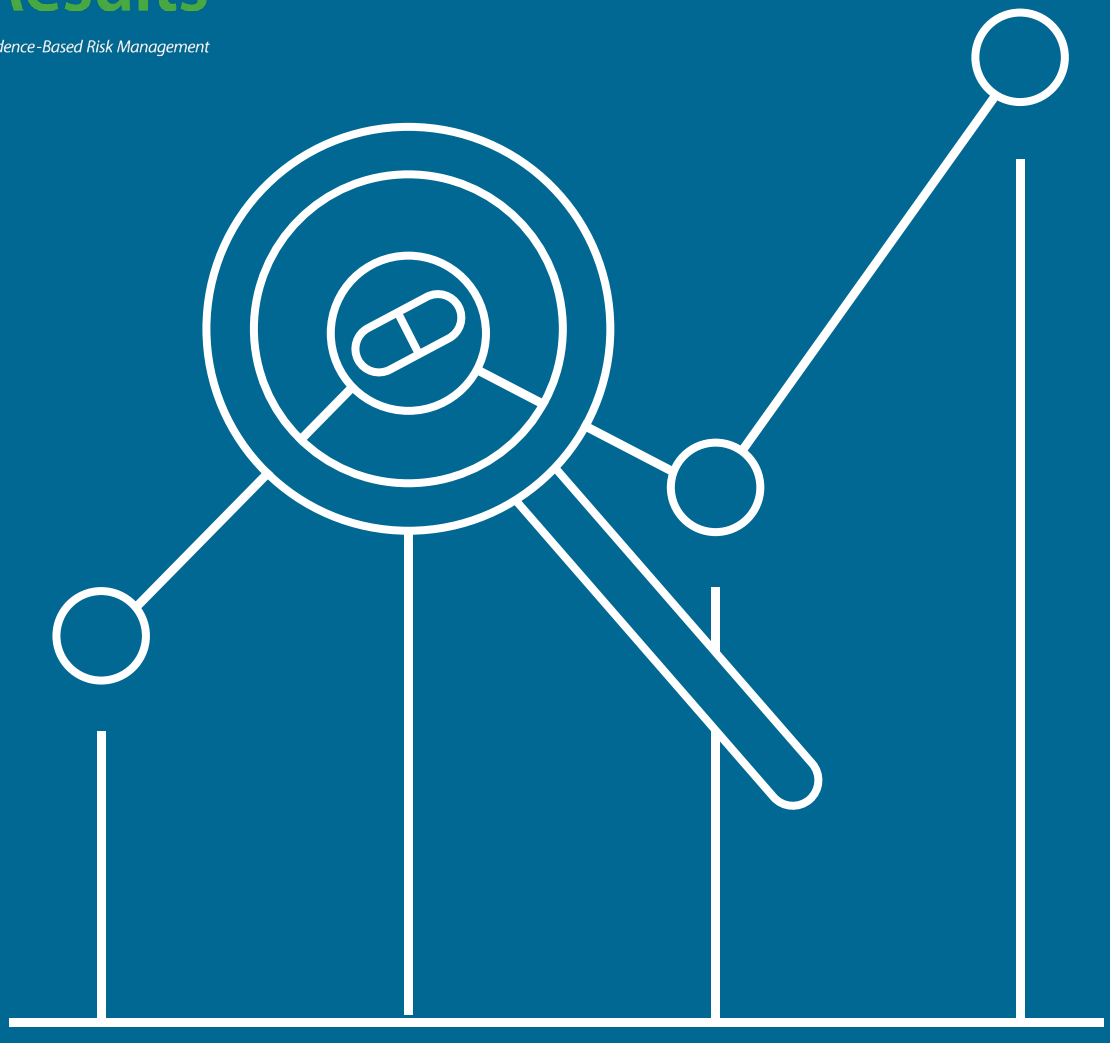
INDUSTRY OUTLOOK

Specialty Drug Insights VOLUME 1

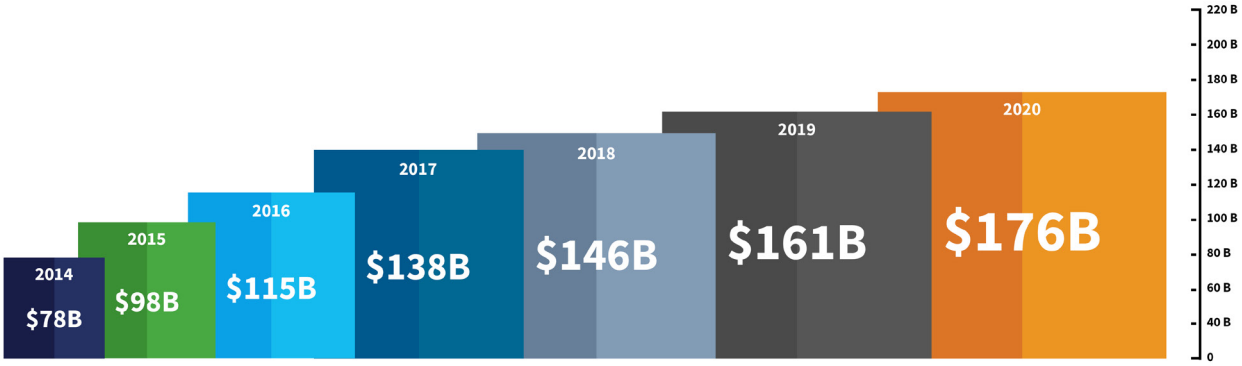
RxResults℠
Evidence-Based Risk Management



Specialty Pharmacy Revenue
Industry Outlook

Specialty Pharmacy Revenue

The infographic below tracks specialty pharmacy revenue across the industry. In 2014, specialty pharmacy was a $78 billion industry and you can see over the years how much this figure has increased. Specialty pharmacy revenue reached $212 billion in 2020, with this figure predicted to grow in the coming years.



Specialty pharmacy revenue has increased by 125% since 2014

Recently FDA Approved Drugs with High Impact

Cost Comparison HAE Medications

DRUG	ADMINISTRATION	AWP/28 DAYS (80KG)	AWP COST/12 MO
Cinryze	Intravenous (IV)	$254,250	$3,051,002
Berinert	Intravenous (IV)	$272,332	$3,267,993
Haegarda	Subcutaneous (SubQ)	$43,315	$519,780
Takhzyro	Subcutaneous (SubQ)	$54,557	$654,684
Orladeyo (berotralstat)	**Oral**	**$44,744**	**$536,928**

Zokinvy (lonafarnib) Capsules

Place in Therapy: Treatment of rare (1 In 4 million births) autosomal dominant disease Hutchinson-Gilford Progeria Syndrome (HGPS). Currently the only approved treatment for HGPS.
