RISK strategies CONSULTING

Q4 2023
Clinical Pipeline Report

Insight into Recent and Upcoming Drug and Biologic Approvals

November 2023

Includes breaking news on the approval of Zepbound (tirzepatide) for chronic weight management.

Risk Strategies Consulting Clinical Pipeline Report

Our clinical pipeline report provides quarterly updates surrounding recent impactful FDA approvals or additional indications, upcoming generic drug and biosimilar availability, and the cell and gene therapy pipeline. This report is intended to highlight the most impactful pharmacy updates and is not all-inclusive.

We will continue to closely monitor the clinical pipeline and provide our clients with this quarterly publication as a resource.

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Impactful Industry News

GLP-1 Updates

Zepbound (tirzepatide) Approved for Chronic Weight Management

On November 8th, 2023, the FDA approved Zepbound (tirzepatide) injection for chronic weight management in adults with obesity or who are overweight with at least one weight-related condition in addition to a reduced calorie diet and increased physical activity. The active ingredient in Zepbound, tirzepatide, is already FDA-approved for use in type 2 diabetes under the name Mounjaro. Zepbound's list price is about $13,000/yr and will be a direct competitor to Wegovy ($17,500/yr) and Saxenda (16,400/yr). According to the manufacturer, Eli Lilly, Zepbound is expected to be available by the end of 2023. The approval of an additional GLP-1 for obesity will continue to have a groundbreaking impact on the weight management space, with some pharma analysts predicting Zepbound could become the largest selling drug of all time.

GLP-1 Pipeline

In 2023, glucagon-like peptide 1 (GLP-1) agonists emerged as a blockbuster class of drugs. Buzz around GLP-1s usually pertains to their FDA-approved uses for diabetes and obesity. However, there are active trials with some support for their use in preventing major cardiovascular events and to treat non-alcoholic steatohepatitis (NASH). Full results of these clinical trials have not been released. GLP-1s are also being studied for their effects on other body systems beyond those related to diabetes and obesity. Early studies are investigating GLP-1s for treatment of polycystic ovarian syndrome (PCOS), chronic kidney disease (CKD), obstructive sleep apnea (OSA), Parkinson disease (PD), and Alzheimer's disease (AD).

Mounjaro's Impact on Oral Contraceptive Effectiveness

Women of child-bearing age using oral contraceptives and starting on Mounjaro should consider alternative birth control methods as Mounjaro may decrease the efficacy of oral contraceptives. GLP-1s delay the time it takes for food to move through the stomach. It's thought that this delayed gastric emptying may impact how oral contraceptives are absorbed by the body. Another possible reason for the decrease in oral contraceptive efficacy is that vomiting, a known side effect of GLP-1s, can prevent the tablet from being absorbed in the body. Alternative contraceptive options which are not impacted by GLP-1s should be considered including intrauterine devices (IUDs), birth control implant, hormonal vaginal ring, IM injection, and condoms. The labeling for Mounjaro includes a warning that it can decrease the efficacy of oral contraceptives, though other GLP-1s do not include this warning. As the number of individuals utilizing GLP-1s increases, experts predict there will be an increase in what has been termed "Mounjaro babies" due to the drug interaction.

Ozempic Safety Updates

At the end of September 2023, the FDA required Ozempic to make two drug safety-related label changes. The first was a drug-interaction warning, reiterating a warning mentioned in another section of the label, that GLP-1 drugs can interact with other select drugs (sulfonylureas, insulin) and result in an increased risk for hypoglycemia. The second label addition was to the post-marketing section of the adverse reactions which identified gastrointestinal ileus (issues with bowel contraction) as a potential serious side effect.

Recent FDA Approvals & Additional Indications

Entyvio & Infliximab Now Available in Subcutaneous Formulations

Entyvio Subcutaneous (vedolizumab) – *Takeda*
Zymfentra Subcutaneous (infliximab) – *Celltrion*

Indication

Entyvio, first approved in 2014, and infliximab, first available as Remicade in 1998, were historically only available in intravenous (IV) forms and are now available in subcutaneous (SC) forms. Both Entyvio and Zymfentra treat moderately to severely active ulcerative colitis (UC) and Zymfentra is approved for moderately to severely active Crohn's disease (CD).

