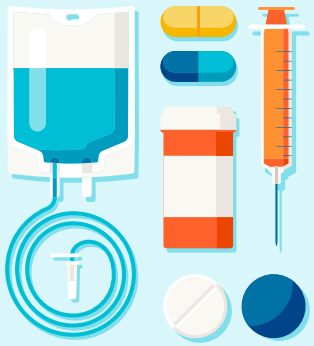
Optum Rx Report: Notable New Drugs™

Fall 2024



Welcome to this edition of the Optum Rx Notable New Drugs report, our ongoing series of commentaries that highlight key new drugs. The drugs in this issue already have, or are expected to receive U.S. Food and Drug Administration (FDA) approval before the end of 2024.

As always, our pipeline surveillance team continuously monitors and evaluates the drug development pipeline to share important upcoming drug approvals.

Please refer here for additional technical background and supplemental sources.

Hympavzi™ (marstacimab-hncq)

FDA approved Oct. 11, 2024

The FDA recently approved Hympavzi to prevent or reduce the frequency of hemophilia bleeding episodes. It is indicated for adult and pediatric patients aged 12 years and older with either hemophilia A or B, but who **have not** developed resistant antibodies.[1]

Analysis

An estimated 33,000 males are living with hemophilia in the U.S.

The most common treatment for hemophilia is clotting factor replacement therapy. The preventive (prophylaxis) factor is administered several times per week, and can cost between $300,000 and $776,000 per year.[3] However, a certain percentage of people will develop a resistance to factor replacement therapy.

Hympavzi blocks a protein in the clotting process that prevents blood clots from forming. This mechanism is expected to work in people with

Key points

Why this drug matters: Hympavzi (marstacimab) offers a first-in-class treatment option for preventive treatment of both hemophilia A and B. It will provide new competition for Hemlibra® (emicizumab-kxwh) for hemophilia A.

Estimated cost: The annual wholesale acquisition cost (WAC) for Hympavzi is $795,600.[2]

Trial notes: Promising efficacy with annualized bleeding rates reduced by 35% vs. routine prophylaxis and by nearly 92% vs. on-demand therapy.

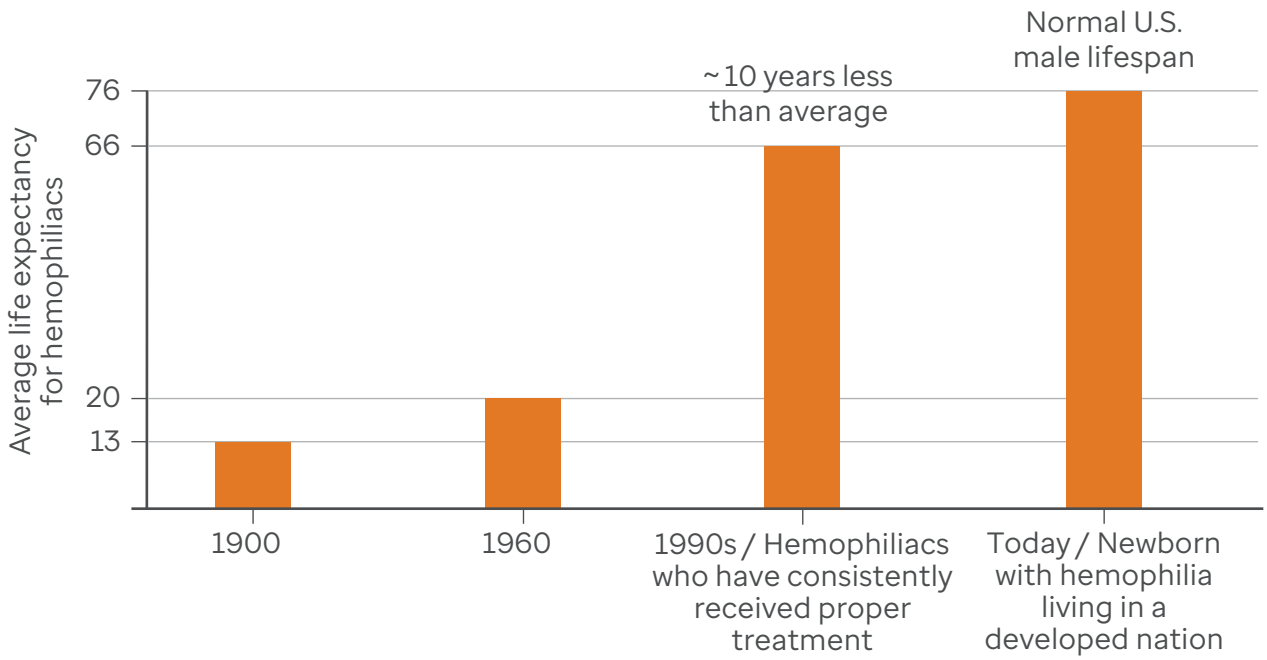
Route of administration: Pre-filled, auto-injector pen for once-weekly subcutaneous injection.

