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Expedited Drug Review Processes for Approval in the United States and European Union with an Illustration

SSND Balakrishna Ch*, Sai Pavan Dwarapudi, Ravi Kumar Reddy Juturi, Venkateswara Raju K.
Department of Pharmaceutical Regulatory Affairs, Shri Vishnu College of Pharmacy (Autonomous), Bhimavaram -534202, Affiliated to Andhra University, Visakhapatnam, Andhra Pradesh, INDIA.

ABSTRACT

Expedited approval processes push new drugs to the market faster than ever. Regulatory Authorities of the United States (US) and European Union (EU) are using different approval pathways to cut down the time it takes to conduct a clinical review. Conventional drug discovery is a costly and time-consuming process. A study found that pharmaceutical industries spend an average of $3 billion in R&D activities, and more than 10 years are required to develop and market one new drug. Patients can hardly wait 10 years for a lifesaving drug. For this reason, in the field of new drug discovery, Regulatory authorities and pharmaceutical companies are pursuing a strategy that expedites the approval of certain drugs that treat severe conditions and address unmet medical needs. Expedited approval processes could attract attention as a solution to dramatically reduce the time and cost required for the new drug discovery. In this article, it is presented with different expedited approval processes in the US and EU with an illustration of these speedy approval processes by taking Crizotinib drug for a better understanding.

Key words: Expedited Approval, Fast Track Approval, Accelerated Approval, Breakthrough Therapy, Priority Review, Priority Medicines.

Correspondence

Mr. Chilukuri Sri Siva Naga Durga Balakrishna

Department of Pharmaceutical Regulatory Affairs, Shri Vishnu College of Pharmacy (Autonomous), Bhimavaram -534202, Affiliated to Andhra University, Visakhapatnam, Andhra Pradesh, INDIA.

Email: balakrishnachilukuri@gmail.com;
ORCID: 0000-0003-3424-7928

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INTRODUCTION

Expedited approval processes are intended to facilitate and expedite the development and approval of new drug products to treat serious or life-threatening diseases and address an unmet medical need.[1] Regulatory Authorities like Food and Drug Administration (FDA) and European Medicines Agency (EMA) are following different methods to accelerate both the drug discovery and review process timelines to treat serious diseases and fill an unmet medical need. In order to speed up the availability, regulatory authorities of the US and EU have created rapid review and approval pathways. These pathways can also significantly benefit drug developers by reducing the time and cost required for the new drug discovery. Compared to the standard approval process, these pathways also comprise different types and levels of clinical evidence of efficacy.

RATIONALE FOR THE EXPEDITED APPROVAL PROCESS

In 1988, AIDS had reached epidemic proportions in the US. A crowd protested in front of the USFDA in Rockville, Maryland. "42,000 patients died with AIDS," the protestors chanted. "Where was the FDA?" The Center for Disease Control and Prevention concluded that over 62,000 people in the united states had deceased from AIDS by the end of 1988.

The protestors demanded the FDA, "Stop placebo-group studies in clinical trials investigating Acquired Immune Deficiency Syndrome (AIDS) drugs to speed up the availability of new drugs to the patients that showed efficacy." A few days after the protest, the FDA proclaimed that it would initiate to consider approving drug products for serious or life-threatening diseases based on Phase II clinical trial results.[2]

EXPEDITED APPROVAL PROCESSES IN THE US

In the US, there are four regulatory pathways have been put in place from 1992 onwards, such as the "Fast Track Approval" (1988), "Accelerated Approval" and "Priority Review" (1992), and "Breakthrough Therapy" (2012) to expedite the development, approval and, enrich the productivity of novel drugs to treat serious or life-threatening diseases. These pathways use a wide range of approaches, including frequent interactions between companies and FDA staff, greater clinical trial designs, and reduced timelines for evaluation of applications.[3]

Fast Track Approval

USFDA defines Fast Track as a process that facilitates the development and expedites the review of drugs to treat serious or rare diseases and fill an unmet medical need. The Fast Track approval process was introduced in 1988. Sponsors typically request Fast Track designation during the Investigational New Drug (IND) phase of drug development. USFDA reviews the application and makes a decision within 60 days. The main purpose is to get new drugs to the patients earlier. Fast Track approval addresses a wide range of serious conditions. AIDS, Cancer, Alzheimer's, and Heart failure are evident examples of serious conditions. However, diseases such as Diabetes, Epilepsy, and Depression are similarly considered to be serious conditions.[4]