Disease State & Population

An estimated 1.6 million people in the United States have either CD or UC. As many as 70,000 new cases of CD or UC are diagnosed each year in the United States. Approximately 15% of individuals with UC and 10-30% of individuals with CD are classified as moderate-severe.

Place in Therapy

Patients can transition to SC Entyvio and SC Zymfentra following induction with IV Entyvio and IV infliximab, respectively. Both Entyvio and infliximab are considered first-line agents for moderate to severe UC and CD and are recommended as a first-line option for biologic agent-naïve patients by treatment guidelines. Many other first-line treatments exist for UC & CD and include but are not limited to Stelara, Humira, and Xeljanz.

Payor Impact

Entyvio SC is administered every 2 weeks and will cost about $76,500 per year, over $20k more than Entyvio IV administered every 8 weeks. Celltrion has not yet released the cost for Zymfentra. The approval of SC Entyvio and SC infliximab could shift utilization from the medical to the pharmacy benefit as these SC formulations are self-administered.

New Alternative Treatment for Pompe Disease

Pombiliti + Opfolda (cipaglucosidase alfa-atga + miglustat) – *Amicus Therapeutics*

Indication

Adults with late-onset Pompe disease (LOPD) weighing ≥40 kg and who are not improving on their current enzyme replacement therapy (ERT). Pombiliti is an ERT and Opfolda is an enzyme stabilizer for Pombiliti.

Disease State & Population

Pompe disease (PD) is a rare genetic disease caused by a specific enzyme deficiency (acid alpha-glucosidase, GAA) that results in progressive weakness of the heart and skeletal muscles. LOPD is a partial deficiency in GAA and can occur anywhere from early childhood to well into adulthood and typically does not impact the heart. In the United States, about 1 in 40,000 individuals have PD.

Place in Therapy

The current standard of care for LOPD is ERT. Other available ERTs are Lumizyme and Nexviazyme. All 3 ERTs are approved for LOPD but Lumizyme has an additional indication for infantile-onset Pompe disease (IOPD). Pombiliti + Opfolda will serve as a secondary treatment option following other ERT therapy, as it is approved for use when current ERT is not working.

Payor Impact

Pombiliti is administered via IV infusion and Opfolda is taken orally. The combined average cost per year (weight-based dosing) is about $675,211. This is slightly less expensive than existing ERTs, with Lumizyme costing about $740,083 per year and Nexviazyme costing about $711,617 per year. Given the extremely high cost and very specific patient population, prior authorization is recommended. Pombiliti + Opfolda will be a specialty pharmacy drug with limited distribution.

Recent FDA Approvals & Additional Indications

A New Treatment Option for Major Depressive Disorder

Exxua (gepirone) – *Fabra-Kramer Pharmaceuticals*

Indication

Treatment of major depressive disorder (MDD) in adults.

Disease State & Population

An estimated 2.1 million adults in the United States (8.3% of the total population) experienced at least one depressive episode in 2021. On average, women (10.3%) experience MDD more than men (6.2%). Individuals aged 18-25 are the most likely to experience MDD (18.6%).

Place in Therapy

Exxua is the first drug in its class, a selective serotonin 1A receptor agonist. There are many drugs, both brand and generic, approved to treat MDD including but not limited to SSRIs (Zoloft, Celexa, etc.), SNRIs (Cymbalta, Effexor), Trintellix, and Fetzima. Exxua does not cause sexual dysfunction or weight gain and may be beneficial for patients who experience these issues with other MDD agents.

Payor Impact

The manufacturer has not yet released the cost for Exxua, but it is estimated to cost somewhere between $10,000-$13,000 per year, like other new brand-name antidepressants. Given the availability of numerous generic antidepressants, it is likely Exxua will serve as a second or third-line option for the treatment of MDD. Exxua management should include prior authorization and step therapy of at least one or more generic antidepressants.