Clinical Insights: Current management of HGPS, characterized by accelerated aging, involves supportive care including nutritional support and treatment of complications.

AVAILABLE	DOSING	ESTIMATED COST
Capsules (Zokinvy Oral) 50 mg: $860.40 75 mg: $1,290.60	**Weight based**, dosed twice daily (150 mg/m2/dose) *Average BSA = 1.7 m2	**30-day:**$258,120 **12-months:** $3,097,440

Imcivree (Setmelanotide) Solution

Place in Therapy: First treatment approved for rare genetic mutations that result in morbid obesity.
Clinical Insights: Studies have identified nearly 5% of individuals with morbid obesity have one of these rare mutations and individuals with these mutations likely experience obesity beginning at infancy.

AVAILABLE	DOSING	ESTIMATED COST
Solution (Imcivree Subcutaneous) 10mg/mL (permL): $3,960.00	**Maximum Dose:** 3mg SubQ/day *Trial weight loss target was 2-3 kg/wk	**30-day:** $35,640 **12-months:** $427,680

Orladeyo (Berotralstat) Capsules

Place in Therapy: First oral treatment indicated for prophylaxis to prevent attacks of HAE.
Clinical Insights: Alternative treatments for HAE include Cinryze, Berinert, Haegarda, and Takhzyro.