Eligibility for Fast Track designation

Fast Track designation can be given based on non-clinical or clinical data and may be available with relevant, pre-clinical data prior to clinical benefit in human clinical studies. A drug product must demonstrate some benefit over existing treatment in order to get a fast track designation, such as:

- Showing superior efficacy than existing therapies
- Avoiding serious adverse effects of an existing therapy or treatment
- Improving the diagnosis of a serious or life-threatening disease where initial diagnosis results in an improved outcome
- Clinically reducing significant toxicity of an existing therapy
- Addressing an emerging public health need.

Benefits of Fast Track designation

- More frequent meetings to discuss development plan with FDA
- More frequent written correspondence
- Eligibility for Priority Review and Accelerated Approval, if appropriate standards are met
- Rolling Review, which means FDA reviews completed sections of Biologic License Application (BLA) or New Drug Application (NDA) submitted by a drug company, instead of waiting until every single section of the BLA or NDA is completed.

Breakthrough Therapy

Breakthrough Therapy designation is a process that accelerates the development and review of drug products that are intended to treat life-threatening diseases. Preliminary clinical evidence must be needed to show substantial improvement over available treatment on a clinically significant endpoint(s). Breakthrough Therapy was introduced in 2012. The sponsor requests a Breakthrough Therapy designation, and the FDA will respond to the request within 60 days. The application request for Breakthrough Therapy designation should be received by the FDA no later than the end of phase II clinical trials.[4] Refer to Figure 1 for number of Fast Track and Breakthrough Therapy Designation requests from January 1, 2015 to December 31, 2020.[5,6]

Qualifying criteria for Breakthrough Therapy designation

- If the drug is for a life-threatening disease
- Preliminary clinical evidence is essential
- May demonstrate substantial improvement on a clinically significant endpoint(s)

Primary considerations for Breakthrough Therapy designation

The FDA relies on three primary considerations

- The quantity and quality of the clinical evidence being submitted in a designation request
- The available therapies that the drug is being compared to can be provided
- The magnitude of the therapeutic effect is shown

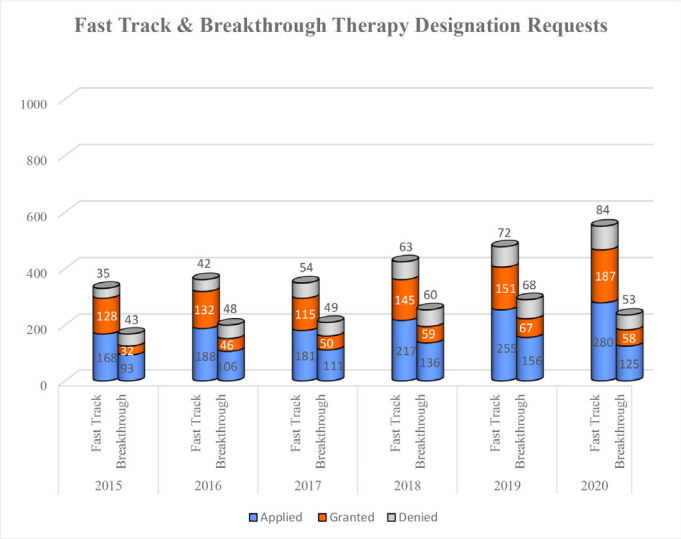

Figure 1: Fast Track and Breakthrough Therapy requests

Benefits of Breakthrough Therapy designation

- All Fast Track designation features can be applicable for Breakthrough Therapy.
- Organizational commitment involving experienced review staff and senior managers

Accelerated Approval

When reviewing a new drug molecule, it can take many years to realize whether a drug provides a real therapeutic effect on patient survival rate and functions. Clinically meaningful positive therapeutic effect in the context of a proposed disease is known as "Clinical Benefit." In 1992, FDA introduced the *Accelerated Approval* regulations and amended them in 2012. These regulations allow early patient access to new drug products that treat serious or life-threatening diseases based on a surrogate endpoint.[7] Drugs approved through FDA Accelerated Approval Program still need to be verified in clinical trials using endpoints that demonstrate clinical benefit, and those studies are called phase II confirmatory trials. If the drug later proves incapable of demonstrating clinical benefit to patients, then FDA may withdraw an Accelerated approved drug.

