

To estimate the **Potential Peak Sales** for pembrolizumab (Keytruda) in the indication of advanced endometrial carcinoma (non-MSI-H or dMMR, with disease progression following prior systemic therapy and not candidates for curative surgery or radiation) in the US, EU5 (France, Germany, Italy, Spain, UK), China, and Japan, as well as the **\$ value of a 1% share of treated patients** in these geographies, we need to follow a structured approach. Since specific data on patient populations, pricing, and market penetration may not be fully available, I will outline the methodology and provide reasonable assumptions based on publicly available data and industry trends. The final numbers are illustrative and should be validated with real-world data.

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## **Step 1: Define the Target Patient Population**

The indication is for **advanced endometrial carcinoma (non-MSI-H or dMMR)** patients with disease progression after prior systemic therapy who are not candidates for curative surgery or radiation. We need to estimate the eligible patient population in each geography.

### #### Incidence and Prevalence of Endometrial Cancer:

- Endometrial cancer is the most common gynecologic cancer in developed countries.
- According to estimates (e.g., GLOBOCAN 2020), the annual incidence of endometrial cancer is approximately:
  - **US**: ~66,000 new cases
  - **EU5**: ~60,000 new cases (combined for France, Germany, Italy, Spain, UK)
  - **China**: ~82,000 new cases
  - **Japan**: ~17,000 new cases
- Of these, ~15-20% are diagnosed at an advanced stage (Stage III/IV).
- Additionally, ~70-80% of endometrial cancers are non-MSI-H or dMMR (based on molecular profiling studies).
- Of advanced cases, a subset will progress after prior systemic therapy and not be candidates for surgery or radiation. Let's assume this is ~50% of advanced cases.

### #### Eligible Patient Population Estimate:

- **US**: 66,000 new cases x 20% advanced x 75% non-MSI-H/dMMR x 50% progressed and ineligible for surgery/radiation = ~4,950 patients/year.
- **EU5**: 60,000 x 20% x 75% x 50% = ~4,500 patients/year.
- **China**: 82,000 x 20% x 75% x 50% = ~6,150 patients/year.
- **Japan**: 17,000 x 20% x 75% x 50% = ~1,275 patients/year.
- **Total across geographies**: ~16,875 patients/year.

Note: These are rough estimates and do not account for prevalent cases (existing patients who may become eligible over time). For simplicity, we'll use incident cases as a proxy for annual treatable patients.

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## **Step 2: Estimate Market Penetration**

The problem assumes a **20% to 30% share of treated patients** for pembrolizumab in this indication. This accounts for competition from other therapies, physician adoption, payer restrictions, and patient access.

- **Low-end penetration (20%):**  $16,875 \times 20\% = 3,375$  treated patients/year.
- **High-end penetration (30%):**  $16,875 \times 30\% = 5,063$  treated patients/year.

#### Breakdown by Geography:

- **US:** 4,950 patients  $\times$  20-30% = 990 to 1,485 treated patients/year.
- **EU5:** 4,500 patients  $\times$  20-30% = 900 to 1,350 treated patients/year.
- **China:** 6,150 patients  $\times$  20-30% = 1,230 to 1,845 treated patients/year.
- **Japan:** 1,275 patients  $\times$  20-30% = 255 to 383 treated patients/year.

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## **Step 3: Estimate Pricing per Patient**

Pembrolizumab is a high-cost immunotherapy. Pricing varies by geography due to differences in healthcare systems, negotiations, and purchasing power.

- **US:** Annual cost of pembrolizumab is ~\$150,000–\$175,000 per patient (based on list prices and typical dosing regimens for advanced cancers).
- **EU5:** Prices are typically 30-50% lower than the US due to negotiations with health authorities. Assume ~\$90,000–\$110,000 per patient/year.
- **Japan:** Pricing is similar to EU5, ~\$90,000–\$110,000 per patient/year.
- **China:** Pricing is significantly lower due to volume-based procurement and local policies. Assume ~\$40,000–\$50,000 per patient/year (post-negotiation discounts or inclusion in the National Reimbursement Drug List).