AVAILABLE	DOSING	ESTIMATED COST
Capsules (Orladeyo) 110 mg: $1,599 150 mg: $1,599	150 mg by mouth once daily	**28-day:** $44,744 **12-months:** $536,928

Tepmetko (tepotinib) Tablet

Place in Therapy: Treatment of adult patients with metastatic non-small cell lung cancer (NSCLC) harboring MET exon 14 skipping alterations.
Clinical Insights: Tepmetko will compete with Tabrecta (capmatinib), which came to the market May 2020 as the first treatment approved for metastatic NSCLC with METex14 skipping (costs ~$292,176/year).

AVAILABLE	DOSING	ESTIMATED COST
Tablet (Tepmetko) 225 mg:$548.42	450 mg by mouth daily	**30-day:** $32,905 **12-months:** $394,862

Breyanzi (lisocabtagene maraleucel) Infusion

Place in Therapy: Cell-based gene therapy to treat adults with specific types of large B-cell lymphoma.
Clinical Insights: Yescarta (CAR-T immunotherapy) has the same indications but is ~10% cheaper ($373K).

AVAILABLE	DOSING	ESTIMATED COST
Chimeric Antigen Receptor (CAR) T-cell Immunotherapy supplied as a suspension for IV infusion	50 to 110 × 106 CAR-positive viable T cells IV x 1	$410,000 /infusion

Evkeeza (evinacumab-dgnb) Infusion

Place in Therapy: Novel monoclonal antibody and potent LDL-lowering medication used as adjunctive therapy in patients with homozygous familial hypercholesterolemia (HoFH).
Clinical Insights: Currently approved for intravenous use with future development to have a subcutaneous formulation. Standard of care to treat HoFH is typically <$300/month.

AVAILABLE	DOSING	ESTIMATED COST
Solution (Evkeeza Intravenous) 345MG/2.3ML (per mL): $5,625.00 1200 mg/8 mL (per mL): $5,625.00	15 mg/kg infused every 4 weeks *Based upon 100 kg patient	**28-day:** $56,250 **12-months:** $675,000

Ponvory (Ponesimod) Tablet

Place in Therapy: Ponvory joins Gelenya, Mayzent, and Zeposia as the 4th S1P receptor modular. Ponvory is selective for a single receptor (S1P1) and has a shorter half-like than the S1P modulators.

DRUG S1P	DRUG CLAS/MOA	AWP COST/12 MO
Gilenya (fingolimod)	S1P-receptor modulator	$130,971
Mayzent (Siponimod)	S1P-receptor modulator	$116,031
Zeposia (ozanimod)	S1P-receptor modulator	$106,365
Ponvory (Ponesimod)	**S1P-receptor modulator**	**$114,403**

Bylvay (Odevixibat) Oral Pellets and Capsule

Place in Therapy: First drug approved for the treatment of pruritus in all subtypes of progressive familial intrahepatic cholestasis (PFIC).

AVAILABLE	DOSING	ESTIMATED COST
Capsule (Bylvay (Pellets) Oral) 200 mcg (per each): $264.00 600 mcg (per each): $792.00	**Weight based:** max dosing varies from 600 mcg-6,000 mcg once daily *Oral pellets are intended for use by patients <19.5 kg, oral capsules are intended for use by patients ≥19.5 kg	**30-day:** $23,760 - $237,600 **12-months:** $285,120 - $2,851,200

Nexviazyme (Avalglucosidase alfa-NGPT) IV Infusion

Place in Therapy: Treatment of late-onset Pompe disease (lysosomal acid alpha-glucosidase [GAA] deficiency) in patients ≥1 year of age

Clinical Insights: Pompe disease is rare, affecting 1 in 21,979 in the US for early and late forms combined. Pompe disease is an inherited and often fatal disorder that disables the heart and skeletal muscles.

