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Withdrawn approvals for cancer therapies: Why it's happening and how it impacts you

New innovations in oncology research and technology have led to the development of novel therapies that constantly change how we treat cancer. From CAR T-cell therapies and immune checkpoint inhibitors to oral oncolytics and molecular-based targeted agents, practice-changing oncology treatments have emerged at a rapid pace. The Food and Drug Administration (FDA) granted 58 new approvals to date in 2021 and 64 new approvals for hematology/oncology indications in the prior year.[1]

The high volume of oncology drugs currently available can be largely attributed to the FDA's Accelerated Approval program, which has accounted for 18 of the 58 approvals.[2] This expedited pathway to drug approval was initiated in 1992 and amended in 2012 to allow for early approval of drugs indicated for serious conditions that fill an unmet medical need.[3] Compared to traditional FDA drug approvals, the use of a surrogate or intermediate clinical endpoint in accelerated approvals notably shortens the time to approval by reviewing markers that predict clinical benefit (laboratory values, physical signs, radiology imaging, etc.) as opposed to waiting to determine whether a drug actually extends overall survival benefit.

Since these surrogate and intermediate clinical endpoints are only considered "reasonably likely to predict" a clinical benefit, drug manufacturers are still required to verify clinical benefit through conducting phase 4 confirmatory trials.[4] If the confirmatory trial does not demonstrate that the drug provides clinical benefit, the FDA may withdraw the accelerated approval of a drug or the labeled indication.

The FDA's Accelerated Approval program accounts for 18 of the 58 new drug approvals in 2021.

While the accelerated approval program has brought numerous oncology drugs to market, the increasing rate of withdrawals and rescinded indications add further complexity to managing the care of oncology patients. Some notable examples of recently withdrawn FDA-accelerated approvals include:

- **Peptaxto®** (melphalan flufenamide) was withdrawn from the U.S. market in October 2021, after results from the phase 3 trial (OCEAN) demonstrated a negative effect on overall survival. The FDA granted Peptaxto® accelerated approval in February 2021 for use in combination with dexamethasone for the treatment of relapsed or refractory multiple myeloma in adult patients who have received at least four prior lines of therapy, and whose disease is refractory to at least one proteosome inhibitor, one immunomodulatory agent, and one CD38-directed monoclonal antibody.[5]

- After confirmatory trials did not meet overall survival endpoints, respective drug manufacturers voluntarily withdrew the indication to treat metastatic small cell lung cancer (SCLC) for **Opdivo®** (nivolumab) in December 2020 and **Keytruda®** (pembrolizumab) in March 2021. Based on early phase 1 and 2 data, the FDA granted accelerated approval for Opdivo® in August 2018 and Keytruda® in June 2019 for metastatic SCLC with progression after platinum-based chemotherapy and at least one prior line of therapy.[6]

- In October 2021, the manufacturer of **Tecentriq®** (atezolizumab) voluntarily withdrew its indication to treat triple negative breast cancer (TNBC) after not demonstrating a statistically significant improvement in the study's primary endpoint of progression free survival. Tecentriq® received accelerated approval in March 2019 in combination with paclitaxel protein-bound for unresectable locally advanced or metastatic TNBC whose tumors express PD-L1 (PD-L1 stained tumor-infiltrating immune cells of any intensity covering = 1% of the tumor area), as determined by an FDA-approved test.[7]

Recent findings presented at the 2021 European Society for Medical Oncology (ESMO) annual meeting shared research indicating both patients and providers have found it challenging to keep up with the pace of change in oncology.[8,9] They are calling for more education to increase awareness and for more collaboration across health care industries to keep up with the latest relevant data.[10]

Notable examples of withdrawn FDA-accelerated approvals include indications treated by:

- **Peptaxto®**
- **Opdivo®**
- **Keytruda®**
- **Tecentriq®**

Fortunately, the Optum® Cancer Guidance Program (CGP) is well positioned to help address these challenges. Our oncology clinicians actively monitor and evaluate the latest changes in oncology trends, from new and accelerated drug approvals to expanded FDA indications and market withdrawals, in order to provide our clients with a highly adaptable and configurable benefit management solution for an ever-evolving oncology landscape.

With precision oncology as a core driver of therapy decisions, CGP ensures our automated prior authorization platform delivers patient, indication and tumor-specific therapy recommendations and prior authorization determinations that incorporate the rapid changes in literature that reflect oncology practice today. We incorporate 270 such updates annually.

Learn more about CGP by visiting optum.com/business/solutions/employer/medical-benefit-management/oncology-management/cancer-guidance-program.html.

Sources

1. US Food and Drug Administration. Oncology (Cancer) / Hematologic Malignancies Approval Notifications. Available at: fda.gov/drugs/resources-information-approved-drugs/oncology-cancer-hematologic-malignancies-approval-notifications. Accessed January 13, 2022.
2. US Food and Drug Administration. Ongoing | Cancer Accelerated Approvals. Available at: fda.gov/drugs/resources-information-approved-drugs/ongoing-cancer-accelerated-approvals. Accessed January 13, 2022.
3. US Food and Drug Administration. Accelerated Approval. Available at: fda.gov/patients/fast-track-breakthrough-therapy-accelerated-approval-priority-review/accelerated-approval. Accessed January 13, 2022.
4. Ibid.
5. US Food and Drug Administration. Withdrawn | Cancer Accelerated Approvals. Available at: fda.gov/drugs/resources-information-approved-drugs/withdrawn-cancer-accelerated-approvals. Accessed January 13, 2022.
6. Ibid.
7. Ibid.
8. Abstract 1510MO_PR 'European cancer patients' perspectives on immunotherapy'. Annals of Oncology, Volume 32, 2021 Supplement 5.
9. Abstract 1723P_PR 'Therapeutic nihilism or therapeutic realism: Perceptions of non-oncologist physicians regarding cancer patients' prognosis'. Annals of Oncology, Volume 32, 2021 Supplement 5.
10. Critical Practice Gaps in Oncology: Implications for Development of Effective CME to Meet Accelerating Educational Needs, A Clinical Care Options (CCO) white paper. September 2015. Available at: clinicaloptions.com/-/media/publications/2016/6_2016_cme_resources/pdf_04/04.pdf?rev=d93264565a5a4befa09ffed405ec8bdd. Accessed January 13, 2022.

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11000 Optum Circle, Eden Prairie, MN 55344