Biologic Demonstrating Superiority Enters Psoriasis Market

Bimzelx (bimekizumab) – *UCB*

Indication

Moderate to severe plaque psoriasis (PsO) in adults who are candidates for systemic therapy or phototherapy.

Disease State & Population

Over 7.5 million adults in the United States have psoriasis, with approximately 80-90% of those individuals having plaque PsO, the most common psoriasis subtype. Approximately 20% of individuals with plaque PsO are classified as having a moderate to severe form of the disease.

Place in Therapy

Bimzelx will compete with several other biologics indicated to treat moderate to severe plaque PsO, including IL antagonists like Bimzelx (Cosentyx and Taltz), as well as Humira and Stelara. In clinical trials, Bimzelx demonstrated superior efficacy over Stelara, Humira, and Cosentyx in the BE VIVID, BE SURE, AND BE RADIANT trials, respectively. Biosimilars for Stelara are expected to enter the market in January 2025, and this may have a further impact on Bimzelx's uptake.

Payor Impact

Bimzelx is administered via autoinjector every 8 weeks and is estimated to cost approximately $94,000 per year. Given the cost and specific patient population, as well as other available treatments in the market, prior authorization is recommended.

Upcoming Significant Approvals

Products Anticipated to Reach Market by 2H 2024

Drug	Indication	Anticipated Approval	Place in Therapy & Est. Cost
Capivasertib	HR+ Breast Cancer	Q4 2023	Would be used in combination with existing treatment (fulvestrant) Est. cost $200-300k per year
Donanemab	Alzheimer's Disease	Q4 2023	3rd in class option, dosed less frequently Est. cost $26k per year
Apadamtase alfa; Cinaxadamtase alfa	Thrombotic Thrombocytopenic Purpura (TTP)	Q4 2023	1st enzyme replacement therapy for TTP Est. cost $300-500k per year
Nirogacestat	Desmoid Tumors / Aggressive Fibromatosis	11/27/23	1st FDA-approved treatment for DT/AF Est. cost $200-300k per year
Iptacopan	Paroxysmal Nocturnal Hemoglobinuria	12/2023	1st oral monotherapy treatment for PNH Would compete with existing treatments Est. cost $300-500k per year
Roluperidone	Negative Symptoms of Schizophrenia	2/26/24	1st FDA-approved treatment for negative symptoms of schizophrenia Est. cost $20-50k per year
Resmetirom	**Non-alcoholic Steatohepatitis**	**3/14/24**	**1st FDA-approved treatment for NASH Est. cost of $20-50k per year**
Insulin Icodec	**Type 1 & 2 Diabetes**	**2Q 2024**	**1st long-acting insulin dosed weekly Est. cost $5,000 per year**
Xanomeline-Trospium	Schizophrenia	2H 2024	1st in-class option, potential to be new monotherapy standard Est. cost $20-50k per year

What You Should Know

Resmetirom has the potential to be the first-ever FDA-approved treatment for NASH, which is poised to become the next emerging drug class and is anticipated to have a significant impact on pharmacy spend. If approved, insulin icodec would be the first weekly basal insulin for diabetes compared to once-daily formulations that are currently on the market. Initial results from phase 3 clinical trials have shown that insulin icodec is just as effective as Lantus and Tresiba. It is possible that, given the longer dosing interval, the price for insulin icodec may be at a premium compared to long-acting insulins currently on the market, though the longer-acting formulation may be a good option for those individuals who struggle with compliance on daily dosing formulations.