AVAILABLE	DOSING	ESTIMATED COST
Solution (reconstituted) (Nexviazyme IV) 100 mg (per each): $2,057.88	**IV:** 40 mg/kg every 2 weeks (weight <30 kg) **IV:** 20 mg/kg every 2 weeks (weight ≥30 kg) *Calculation based on 80 kg patient	**30-day:** $65,824 **12-months:** $789,888

Fyarro (sirolimus) IV Infusion

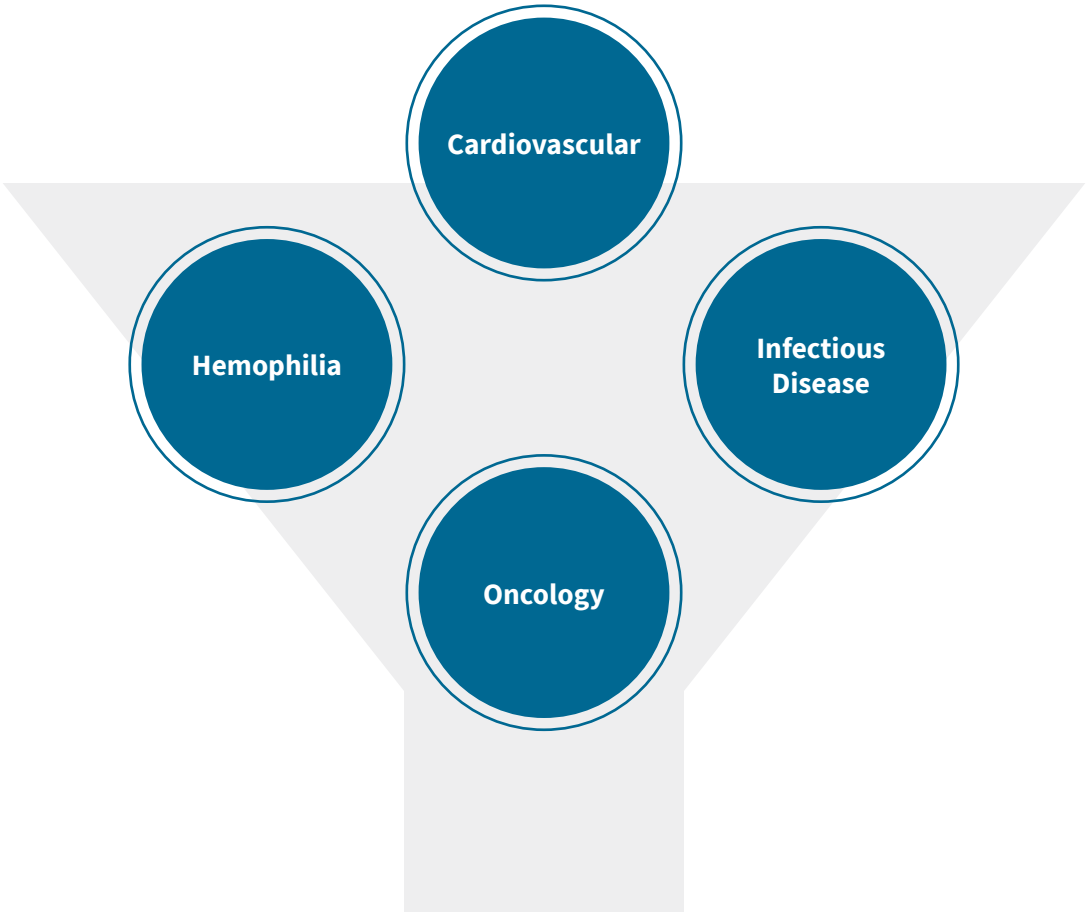
Place in Therapy: Used to treat adults with locally advanced unresectable or metastatic malignant perivascular epithelioid cell tumor (PEComa).

Clinical Insights: This is the first IV formulation of sirolimus, which is also available in oral formulation.

AVAILABLE	DOSING	ESTIMATED COST
Suspension (reconstituted) (Fyarro IV) 100 mg (per each): $8,142.00	100mg/m^2 on days 1 and 8 every 21 days. *Based on a BSA =2	**30-day:** $46,525 **12-months:** $558,300

The Pipeline of Specialty Medications

There are several specialty drug classes with notable products in the pipeline



Cardiovascular

Mavacamten

Under FDA Review: Decision Anticipated April 2022

Epidemiology: Hypertrophic cardiomyopathy (HCM) is a genetically determined heart muscle disease mostly caused by mutations that is estimated to affect 1 in 500. Some patients with HCM will live a normal life span and many are asymptomatic making these patients high risk for heart failure and stroke.

Place in Therapy: If approved, first FDA approved treatment for obstructive HCM. Current therapy for patients with HCM are typically treated with beta-blockers, calcium-channel blockers, diuretics, and lifestyle modifications.

