

Umbralisib (Ukoniq) received accelerated approval from the U.S. Food and Drug Administration (FDA) on February 5, 2021, for the treatment of adult patients with relapsed or refractory marginal zone lymphoma (MZL) who have received at least one prior anti-CD20-based regimen, and for adult patients with relapsed or refractory follicular lymphoma (FL) who have received at least three prior lines of systemic therapy. However, please note that in May 2022, TG Therapeutics announced the voluntary withdrawal of umbralisib from the market in the U.S. due to concerns about increased risk of death in clinical trials, and the FDA subsequently withdrew its approval for these indications. Despite this, I will proceed with the hypothetical analysis of potential peak sales and the value of a 1% share of treated patients for umbralisib in the specified geographies (US, EU5, China, and Japan) for the originally approved indications, assuming the drug is still on the market or under consideration for approval.

To estimate the **Potential Peak Sales** and the **value of a 1% share of treated patients** for umbralisib in the indication of relapsed or refractory MZL and FL, we need to make several assumptions and follow a structured approach. Since specific data on umbralisib's pricing, patient population, and market penetration may not be fully available or up-to-date due to its withdrawal, I will base this analysis on general market data for similar drugs in these indications, epidemiology of MZL and FL, and standard assumptions for market share and pricing.

Step 1: Define the Target Patient Population

The indications are for relapsed or refractory MZL and FL in patients who have received prior therapies. We will estimate the eligible patient population in the US, EU5 (Germany, France, Italy, Spain, UK), China, and Japan.

Epidemiology of Marginal Zone Lymphoma (MZL) and Follicular Lymphoma (FL)

- **MZL** accounts for approximately 5-10% of non-Hodgkin lymphomas (NHL). The incidence of NHL is roughly 19-20 per 100,000 people in the US and EU, with lower rates in China and Japan.

- **FL** accounts for about 20-25% of NHL cases.

- Relapsed/refractory patients are a subset of the total diagnosed population. For MZL, we assume patients have received at least one prior anti-CD20 therapy, and for FL, at least three prior therapies. Typically, 20-30% of diagnosed patients may reach relapsed/refractory status eligible for later-line therapies.

Estimated Annual Incidence (New Cases) of NHL and Subtypes

- **US:** ~80,000 new NHL cases/year (FL: ~20,000; MZL: ~6,000). Relapsed/refractory eligible for umbralisib: ~30% of these, i.e., FL: ~6,000; MZL: ~1,800 (Total ~7,800).

- **EU5:** ~100,000 new NHL cases/year (FL: ~25,000; MZL: ~7,500). Relapsed/refractory: ~30%, i.e., FL: ~7,500; MZL: ~2,250 (Total ~9,750).

- **China:** ~90,000 new NHL cases/year (lower incidence rate, but large population; FL: ~18,000; MZL: ~5,400). Relapsed/refractory: ~30%, i.e., FL: ~5,400; MZL: ~1,620 (Total ~7,020).

- **Japan:** ~30,000 new NHL cases/year (FL: ~7,500; MZL: ~2,250). Relapsed/refractory: ~30%, i.e., FL: ~2,250; MZL: ~675 (Total ~2,925).

Total eligible treated patient pool across geographies (assuming 100% treatment rate for simplicity, though real-world rates are lower due to access and other factors):

- US: ~7,800
- EU5: ~9,750
- China: ~7,020
- Japan: ~2,925
- **Total:** ~27,495 patients annually.

Step 2: Market Share Assumption

The query assumes a **20% to 30% share of treated patients** for umbralisib. This is a reasonable estimate for a novel targeted therapy in a niche indication like relapsed/refractory MZL and FL, where competition exists from other therapies (e.g., BTK inhibitors like ibrutinib, other PI3K inhibitors, and anti-CD20 therapies).

- **Low-end (20%):** 20% of 27,495 = ~5,499 patients.
- **High-end (30%):** 30% of 27,495 = ~8,249 patients.