Manufacturer: Pfizer

hemophilia A or B, **despite any developed resistance.**[4] An ongoing branch of the phase 3 trial is studying the effect of Hympavzi on people who **have** developed resistance to replacement therapy. Results are expected in the third quarter of 2025.

Hympavzi continues the trend toward more effective treatments for hemophilia, resulting in increasing life spans for patients:

Better treatments have increased Hemophiliac life expectancy



Optum Rx image adapted from: 1900 & 1960: National Bleeding Disorders Foundation. History: From 2 AD to the present. Accessed October, 2024. 1990's & Current: MyHemophiliaTeam. Hemophilia A Prognosis: What Is the Life Expectancy? Published October 17, 2023.

The data for Hympavzi in both hemophilia A and B patients without inhibitors is promising. As noted, annualized bleeding rates were reduced by 35% vs. routine prophylaxis and by nearly 92% vs. on-demand therapy.

Other replacement therapies are currently in development for hemophilia, including Novo Nordisk's anti-TFPI, concizumab, and Sanofi's RNAi therapeutic, fitusiran. Both products could be approved by the end of the first quarter 2025 and would be potential competitors to Hympavzi.

The annual wholesale acquisition cost (WAC) for Hympavzi is $795,600.

Itovebi™ (inavolisib)

FDA approval: Oct. 10, 2024

Itovebi is a new first-line option for people with HR-positive breast cancer with a PIK3CA mutation. The approval stipulates Itovebi will be used in combination with Ibrance® (palbociclib) and fulvestrant.

Analysis

In 2024 there will be nearly 310,700 new cases of breast cancer in the U.S., or, about 15% of all cancers. And, approximately 42,250 deaths are expected due to breast cancer this year.[6]

Ibrance plus fulvestrant is a recommended first-line treatment for the approximately 87,000 new patients with advanced or metastatic HR-positive breast cancer with a PIK3CA mutation.

In a clinical study, patients who added Itovebi to the standard care regimen experienced better outcomes (57% reduction in the risk of disease

Key points

Why this drug matters: Itovebi showed promising progression-free survival results versus standard of care therapy, plus a reasonable safety profile vs. other drugs in the same class.

Estimated cost: The WAC is $274,400 per year.[5] The WAC for a competitor, Piqray® (alpelisib), is approximately $287,000 per year.

Trial notes: Combination therapy with Itovebi, Ibrance and fulvestrant demonstrated a 57% reduction in the risk of disease worsening or death vs. Ibrance and fulvestrant alone.

Route of administration: Orally once daily.

Manufacturer: Genentech

~87,00 treatable patients/year for Itovebi

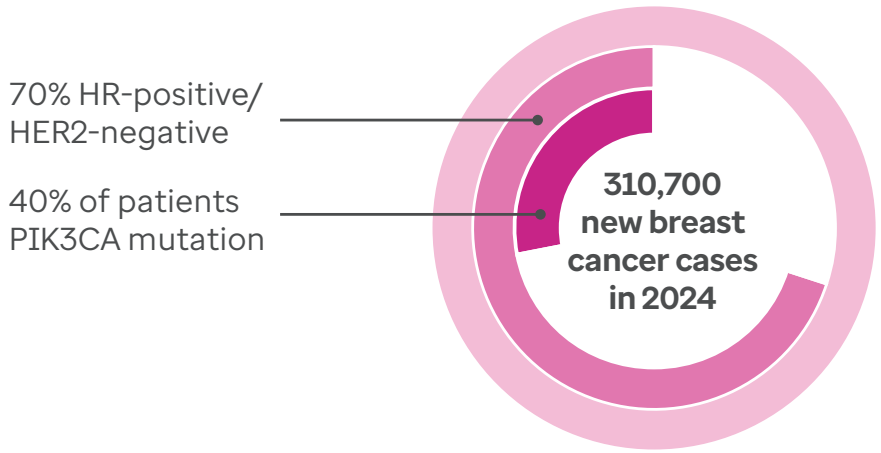


Image citation: 310,700 new cases: National Institutes of Health, National Cancer Institute. Cancer Stat Facts: Female Breast Cancer. Accessed October 14, 2024. 70% HR/HER2; 40% PIK3CA; $22,867: Formulary Watch. FDA Approves Itovebi for Metastatic Breast Cancer. Published October 11, 2024.

worsening or death) than those who only received standard of care alone. Based on these outcomes, the new three-way combination could become a first-line standard of care in this setting.