Clinical Insights: Once daily, oral tablet with a mechanism that decreases the stress on the heart muscles. Cost information is unknown at the time-this could be a game changer to decrease cardiovascular related hospitalization.

Infectious Disease

Reltecimod

Phase 3 Trial Underway: FDA Decision Status Unknown

Epidemiology: Necrotizing soft tissue infection (NSTI) is a rare, life-threatening disease that spreads rapidly to other areas of the body. Multi-organ failure frequently occurs.

Place in Therapy: There are currently no therapies approved to treat severe NSTI. The proposed indication would be the treatment of suspected organ dysfunction in patients >12 years of age with NSTI. If approved, Reltecimod would be the first IV therapy.

Clinical Insights: Current management consists of early and aggressive surgical debridement, broad spectrum antibiotics, and supportive intensive care. Despite these measures, there are high rates of mortality.

Hemophilia (B)

Etranacogene dezaparvovec

In Development: FDA Decision Status Unknown

Place in therapy: If approved, this would be the first gene therapy for hemophilia B. Administered as a one-time IV infusion, this therapy utilizes a viral vector to combine a naturally occurring factor IX variant.

Clinical Insights: Another gene therapy for hemophilia B is being developed by Pfizer and Spark Therapeutics, also expected to file with the FDA by 2022. All hemophilia A and B therapies costs several hundred of thousand dollars per year.

Oncology: Leukemia

Pacritinib

In Development: FDA Decision Status Unknown

Epidemiology: Myelofibrosis is a rare type of chronic leukemia which results in excessive blood cell production in the bone marrow causing anemia, weakness, fatigue, and an enlarged spleen. Myelofibrosis has a prevalence of an estimated 17,000 patients in the U.S each year and is associated with several generic mutation (most commonly JAK-2).

Place in Therapy: If approved, pacritinib will compete with two other JAK-inhibitors, Inrebic and Jakafi to treat intermediate or high-risk myelofibrosis in patients with thrombocytopenia.

DRUG S1P	DRUG CLAS/MOA	AWP COST/12 MO
Inrebic (fedratinib)	JAK-inhibitor	$316,008
Jakafi (ruxolitinib)	JAK-inhibitor	$204,292
Pacritinub	JAK2-selective	???

Biosimilars: the Potential Savings When You Switch

Generics vs. Biologics vs. Biosimilars

GENERICS	BIOLOGICS	BIOSIMILARS
• Produced by a chemical process • Predictable chemical formula, exact copy of the brand product is possible • May be substituted for the brand product by a pharmacist without intervention of the prescriber	• Created from living organisms • Slight differences between manufactured lots of the same biologic • Original approval is referred to as "reference product" and approval is based on full efficacy and safety review	• "Highly similar" with "no clinically meaningful difference" • Produced using the same amino acid sequence as the reference product • Avoids costly clinical trials to independently establish efficacy and safety • Pharmacists cannot substitute a biosimilar for the reference biologic

Products with Biosimilars

IN THE MARKET	APPROVED BUT UNAVAILABLE	PIPELINE
Avastin (2)	Humira (6)	Lucentis
Epogen (1)	Enbrel (2)	Eylea
Herceptin (5)		Actemra
Neulasta (4)		Soliris
Neupogen (2)		Xgevia
Remicade (3)		
Rituxan (3)		

Example of Savings

Prescriber Changed Request from REMICADE to AVSOLA	
9 Cycles of Remicade	**9 Cycles of Avsola**
	
$50,450	**$21,600**
Estimated Savings: $28,850	

Remicade Biosimilars

Pricing
US (AWP 100 mg per each)