Eligibility for Accelerated approval designation

- If there is a serious condition
- A Meaningful advantage over available therapy
- Sponsors must agree to conduct adequate and well-controlled post-marketing confirmatory studies that validate the surrogate endpoint

Benefits of Accelerated approval

- Discussions with reviewing division early in the development process (pre-IND meeting)
- Drugs under Accelerated Approval can be approved based on an unestablished surrogate endpoint.
- Shortens overall development time

Priority Review

A Priority Review is an expedited program introduced in 1992 that will direct complete attention to the evaluation of priority drug applications that, if approved, would play a major role in the increased effectiveness of the Diagnosis, treatment, or prevention of serious diseases when compared to normal applications.[1] Refer to Figure 2 for number of Accelerated and Priority Review Approvals from 2015 to 2019.[8,9,10,11,12,]

Eligibility for Priority Review designation

- The proposed drug must treat a Serious Disease or Condition.
- The drug product must demonstrate a clinically meaningful improvement in safety or effectiveness

Benefits of Priority review

A drug review process can be completed in 6 months instead of 10 months under standard review.

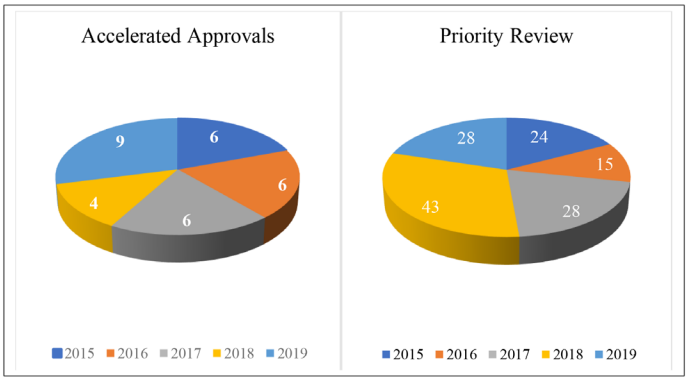

Figure 2: Accelerated and Priority review approvals

EXPEDITED APPROVAL PROCESSES IN EUROPEAN UNION

In the EU, The European Medicines Agency (EMA) is a decentralised regulatory body providing authorization to speed up the development and approval of new therapeutic products in situations of unmet medical need to treat serious or life-threatening diseases. EMA provides various expedited routes for early patient access to novel medicines that address public health needs such as PRIME (Priority Medicines), Accelerated Assessment, Conditional Marketing Authorisation, Compassionate Use, Exceptional Circumstances.[13]

PRIME - Priority Medicines

EMA launched the PRIME scheme in March 2016. The scheme focuses on drug products that show a greater therapeutic effect over available treatments or benefit patients with no available treatments. PRIME provides enhanced scientific and regulatory support to optimize development and enable accelerated assessment of drugs that can address patients' unmet medical needs.[13]

Eligibility for PRIME designation

- When the drug is for a serious life-threatening disease or condition where there is no major therapeutic efficacy over existing treatments or no available medication to treat a patient
- A medicinal product should demonstrate the potential to help patients with no existing treatments based on pre-clinical data

Benefits of PRIME approval

- PRIME helps developers of promising new drugs to optimize development plans.
- Initial Marketing Authorization (MA) and Centralized procedure.
- PRIME eligible products may also qualify for Conditional Marketing Authorization (CMA).
- It fosters early dialogue with EMA to facilitate robust data collection and high-quality marketing authorization applications.
- It speeds up an evaluation so that patients hoping for earlier access to safe therapies for their unmet medical needs, such as AIDS, Cancer, Alzheimer's disease.
- Early Rapporteur appointment from the Committee for Medicinal Products for Human Use (CHMP) or the Committee for Advanced Therapies (CAT), to deliver continuous support to build knowledge ahead of Marketing Authorization Application (MAA).
- Organizes an initial meeting with the CHMP/CAT rapporteur and a multidisciplinary group of experts from working parties and relevant EMA scientific committees.
- Issues preliminary guidance on a company's entire development plan and regulatory approach.
- Assign a dedicated EMA contact person.
- Provides scientific advice during the development stage.
- Medicines eligible for PRIME are also potentially qualified for accelerated assessment at the time of an application for marketing authorization.