Other drugs that target PIK3CA mutations [i.e., Piqray® (alpelisib) and Truqap® (capivasertib)] have been plagued with tolerability issues, including side effects like high blood sugar and diarrhea. These side effects appear to occur at a lower rate with Itovebi.

While the progression-free survival data is encouraging, overall survival data at this point is still not mature (although a positive trend has been observed).

The WAC is $274,400 per year.

Acoramidis

Expected FDA decision: Nov. 29, 2024

Acoramidis is intended to treat cardiomyopathy associated with transthyretin amyloidosis (ATTR-CM).

- **Cardiomyopathy (CM)** is any disorder that causes the heart to lose its ability to pump blood effectively.[7]
- **Transthyretin (TTR)** is a protein used to circulate essential chemicals in the blood. Amyloidosis is when the body produces faulty TTR proteins.[8]
- **ATTR amyloidosis** is when these abnormal TTR proteins form clumps of amyloid fibrils. When fibrils build up in the heart, the ventricle walls become stiff and weak.[9] The resulting loss of heart function reduces life expectancy by two–six years from diagnosis.[10]

Key points

Why this drug matters: Potential competitor to Pfizer's Vyndamax® (tafamidis) — the only other drug currently approved for ATTR-CM.

Estimated cost: Prices not yet released. The WAC for Vyndamax is approximately $270,000 per year.

Trial notes: At month 30, the survival rate was 81% with acoramidis vs. 74% with placebo. This represents a 25% relative reduction in death risk.

Route of administration: Orally twice daily.

Manufacturer: BridgeBio Pharma

Analysis

If approved, acoramidis would be the second transthyretin stabilizer available for ATTR-CM and a direct competitor to Pfizer's Vyndamax® (tafamidis), the only other drug currently approved for the disease.

ATTR-CM is relatively rare. In the U.S., an estimated 120,000 adults have ATTR-CM, with 5,000 to 7,000 new cases each year.[11] Still, ATTR-CM is a large and growing drug class. The Vyndamax family (tafamidis meglumine, tafamidis) earned Pfizer $3.3B in 2023 sales — up more than 35% from 2022.[12]

Vyndamax utilization has been surging. Utilization may be up because diagnosis rates/education about the condition have increased over time. Analysts also believe the increase may in part be due to the Inflation Reduction Act, which caps out-of-pocket costs for people covered by Medicare Part D in 2024.[13]

The basic product patent for Vyndamax is set to expire at the end of 2024. Pfizer has filed requests for patent term extensions through 2028; these are currently pending.[14]

Trial results for acoramidis appear robust across a range of clinical outcomes, including death from any cause and cardiovascular-related hospitalization. However, at this point we do not have head-to-head trials evaluating acoramidis against Vyndamax.

Assuming it gains approval, both acoramidis and Vyndamax may face additional competition for ATTR-CM with Alnylam's Amvuttra® (vutrisiran). Amvuttra is currently approved for polyneuropathy of hereditary ATTR but recently Alnylam announced positive results for ATTR-CM.

Unlike Vyndamax and acoramidis which require daily oral administration, Amvuttra is administered via subcutaneous injection once every three months. Alnylam has submitted to the FDA for the ATTR-CM indication and a decision is possible in April 2025.

The WAC for Vyndamax is approximately $270,000 per year.

Pipeline awareness informs coverage and cost management

Optum Rx continuously monitors medications throughout their lifecycle, beginning with the drug development pipeline. The independent Optum Rx Pharmacy and Therapeutics Committee (P&T) appraises new and existing drugs based on clinical evidence. From these assessments, the Committee determines whether a drug has unique therapeutic benefit, comparable safety and efficacy, or whether the risk of harm outweighs the benefits.

Our **First Mover** process targets pipeline drugs that have high potential cost or safety concerns for patients. By expediting pre-FDA approval P&T clinical review of select high-impact drugs, Optum Rx can begin to develop sound clinical and financial management strategies before the drug is even available.

Your Optum Rx team will work with you to customize your plan from our full suite of utilization management strategies and programs, including prior authorization, step therapy and quantity limits. These programs work together to help ensure that your members get clinically effective medications that also make the best use of their pharmacy benefits.

References

Unless otherwise specified, all citation taken from RxOutlook® 3rd Quarter 2024.

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