Reference Product
Remicade : $1,401.38

Biosimilars:
Avsola: $600.00
Inflectra: $1,135.54
Renflexis: $904.07

The average regimen for a 170 lb patient = 400 mg IV every six weeks

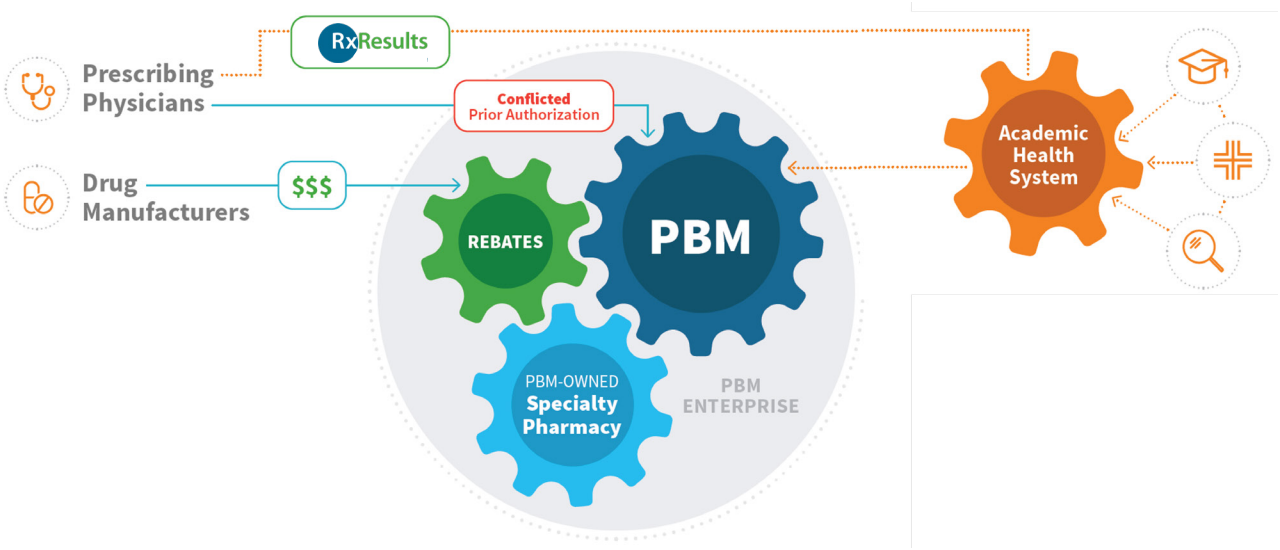
Biosimilars will result in roughly $160 billion in lower spending over the next five years compared to a market without Biosimilars*

*IQVIA Institute for Human Data Science. The Global Use of Medicine in 2019 and Outlook to 2023. January 29, 2019.
URL: https://www.iqvia.com/institute/reports/the-global-use-of-medicine-in-2019-and-outlook-to-2023. Accessed August 2020.

The Specialty Drug Conflict of Interest

In the current industry model, many PBMs own the specialty pharmacy and they complete the prior authorization of the specialty drugs. The approval of specialty drugs can produce revenue for the PBM in the fulfillment of the drug via their specialty pharmacy and through potential rebates with the drug manufacturers.

RxResults removes the conflict of interest. Our model is designed to make certain the right member meeting the right clinical criteria gets the right drug at the right time in an effort to achieve the best clinical outcome.



Evidence-Based Pharmacy Risk Management

Evidence-Based Pharmacy Risk Management is changing the benefits landscape.

A Pharmacy Risk Manager doesn't replace a PBM. It serves to enhance a PBM model as an advocate for the plan sponsor and its plan participants. RxResults leverages proprietary informatics, clinical expertise and business processes to formulate actionable insights and implement evidence-based strategic initiatives to manage pharmacy and specialty pharmacy spend.

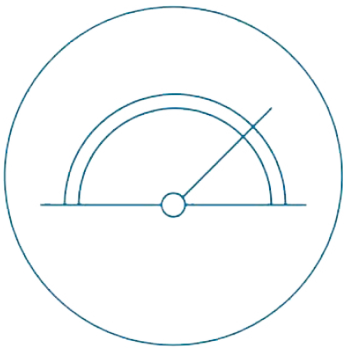
As a Pharmacy Risk Manager, RxResults:

- Provides a team of independent pharmacists & benefit industry experts
- Identifies plan risks and stratifies cost savings opportunities
- Delivers unprecedented insights into drug costs and utilization trends
- Utilizes a proprietary analytics platform and clinical rules engine

RxResults℠
Evidence-Based Risk Management

Analyze

Implement



Measure

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