Accelerated Assessment

The Accelerated Assessment was launched in November 2005 by the revised EU pharmaceutical legislation. This regulatory tool aims to speed up patients' access to new medicines of major public-health interest by reducing the review time of a Marketing Authorisation Application. According to Article 14 (9) of Regulation (EC) No 726/2004, when an application is submitted for marketing authorization in respect of drug products for unmet medical needs or constitutes a significant improvement over the existing methods of diagnosis, treatment, and prevention of a serious condition human use which is of major public interest from the point of health, the applicant or companies can request an Accelerated Assessment. The European Medicines Agency's Committee for Medicinal Products for Human Use reviews a Marketing Authorization Application for Accelerated Assessment.[14]

Eligibility for Accelerated Assessment

- Accelerated assessment requests should be made at least two months before submitting the MAA.
- EMA recommends that applicants can ask for a pre-submission meeting six months before final submission to plan for review under Accelerated assessment.

Benefits of Accelerated Assessment

- Evaluating a MAA under a Centralized Procedure can take up to 210 days. The CHMP can decrease the timeline to 150 days if the applicant gives appropriate reason for an Accelerated Assessment.
- Accelerated Assessment pathways use both clinical and surrogate endpoints.
- For products undergoing Accelerated Assessment based on surrogate endpoints, the real therapeutic benefit of the drug products approved for marketing may never be found because there is no consistent requirement for confirmatory post-marketing studies.

Conditional Marketing Authorisation

The EMA introduced conditional Marketing Authorisation (CMA) in 2005 as an early access pathway for medicines that address unmet medical needs and treat patients' life-threatening or rare diseases. In the interest of public health, applicants may be granted a CMA for such medicinal products where the benefit of immediate accessibility outweighs the risk based on less data than usually required. The marketing authorization holder will submit complete clinical data at a later stage. CMA is valid for one year and it can be renewed annually.[14]

Eligibility for Conditional Marketing Authorisation

- The anticipated benefits justify the risks.
- The applicant is invited to inform the EMA about his purpose to request a CMA as part of the "Letter of Intent" to be sent to the EMA in advance about the submission of MAA.

- The applicant must be able to give complete data after marketing authorization.
- Unmet medical needs of the patients will be fulfilled.
- The benefit to public health of the drug product's availability on the market outweighs the possible risks.
- Medicines designated as orphan drugs are also eligible for CMA.

Benefits of Conditional Marketing Authorisation

- CMA can speed up earlier patient access to new medicines.
- Once complete data on the drug product have been submitted, the marketing authorization can be switched into a standard marketing authorization. Initially, this is valid for five years and then it can be renewed for unlimited validity.
- For medicinal products deemed suitable for CMA, applicants are also encouraged to request an Accelerated Assessment.

Compassionate Use

Compassionate Use is a treatment choice that permits the use of unauthorized medicine. Under severe conditions, drug products in the development phase can be made accessible to seriously ill patients with no available treatments. EMA gives recommendations through the CHMP, but these do not make a legal framework. Compassionate use programs are executed by the Member States, which have their own rules and regulations.[15]

Eligibility for Compassionate use

- Compassionate use programs are put in place if the drug product is likely to help patients suffering from long-lasting, or seriously life-threatening diseases, which cannot be treated satisfactorily with any currently authorized drug products.
- Every member state of the EU has developed its own legislation for Compassionate use programs based on the EMA recommendations and legal framework. Therefore, stakeholders such as health professionals, pharmaceutical companies, patients and patient organizations, and policymakers need to be informed of regulations and processes that enable early access to innovative medicines.

Benefits of Compassionate use

- Compassionate Use Programme (CUP) benefits patients who are incapable to participate in clinical. Participation in clinical trials is a difficult choice for patients with life-threatening, long-lasting diseases.
- Patients get early access to investigational drugs or drugs that have not yet received marketing authorization in the European Union.
- Patients have access to promising drugs at an earlier stage during the life cycle, for instance, post Phase II.
- The market authorization holders in the EU get the opportunity to resolve any product-related issues and can overcome challenges or issues encountered by pre-approved drugs through early access.

Exceptional Circumstances

In 1993, the European Union introduced an instrument to approve drugs under Exceptional Circumstances (ECs). Early market access could be granted to drug products where the applicant is incapable to provide complete data on the safety and efficacy under regular conditions of use because the condition or illness to be treated is rare or collection of complete information is not possible or is unethical. The sponsors need to perform further studies to meet specific obligations after obtaining marketing approval.[16] Drugs that are approved under Exceptional Circumstances are reviewed annually to check the risk-benefit balance.

