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Drug Approval Processes During Emergency Situations: Emergency Use Authorization (Eua)

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ABSTRACT

A pharmaceutical company trying to manufacture a drug, cosmetic, vaccine, or medical device must first establish its safety and efficacy. This is done by conducting preliminary investigations in animals, followed by establishing clinical efficacy through clinical trials. This whole process spans years before the FDA or other regulatory bodies approve the drug or vaccine for marketing and distribution. In situations involving public health emergencies, pandemics, or potential threats such as chemical, biological, or nuclear incidents, the FDA allows for Emergency Use Authorisation (EUA). This regulatory approach allows for fast-track authorization of unapproved medical products or unauthorized indications of medical products. The FDA also allows the use of EUA when there are no adequate alternative treatment options available.EUA acts as an essential resource for medical practitioners and healthcare professionals during a public health crisis by using all possible medical products and treatments available during the emergency period. The EUA is activated once the government declares a crisis and remains in effect until the end of the said specific crisis it was activated for. For a medical product or treatment to be approved by the EUA, it must be "safe and effective," and its potential benefits must outweigh its potential risks.

Keywords: *Emergency Use Authorization, FDA Approval Process, remdesivir, Emergency pathways.*

INTRODUCTION

"The Emergency Use Authorisation (EUA)" framework was established in 2004 during "The Project Bioshield Act 2004", in the "Federal Food, Drug and Cosmetic Act", to ratify the use of specific medical products during emergency health situations [1]. It acts as an essential resource for medical practitioners and healthcare officials engaged in a public health crisis to use all possible medical products available to detect, prevent, treat, or mitigate the disease/disorder [2]. In situations where there are no adequate approved alternatives available, the Emergency Use Authorisation (EUA) sanctions the use of medicines or treatments that have not yet received full approval but are considered necessary and appropriate. An EUA's duration aligns with the duration of the declared public health emergency for which it was issued [2][3].

EUA was appropriately used for the first time during the H1N1 outbreak. Before its increased use amidst the COVID-19 pandemic, the Emergency Use Authorisation (EUA) had been utilised on two occasions [4].

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The first instance was for medication aimed at preventing inhalation anthrax, while the second was for antibiotic emergency kits. Peramivir was the first unapproved investigational new drug to be authorized under the EUA to treat suspected and confirmed cases of H1N1 influenza virus (a communicable viral disease that causes upper and lower respiratory tract infections) in adult and pediatric patients receiving hospital care,[5] the EUA issued for peramivir expired on June 23, 2010 with conclusion of H1N1 influenza virus as a urgent health concern [6]. Peramivir marked the first instance of an EUA being granted for an unapproved drug by the FDA [7].

EUA of a drug can be revoked by the FDA if it shows no significant effect in treating the disease or outbreak,[8] Example- a EUA was issued for hydroxychloroquine in the initial period of the COVID-19 pandemic, but was revoked after it was found that it posed potential risks to the patients but offered no substantial benefit [9][10].

As the COVID-19 outbreak progressed, small laboratories and multinational pharmaceutical companies tried to develop potential drugs and vaccines that could control and combat the ongoing pandemic [11]. In just a few months, numerous clinical trials were initiated to investigate potential COVID-19 treatments.

Remdesivir, a therapeutic developed by Gilead Sciences in a joint effort with the U.S. Centers for Disease Control and Prevention (CDC), demonstrated significant clinical improvement when administered to COVID-19 patients [12][13]. One of the main reasons for the investigation of remdesivir was that it was the most clinically advanced nucleoside against SARS-CoV-2 when compared to other therapeutic counterparts [14]. During the clinical trial led by the U.S. National Institute of Allergy and Infectious Diseases (NIAID) conducted on remdesivir among 1,063 hospitalised patients with severe illness across different sites in the US, EU, and Asia, study demonstrated that patients receiving remdesivir experienced a 31% shorter recovery time compared to the placebo group [15][16].