Breakdown by geography (proportional to patient pool):

- **US:** 20-30% of 7,800 = 1,560 to 2,340 patients.
- **EU5:** 20-30% of 9,750 = 1,950 to 2,925 patients.
- **China:** 20-30% of 7,020 = 1,404 to 2,106 patients.
- **Japan:** 20-30% of 2,925 = 585 to 878 patients.

Step 3: Pricing Assumption

Pricing for targeted therapies like PI3K inhibitors in oncology varies by region due to healthcare systems and reimbursement policies. Umbralisib's list price in the US before withdrawal was approximately **\$14,000 per month**, or ~\$168,000 per year (assuming 12 months of treatment, though real-world duration may be shorter, e.g., 6-9 months). For simplicity, we assume an annual cost per patient, adjusted for regional pricing differences:

- **US:** \$150,000/year (after discounts/rebates).
- **EU5:** \$100,000/year (lower due to price controls and negotiations).
- **Japan:** \$120,000/year (similar to EU5 but slightly higher due to premium pricing for innovative drugs).
- **China:** \$50,000/year (significantly lower due to affordability and local pricing policies).

Step 4: Calculate Potential Peak Sales

Peak sales are calculated as (Number of treated patients) x (Annual cost per patient) for each region, using the 20-30% market share range.

At 20% Market Share:

- **US:** 1,560 patients x \$150,000 = **\$234 million.**
- **EU5:** 1,950 patients x \$100,000 = **\$195 million.**
- **China:** 1,404 patients x \$50,000 = **\$70.2 million.**
- **Japan:** 585 patients x \$120,000 = **\$70.2 million.**
- **Total Peak Sales (20%):** \$234M + \$195M + \$70.2M + \$70.2M = **\$569.6 million.**

At 30% Market Share:

- **US:** 2,340 patients x \$150,000 = **\$351 million.**
- **EU5:** 2,925 patients x \$100,000 = **\$292.5 million.**
- **China:** 2,106 patients x \$50,000 = **\$105.3 million.**
- **Japan:** 878 patients x \$120,000 = **\$105.4 million.**
- **Total Peak Sales (30%):** \$351M + \$292.5M + \$105.3M + \$105.4M = **\$854.2 million.**

Thus, **Potential Peak Sales for umbralisib** in the US, EU5, China, and Japan for the given indications range from **\$570 million to \$854 million annually**, assuming a 20-30% market share.

Step 5: Calculate Value of 1% Share of Treated Patients

A 1% share of treated patients corresponds to 1% of the total eligible patient pool (27,495), i.e., ~275 patients annually. Using the same pricing assumptions per region:

- **US:** 1% of 7,800 = 78 patients x \$150,000 = **\$11.7 million.**
- **EU5:** 1% of 9,750 = 98 patients x \$100,000 = **\$9.8 million.**
- **China:** 1% of 7,020 = 70 patients x \$50,000 = **\$3.5 million.**
- **Japan:** 1% of 2,925 = 29 patients x \$120,000 = **\$3.5 million.**
- **Total Value of 1% Share:** \$11.7M + \$9.8M + \$3.5M + \$3.5M = **\$28.5 million.**

Thus, the **value of a 1% share of treated patients** across the US, EU5, China, and Japan is approximately **\$28.5 million annually**.

Final Answer:

1. **Potential Peak Sales for umbralisib** in the US, EU5, China, and Japan for relapsed/refractory MZL and FL (assuming 20-30% market share):

- **\$570 million to \$854 million annually.**

2. **Value of 1% share of treated patients** in these geographies:

- **\$28.5 million annually.**

Caveats: This analysis is hypothetical and based on assumptions about patient numbers, market share, and pricing. Real-world sales would depend on regulatory status (noting umbralisib's withdrawal in the US), competition, reimbursement, treatment duration, and market access challenges, especially in China. Adjustments may be needed based on more specific or updated data. If you have additional information (e.g., specific pricing or patient numbers), I can refine the calculations.