Refer to Figure 3 for Bar graph representation of CMA, Accelerated Assessment, Exceptional Circumstances, & PRIME from 2017-2019.[17,18,19]

Eligibility for approval under Exceptional Circumstances

- Drug products for which the applicant is incapable to provide comprehensive efficacy and safety data due to the rarity of the indication.
- If it is unethical to collect the comprehensive safety and efficacy data for a standard approval.
- Inability to provide comprehensive data due to the present state of knowledge and the applicant should explain what scientific knowledge would be needed to conduct such trials and justify the lack of such knowledge.

Benefits of approval under Exceptional Circumstances

- Accelerated Assessment can be applicable for drug products that are approved under Exceptional Circumstances.
- Marketing authorization of medicinal products under Exceptional Circumstances may be varied with the addition of new indication(s).

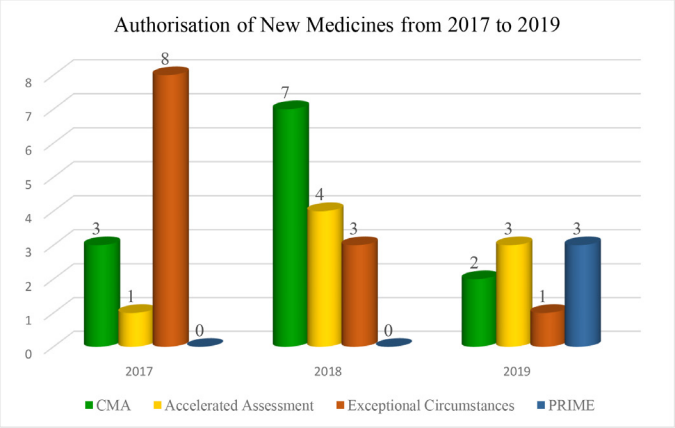

Figure 3: CMA, Accelerated Assessment, Exceptional Circumstances, & PRIME approvals

In such cases, the marketing authorization will still remain under Exceptional Circumstances.

ILLUSTRATION OF EXPEDITED APPROVAL TIMELINE OF CRIZOTINIB

Crizotinib for Non-Small Cell Lung Cancer (NSCLC).

Sponsor: Pfizer, Inc.

Crizotinib is an oral drug indicated for the treatment of NSCLC. Crizotinib is designed to block a protein called ALK (Anaplastic Lymphoma Kinase), which is involved in Cancer cell growth and survival. NSCLC is usually caused by smoking. It also occurs in people who work near asbestos, certain alloys, paints, pigments, and preservatives. Symptoms of NSCLC comprise chest pain, coughing up blood, shortness of breath, loss of appetite, and fatigue.

2007: *ALK* was first identified as a molecular target in NSCLC.[20]

September 13, 2010: Crizotinib acquired Orphan drug designation from the USFDA.[21]

December 6, 2010: FDA granted Fast Track designation for Crizotinib.[21]

January 11, 2011: Initiated the Rolling submission of a New Drug Application (NDA) to the FDA for Crizotinib.[22]

March 30, 2011: Crizotinib New Drug Application (NDA) was submitted.[23]

May 16, 2011: NDA for Crizotinib was accepted and granted Priority Review status by the FDA.[24]

July 28, 2011: Pfizer submitted MAA to the EMA for Crizotinib through the Centralized Procedure.[25]

August 26, 2011: USFDA Approves Pfizer's (crizotinib) as the first and only therapy specifically to treat certain late-stage Non-Small Cell Lung Cancers that express the abnormal anaplastic lymphoma kinase gene by the USFDA. The early approval of Crizotinib was based on clinical trial data of 255 patients registered in two clinical trials, specifically Phase II Profile 1005 and Phase I Study 1001 have demonstrated impressive clinical benefit.[26]

October 23, 2012: The European Commission has given conditional marketing authorisation valid throughout the European Union for Crizotinib.[23]

November 20, 2013: Crizotinib obtained regular approval based on an increased survival rate in patients with metastatic ALK-positive NSCLC initially treated with one platinum-based chemotherapy regimen.[26]

April 21, 2015: The USFDA granted Breakthrough Therapy designation to Crizotinib for the treatment of patients with ROS1-positive NSCLC.[27]

