Drug	*Rx Drug Indication*	Adult/Pediatric	2019 % DIFF
Galafold	*Treatment of Fabry Disease (orphan drug)*	*Adult*	19.26%
Cimzia	*Multiple Indications*	*Adult*	18.57%
Trexall/Generic Methotrexate	*Multiple Indications*	*Adult*	18.39%
Sabril	*Treatment of Complex Partial Seizures*	*Adult*	15.84%
Simponi	*Multiple Indications*	*Adult*	15.40%

Though we have come to expect that specialty drugs keep escalating in price, competition from generics, more cost-effective treatment options, and other factors do contribute to price reductions as well.

DOLLAR DECREASE: Because the first and second place drugs with the biggest yearly declines (Orfadin and Clolar) have multiple indications we've included two others in order to have five unique drugs on the list below.

Rx Drug	*Rx Drug Indication*	Adult/Pediatric	2020 $ DIFF
Orfadin	*Treatment of Hereditary Tyrosinemia Type 1 (HT-1; Hepatorenal Tyrosinemia)*	*Adult*	-$31,984
Clolar	*Treatment of Langerhans Cell Histiocytosis*	*Pediatric*	-$16,506
Orfadin	*Treatment of Hereditary Tyrosinemia Type 1 (HT-1; Hepatorenal Tyrosinemia)*	*Pediatric*	-$15,992
Doptelet	*Treatment of Thrombocytopenia*	*Adult*	-$12,531
Clolar	*Treatment of Acute Myeloid Leukemia (AML)*	*Adult*	-$10,316
Dacogen	*Treatment of Myelodysplastic Syndrome (MDS)*	*Adult*	-$3,919
Remicade	*Treatment of Ankylosing Spondylitis*	*Adult*	-$2,822

PERCENTAGE DECREASE: Far & away Doptelet set itself apart from the other four drugs that went down in price.

Rx Drug	*Rx Drug Indication*	Adult/Pediatric	2020 % DIFF
Doptelet	*Treatment of Thrombocytopenia*	*Adult*	-201.89%
Trisenox	*Treatment of Acute Promyelocytic Leukemia (APL)*	*Adult*	-8.04%
Clolar	*(multiple indications)*	*Pediatric*	-5.87%
Remicade	*(multiple indications)*	*Adult*	-5.16%
Dacogen	*(multiple indications)*	*Adult*	-2.82%

DRUG VIEWS

For the Top 5 researched drugs in PredictRx, there has been a reshuffling from last year. During the 2019 calendar year Keytruda had 2,516 member views, moving it from third place in 2018 up to the lead position. Humira, which ranked fifth last year, was bumped out by Avastin which took its spot.

Trade Name – 2019 Views	2018	2019
Keytruda	1304	2516
Rituxan	1215	2328
Opdivo	1416	2227
Remicade	1327	2009
Avastin	1090	1907

As for which pharmaceuticals were trending higher in terms of member queries, Gamifant had a huge increase in “eyeballs” from 2018 to 2019. Gamifant is indicated to treat Primary Hemophagocytic Lymphohistiocytosis (HLH) in newborns, infants, children, and adults with refractory, recurrent, or progressive disease or intolerance with conventional HLH therapy (i.e.: steroids, etoposide, and methotrexate intrathecal).

Trade Name - Trend	2018	2019	Change from 18-19
Gamifant	4	205	5025%
Nilandron	1	36	3500%
Tabloid	1	28	2700%
Chobham	2	49	2350%
Floxuridine	1	24	2300%

DIAGNOSIS VIEW

Every drug has at least one diagnosis that it is meant to remedy. Included below are the most researched diagnoses within PredictDx, which provides in-depth clinical information and insight as well as key financial analytics. Since Breast Cancer occupied two slots on the Top 5 list, we expanded it to six.

Trigger Diagnosis Name – 2019 Views	2018	2019
Early Stage/Locally Advanced Breast Cancer (Stages I/II/III)	16369	30088
Chronic Renal Failure/End-Stage Renal Disease (ESRD)	13149	19226
Non-Small Cell Lung Cancer (NSCLC)	5663	13924
Colon Cancer/Cancer of the Appendix	5946	13548
Advanced/Metastatic Breast Cancer (Stage IV/Recurrent Disease)	4771	12249
Dilated Cardiomyopathy/Congestive Heart Failure (CHF)	7234	10767

The therapeutic classes (diseases) that have caused the most specialty pharma spend in 2019 and are also projected to keep trending upward are: oncology, Inflammatory/autoimmune conditions, and infectious diseases.

Regarding specific diagnoses that trended higher in terms of PredictDx member queries, Oppositional Defiant Disorder/Conduct Disorders, which pertains to children and adolescents, had the highest escalation from 2018 to 2019.

Trigger Diagnosis Name - Trend	2018	2019	Change from 18-19
Oppositional Defiant Disorder/Conduct Disorders	84	721	758%
Primary CNS Lymphoma (Brain Cancer/Tumor)	186	1437	673%
Renal Pelvis/Ureteral Cancer	135	988	632%
Castleman Disease	54	392	626%
Gestational Trophoblastic Neoplasia/Choriocarcinoma/Placental Cancer	41	292	612%

2019 SPECIALTY DRUG LISTING

In 2019, 36 newly FDA-approved specialty drugs were added to PredictRx. The vast majority of the listed drug indications have a chronic/indefinite duration, which is well worth highlighting because it exacerbates this astonishing statistic: ***The ACP among these newly approved medications averaged out to be over $400,000 per year.***

Some other notable stats regarding PredictRx additions in 2019:

- 13 are Orphan-designated pharmaceuticals
- 15 of the new drugs are indicated to treat various cancers
- 2 are Biosimilars[10]
- 3 are Biologics (BLA-approved)
- 35 additional FDA-approved indications were incorporated into drugs already in PredictRx

Members of Advanced Medical Strategies receive a "Newly Predicted" email notifying them whenever a specialty drug gets approved by the FDA and is added to the AMS PredictRx directory.

The email includes a downloadable Newly Predicted fact sheet which provides the most relevant datapoints about each new drug. First and foremost, Quantity for Cost and ART pricing are listed. Information includes an overview of the drug, physician comments most pertinent to its specific treatment area, available dosages, drug category, HCPCS/J Codes, and Line of Therapy (LOT). It also contains a brief synopsis about its associated diagnosis from PredictDx.

Click below to view all 36 high dollar pharmaceuticals (listed in chronological order of when approved) that have been added to PredictRx in 2019. Note that ACP and Yearly ACP amounts are as of the date the drug was entered into PredictRx. Drug indications that have n/a in the ACP column have not launched as of press time. If there is n/a in the Yearly ACP column only that means those costs cannot be accurately calculated or projected.

Download the list of 36 high-dollar pharmaceuticals

Transparency and clarity are essential for payers within the health and casualty industries to make informed, proactive business decisions concerning specialty drugs, particularly when it comes to pricing, dosing, and treatment analytics. With hundreds of thousands of searches within PredictRx and PredictDx, and associated usage of their respective statistical reporting functionalities, it's clear that the on-demand decision support solutions they both provide have become the gold standard.

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[10] A total of 10 biosimilars were FDA approved in 2019; however, only two launched and were thus entered into PredictRx.