For simplicity, use mid-point estimates:

- US: \$162,500/patient/year
- EU5: \$100,000/patient/year
- Japan: \$100,000/patient/year
- China: \$45,000/patient/year

Note: These are annual costs assuming patients remain on therapy for a full year. Real-world duration of therapy may vary based on progression-free survival (PFS) or overall survival (OS) data from clinical trials (e.g., KEYNOTE-775 trial for pembrolizumab + lenvatinib showed median PFS of ~7-8 months in

this indication). For peak sales, we assume full-year treatment.

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## **Step 4: Calculate Potential Peak Sales**

Peak sales are calculated as: **Number of treated patients x Annual cost per patient.**

#### At 20% Penetration:

- **US:** 990 patients x \$162,500 = **\$160.9 million**
- **EU5:** 900 patients x \$100,000 = **\$90.0 million**
- **China:** 1,230 patients x \$45,000 = **\$55.4 million**
- **Japan:** 255 patients x \$100,000 = **\$25.5 million**
- **Total Peak Sales (20%):** \$160.9M + \$90.0M + \$55.4M + \$25.5M = **\$331.8 million/year**

#### At 30% Penetration:

- **US:** 1,485 patients x \$162,500 = **\$241.3 million**
- **EU5:** 1,350 patients x \$100,000 = **\$135.0 million**
- **China:** 1,845 patients x \$45,000 = **\$83.0 million**
- **Japan:** 383 patients x \$100,000 = **\$38.3 million**
- **Total Peak Sales (30%):** \$241.3M + \$135.0M + \$83.0M + \$38.3M = **\$497.6 million/year**

Thus, **Potential Peak Sales** for pembrolizumab in this indication across the specified geographies range from **\$331.8 million to \$497.6 million per year**.

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## **Step 5: Calculate \$ Value of 1% Share of Treated Patients**

A 1% share of treated patients corresponds to 1% of the total eligible patient population (16,875 patients/year) being treated with pembrolizumab.

- **1% of total patients:** 16,875 x 1% = 169 patients/year.
- Breakdown by geography:
- **US:** 4,950 x 1% = 50 patients
- **EU5:** 4,500 x 1% = 45 patients
- **China:** 6,150 x 1% = 62 patients
- **Japan:** 1,275 x 1% = 13 patients

#### Revenue from 1% Share:

- **US:** 50 patients x \$162,500 = **\$8.1 million**
- **EU5:** 45 patients x \$100,000 = **\$4.5 million**
- **China:** 62 patients x \$45,000 = **\$2.8 million**
- **Japan:** 13 patients x \$100,000 = **\$1.3 million**
- **Total \$ Value of 1% Share:** \$8.1M + \$4.5M + \$2.8M + \$1.3M = **\$16.7 million/year**

Thus, the **\$ value of a 1% share of treated patients** across these geographies is approximately **\$16.7 million per year**.

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### **Final Answer:**

1. **Potential Peak Sales for Pembrolizumab** in this indication (advanced endometrial carcinoma, non-MSI-H/dMMR, progressed after prior therapy, not candidates for surgery/radiation) at 20% to 30% market share:

- **US:** \$160.9M to \$241.3M/year
- **EU5:** \$90.0M to \$135.0M/year
- **China:** \$55.4M to \$83.0M/year
- **Japan:** \$25.5M to \$38.3M/year
- **Total:** **\$331.8M to \$497.6M/year**

2. **\$ Value of 1% Share of Treated Patients:**

- **US:** \$8.1M/year
- **EU5:** \$4.5M/year
- **China:** \$2.8M/year
- **Japan:** \$1.3M/year
- **Total:** **\$16.7M/year**

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### **Caveats and Assumptions:**

- Patient population estimates are based on incidence data and rough proportions for advanced, non-MSI-H/dMMR, and progressed patients. Prevalent cases could increase the pool.
- Pricing assumptions are based on typical costs for pembrolizumab and may vary due to discounts, rebates, or local policies.
- Duration of therapy is assumed to be one year, but real-world data (e.g., from KEYNOTE-775) suggests shorter PFS, which could lower revenue per patient.

- Market penetration (20-30%) is as given, but competition (e.g., other immunotherapies or chemotherapies) and access barriers could impact this.

- These estimates are for illustrative purposes and should be refined with primary data on epidemiology, pricing, and market dynamics.

If you have specific data or trial results (e.g., exact patient numbers or updated pricing), I can adjust the calculations accordingly.