October 8, 2015: Pfizer submitted a supplemental New Drug Application (sNDA) to the USFDA.[28]

December 8, 2015: FDA granted Priority Review for sNDA to Crizotinib.[29]

March 11, 2016: The USFDA approved Crizotinib capsules for the treatment of patients with metastatic NSCLC whose tumours are ROS1-positive. Crizotinib is the first FDA-approved treatment indicated for two Biomarkers, ALK and ROS1, in metastatic NSCLC.[30]

August 31, 2016: Crizotinib receives approval in European Union for ROS1-positive advanced NSCLC.[31]

May 29, 2018: Pfizer's Crizotinib is the first Tyrosine kinase inhibitor to obtain FDA Breakthrough Therapy Designation in two new indications for the treatment of patients with previously treated Metastatic NSCLC with MET Exon 14 alterations and relapsed or refractory systemic Anaplastic Large Cell Lymphoma (ALCL).[31]

September 23, 2020: FDA accepts sNDA for Pfizer's crizotinib for the treatment of patients with pediatric ALK-positive ALCL.[32]

January 14, 2021: FDA approved Pfizer's Crizotinib for the treatment of patients with ALK-positive ALCL in children and young adults.[33]

A recently published study of clinical trials evaluating therapies for advanced NSCLC has proved that the cumulative success rate for new drug products for advanced NSCLC is lesser than the industry-projected rate.[34] However, the study also confirmed that biomarker and receptor-targeted therapies (such as Crizotinib, Bevacizumab, and Erlotinib) substantially increased the clinical trial success rate.

Crizotinib serves as a model for expedited development, review, and approval of novel, highly efficacious and the clinically meaningful drug that demonstrates the potential to address unmet needs for such a life-threatening disease or condition.

POST MARKETING SURVEILLANCE

Post-marketing surveillance programs in the US and EU are capable of identifying the quality, safety, and efficacy of drug products. They will protect public health from the risks posed by falsified drug products. Post-marketing surveillance is essential to the effective regulation of drugs and comprises all regulatory activities that monitor the long-term adverse effects of new medicinal products after launching into the market. In the US, MedWatch is the adverse events reporting program that interacts with FDA's Adverse Event Reporting System (FAERS) which receives voluntary adverse event reports from patients and healthcare professionals. EudraVigilance is an electronic database for analysing, evaluating, and collecting adverse drug reactions related to authorised medicinal products in the EU.[35]

CONCLUSION

Speeding the availability of new drugs that treat life-threatening diseases is in everyone's interest, particularly when the drug products are the first available medication or if the drug has advantages over other available treatments. However, these expedited new drugs may have uncertainty in the efficacy data or undetected serious toxicities at the time of approval. They are not identified until after on the market for several years. Although these drug products may have safety concerns, they were mainly approved based on the determination that the anticipated benefits outweighed potential risks of the drug. All drugs have risks. FDA and EMA have efforts in place to curtail these safety risks, and there are still occurrences where drug products may come to market quickly and lead to safety concerns. Although, many drugs that treat life-threatening diseases or conditions have successfully been brought to market through these expedited pathways and have made a significant impact on disease progression. For example, a number of targeted cancer-fighting drugs and antiretroviral drugs used to treat HIV/AIDS entered the market via a speedy approval process and subsequently altered the treatment paradigm.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