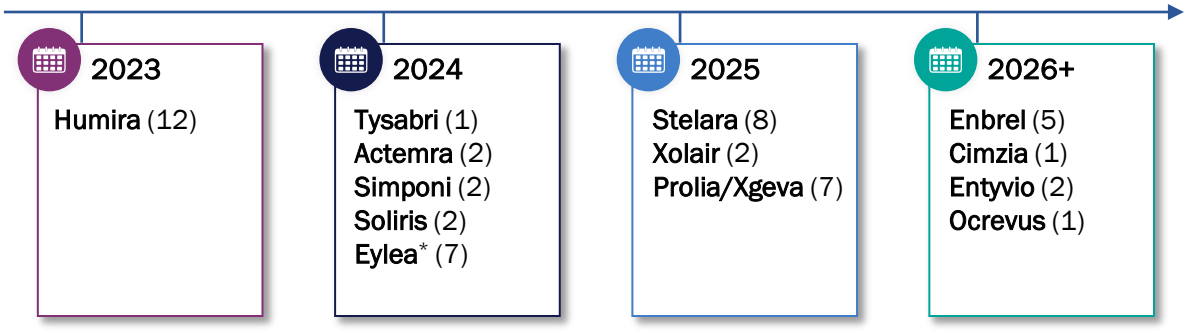
Upcoming Generics & Biosimilars

Newly Available Generics Anticipated by End of Year 2023

Brand	Generic	Indication	Generic Launch %	Anticipated Launch
Prolensa	Bromfenac Sodium	Inflammation Post Cataract Surgery	70%	Q4 2023
Livalo	Pitavastatin Calcium	Reduce LDL Cholesterol	90%	2H 2023
Gattex	Teduglutide Recombinant	Short Bowel Syndrome	50%	2H 2023
Dulera	Formoterol Fumarate; Mometasone Furoate	Asthma	60%	2023
Mydayis	Amphetamine + Dextroamphetamine salts	ADHD	60%	2023
Neupro	Rotigotine	Parkinson's Disease Restless Leg Syndrome	80%	2023
Teflaro	Ceftaroline Fosamil	Skin Infections Pneumonia	60%	2023

Recently Launched & Anticipated Biosimilars

Biosimilars listed by first launch year
(#) indicates total launched biosimilars by the end of the specified year



*Launch depends on patent expiration. Possible launch may extend to 2032.

What You Should Know

Q3 2023 saw the early approval of the first biosimilar for both Tysabri (Tyruko) and Actemra (Tofidence). The expected launch for both biosimilars is in 2024. Tyruko is approved to treat multiple sclerosis (MS) and Crohn's disease (CD). Tofidence is approved to treat rheumatoid arthritis (RA) and juvenile idiopathic arthritis (JIA). The estimated cost and availability date for both drugs is not yet known. The first biosimilar of Stelara, Wezlana, was approved at the end of October 2023. Wezlana has interchangeable status with Stelara and is approved for plaque psoriasis, psoriatic arthritis (PsA), CD, and ulcerative colitis (UC). The expected launch of Wezlana is in 2025, following patent expiration.

Cell and Gene Therapy Pipeline

Cell & Gene Therapies Anticipated by Q3 2024

Exa-cel (gene therapy)
CRISPR & Vertex
Sickle Cell Disease
12/8/2023

Fidanacogene (gene therapy)
Pfizer & Roche
Hemophilia B
Q2 2024

RP-L102 (cell therapy)
Rocket Pharma
Fanconi Anemia
H1 2024

Lovo-cel (gene therapy)
bluebird bio
Sickle Cell Disease
12/20/2023

RP-L201 (gene therapy)
Rocket Pharma
Severe Combined Immunodeficiency
3/31/2024

EB-101 (gene therapy)
Abeona Therapeutics
Epidermolysis Bullosa
Q3 2024

Lifileucel (cell therapy)
Iovance
Melanoma
2/24/2024

OLT-200 (gene therapy)
Orchard
Metachromatic Leukodystrophy
3/18/2024

Recent Approvals

Drug	Indication	Launch
Vyjuvek	Dystrophic Epidermolysis Bullosa	Q3 2023
Elevidys	Duchenne Muscular Dystrophy	Q3 2023
Roctavian	Hemophilia A	Q3 2023

What You Should Know

Cell & gene therapies are a more recent form of groundbreaking therapy that can improve or cure rare, chronic diseases, often in a one-time administration. These medications are ultra-high cost as they are intended as one-time treatments. There are some concerns with the long-term durability of these therapies, so value-based contracting as part of the cell & gene therapy strategy is advised. Plan sponsors must work with their medical carriers to prepare to manage the extremely high costs associated with treatment.

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