1. Van Norman GA. Update to drugs, devices, and the FDA: How Recent Legislative Changes Have Impacted Approval of New Therapies. JACC Basic Transl Sci. 2020;5(8):831-9. doi: 10.1016/j.jacbts.2020.06.010, PMID 32864509.
2. The scientist. Picking Up Pace. 2016.
3. Cauchon NS, Oghamian S, Hassanpour S, Abernathy M. Innovation in Chemistry, Manufacturing, and Controls-A Regulatory Perspective From Industry. J Pharm Sci. 2019;108(7):2207-37. doi: 10.1016/j.xphs.2019.02.007, PMID 30794794.
4. Arjun S, Venkatesh MP, Balamuralidhara V, Kumar TMP. Expedited programs for Drug Development and Approval in USA. Res J Pharm Technol. 2020;13(3):1409-14. doi: 10.5958/0974-360X.2020.00258.9.
5. FDA. CDER FAST track designation requests received; 2020 [cited Jan 2021]. Available from: https://www.fda.gov/media/97830/download.
6. FDA. CDER breakthrough therapy designation requests received by fiscal year; 2020 [cited Jan 2021]. Available from: https://www.fda.gov/media/95292/download.
7. Kraus VB, Simon LS, Katz JN, Neogi T, Hunter D, Guermazi A, Karsdal MA. Proposed study designs for approval based on a surrogate endpoint and a post-marketing confirmatory study under FDA's accelerated approval regulations for disease modifying osteoarthritis drugs. Osteoarthritis Cartilage. 2019;27(4):571-9. doi: 10.1016/j.joca.2018.11.002, PMID 30465809.
8. FDA. NOVEL drugs 2015; 2016 [cited Sep 2020]. Available from: https://www.fda.gov/media/95661/download.
9. FDA. NOVEL DRUGS summary [cited Sep 2020]. Available from: https://www.fda.gov/media/102618/download. Vol. 2017; 2016.
10. FDA. New drug therapy approvals [cited Sep 2020]. Available from: https://www.fda.gov/files/about%20fda/published/2017-New-Drug-Therapy-Approvals-Report.pdf. Vol. 2018; 2017.
11. FDA. New drug therapy approvals [cited Sep 2020]. Available from: https://www.fda.gov/files/drugs/published/New-Drug-Therapy-Approvals-2018_3.pdf. Vol. 2019; 2018.
12. FDA. New drug therapy approvals 2019; 2020 [cited Sep 26 2020]. Available from: https://www.fda.gov/media/134493/download.

13. Detela G, Lodge A. EU regulatory pathways for ATMPs: standard, accelerated and adaptive pathways to marketing authorisation. Mol Ther Methods Clin Dev. 2019;13:205-32. doi: 10.1016/j.omtm.2019.01.010, PMID 30815512.
14. Cox EM, Edmund AV, Kratz E, Lockwood SH, Shankar A. Regulatory affairs 101: introduction to expedited regulatory pathways. Clin Transl Sci. 2020;13(3):451-61. doi: 10.1111/cts.12745, PMID 31909876.
15. Goyal PK, Mathur R, Medhi B. Understanding the challenges and ethical aspects of compassionate use of drugs in emergency situations. Indian J Pharmacol. 2020;52(3):163-71. doi: 10.4103/ijp.IJP_665_20, PMID 32873998.
16. Hofer MP, Hedman H, Mavris M, Koenig F, Vetter T, Posch M, Vamvakas S, Regnstrom J, Aarum S. Marketing authorisation of orphan medicines in Europe from 2000 to 2013. Drug Discov Today. 2018;23(2):424-33. doi: 10.1016/j.drudis.2017.10.012, PMID 29074441.
17. EMA. Human medicines highlights 2017; 2018 [cited Nov 2020]. Available from: https://www.ema.europa.eu/documents/report/human-medicines-highlights-2017_en.pdf.
18. EMA. Human medicines highlights 2018; 2019 [cited Nov 2020]. Available from: https://www.ema.europa.eu/en/documents/report/human-medicines-highlights-2018_en.pdf.
19. EMA. Human medicines highlights 2019; 2020 [cited Nov 19 2020]. Available from: https://www.ema.europa.eu/en/documents/report/human-medicines-highlights-2019_en.pdf.
20. Du X, Shao Y, Qin HF, Tai YH, Gao HJ. ALK-rearrangement in non-small-cell lung cancer (NSCLC). Thorac Cancer. 2018;9(4):423-30. doi: 10.1111/1759-7714.12613, PMID 29488330.
21. Ou SH, Bartlett CH, Mino-Kenudson M, Cui J, Iafrate AJ. Crizotinib for the treatment of ALK-rearranged non-small cell lung cancer: a success story to usher in the second decade of molecular targeted therapy in oncology. Oncologist. 2012;17(11):1351-75. doi: 10.1634/theoncologist.2012-0311, PMID 22989574.
22. Pfizer. Pfizer initiates rolling submission for A new drug application in the U.S.; 2011 [cited Nov 7 2020]. Available from: https://www.pfizer.com/news/press-release/press-release-detail/pfizer_initiates_rolling_submission_for_a_new_drug_application_in_the_u_s_for_its_fast_tracked_investigational_compound_crizotinib_pf_02341066_for_patients_with_alk_positive_advanced_non_small_cell_lung_cancer.
23. Shah RR, Roberts SA, Shah DR. A fresh perspective on comparing the FDA and the CHMP/EMA: approval of antineoplastic tyrosine kinase inhibitors. Br J Clin Pharmacol. 2013;76(3):396-411. doi: 10.1111/bcp.12085, PMID 23362829.
24. Pfizer. Pfizer announces simultaneous filing of new drug applications for crizotinib with U.S. Food and Drug Administration and Japanese Ministry of Health, Labour and Welfare; 2011 [cited Dec 2020]. Available from: https://investors.pfizer.com/investor-news/press-release-details/2011/Pfizer-Announces-Simultaneous-Filing-Of-New-Drug-Applications-For-Crizotinib-With-US-Food-And-Drug-Administration-And-Japanese-Ministry-Of-Health-Labour-And-Welfare/default.aspx.
25. EMA. CHMP assessment report; 2012 [cited Dec 2020]. Available from: https://www.ema.europa.eu/en/documents/assessment-report/xalkori-epar-public-assessment-report_en.pdf.
26. Kazandjian D, Blumenthal GM, Chen HY, He K, Patel M, Justice R, Keegan P, Pazdur R. FDA approval summary: crizotinib for the treatment of metastatic non-small cell lung cancer with anaplastic lymphoma kinase rearrangements. Oncologist. 2014;19(10):e5-11. doi: 10.1634/theoncologist.2014-0241, PMID 25170012.
27. Pfizer. Pfizer Receives U.S. FDA Breakthrough Therapy Designation for XALKORI® (crizotinib) for the Treatment of Patients with ROS1-Positive Non-Small Cell Lung Cancer; 2015 [cited Dec 21 2020]. Available from: https://www.pfizer.com/news/press-release/press-release-detail/pfizer_receives_u_s_fda_breakthrough_therapy_designation_for_xalkori_crizotinib_for_the_treatment_of_patients_with_ros1_positive_non_small_cell_lung_cancer.
28. EMA. Crizotinib in patients with ROS1+ non-small cell lung cancer: rationale and results; 2016 [cited Dec 2020]. Available from: https://www.ema.europa.eu/en/documents/presentation/presentation-crizotinib-patients-ros1-non-small-cell-lung-cancer-rationale-results-mace-l-rothenberg_en.pdf.
29. Pharm Tech. FDA accepts and grants priority review for Xalkori; 2015 [cited Dec 2020]. Available from: https://www.pharmtech.com/view/fda-accepts-and-grants-priority-review-xalkori.
30. Kazandjian D, Blumenthal GM, Luo L, He K, Fran I, Lemery S, Pazdur R. Benefit-risk summary of crizotinib for the treatment of patients with ROS1 alteration-positive, metastatic non-small cell lung cancer. Oncologist. 2016;21(8):974-80. doi: 10.1634/theoncologist.2016-0101, PMID 27328934.
31. Puccini A, Marín-Ramos NI, Bergamo F, Schirripa M, Lonardi S, Lenz HJ, Loupakis F, Battaglin F. Safety and Tolerability of c-MET Inhibitors in Cancer. Drug Saf. 2019;42(2):211-33. doi: 10.1007/s40264-018-0780-x, PMID 30649748.
32. Pfizer Inc. FDA accepts supplemental new drug APPLICATION [internet] (NYSE. PFE); 2020. Available from: https://www.pfizer.com/news/press-release/press-release-detail/fda-accepts-supplemental-new-drug-application-pfizers.
33. Pfizer Inc. Pfizer's XALKORI® (crizotinib) approved by FDA [internet] (NYSE. PFE); 2021. Available from: https://www.pfizer.com/news/press-release/press-release-detail/pfizers-xalkorir-crizotinib-approved-fda-alk-positive.
34. International Association for the Study of Lung Cancer. Clinical trial success influenced by biomarker - and receptor-targeted therapies in NSCLC. Science-Daily. Science. Feb 14 2014.
35. Cano-Sandoval MÁ, López-Armas GC, Perfecto-Avalos Y, Vázquez-Alvarez AO, Brennan-Bourdon LM. Opportunities to improve the electronic reporting system for adverse drug reactions in Mexico: A comparative evaluation with the United States of America and the European Union. Pharmacoepidemiol Drug Saf. 2020;29(11):1523-6. doi: 10.1002/pds.5092, PMID 32838482.

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