There was a decrease in the mortality rates of these patients, with a median recovery time of 11 and 15 days. These preliminary results were provided to regulators globally [17]. The FDA collaborated with NIH to confirm the data's reliability, a critical factor in determining whether remdesivir should be made widely available beyond clinical trials [18].
By April 29, 2020, data from these two completed trials and their interim results had been submitted to regulatory bodies to support the use of remdesivir in covid patients. Based on these positive clinical findings, the U.S. Food and Drug Administration issued an Emergency Use Authorisation (EUA) for the use of remdesivir in hospitalised COVID-19 patients. The FDA had not approved any therapeutic for emergency use during COVID-19, making remdesivir the first therapeutic to obtain an EUA during the pandemic [19][20].

FDA approval process for a new drug:
The manufacturers apply for a "Biologics License Application (BLA)" for the approval of biologics or vaccines, but before filing for a BLA, the manufacturer must follow the following process: [21][22].

1. Drug Discovery and Development: a new drug compound is developed in the laboratory & research is conducted to isolate the most promising lead compound based on its interaction with potential therapeutic targets in man [23].

2. Animal Testing: In this process, the sponsor conducts research on animals to assess drug toxicity and gather essential data on the drug's safety, effectiveness, and quality, which are being investigated [24].

3. Investigational New Drug Application (IND): the drug sponsor files for an IND using data derived from animal experimentation, provides information to the FDA about the composition of the drug and its nature, and a plan is developed for testing the drug on humans [25]. After the IND has been filed, the FDA carefully assesses the application to ensure that the clinical trial poses no unreasonable risks to the trial participants. Additionally, the FDA reviews the informed consent and human subject protection protocols to safeguard the rights and well-being of trial participants [26][27].

4. Clinical development/ Clinical Trial: the testing of an investigational new drug in human subjects occurs in four phases.

i. Phase I: a clinical trial is conducted on a cohort of 20-80 healthy volunteers to determine the safety and tolerability of the new compound in the body, and also determine its metabolism and excretion processes.

ii. Phase II: In Phase II of a clinical trial, typically 100 healthy volunteers are enrolled to evaluate the drug's efficacy and gather preliminary data indicating its potential therapeutic effects against the targeted disease.

iii. Phase III: a trial is conducted on 1000 volunteers to garner additional information on the safety and efficacy of the drug in diverse populations at varying concentrations and study the efficacy of the new drug when given in combination with other medications [28].

iv. Phase IV: Post Marketing Surveillance

5. Labelling: FDA reviews the drug label [29].

6. New Drug Application (NDA): The pharmaceutical company officially petitions the FDA for the endorsement of a drug to be marketed within the United States. NDA encompasses comprehensive data from animal and human trials, along with details on the drug's mechanisms of action within the body. Prior to NDA submission, the FDA holds consultations with the drug sponsor [30].

7. Facility Inspection: the FDA carries out an inspection of the facility where the drug is set to be produced and manufactured [31].

8. Post-Marketing Risk Assessment: these are the studies that are carried out after the drug has been granted approval by the regulatory authorities. The primary purpose of this assessment is to predict safety issues in larger populations and monitor for any adverse effects [32].

FDA approval process of a new drug/ vaccine under emergency use authorisation:
The USFDA provides several regulatory mechanisms that facilitate faster development and review of drugs and biologics for severe diseases where treatment options are limited [33].

Fast Track Designation: it is a process designed to develop and expedite the review of drugs used to treat serious conditions and fill an unmet medical need. The main purpose of this is to get important drugs to the patient earlier. Deciding whether a condition is considered serious involves judgment, typically based on factors such as the drug's potential impact on survival, daily functioning, or the likelihood that the condition will worsen over time if left untreated. Examples of serious conditions include AIDS, Alzheimer's disease, heart failure, and cancer. Addressing an unmet medical need involves offering a therapy where none currently exists or introducing a treatment that could potentially be superior to existing options [34]. A drug intended to treat or prevent a condition without any available therapy is clearly targeting an unmet need. However, if therapies are already available, a fast-track drug must demonstrate a clear advantage over the existing treatments. The Fast-Track designation must be requested by the drug manufacturer. This request can be made at the time of, or any point after, submitting the application to investigate the drug (under section 505(i) or section 351(a)(3) of the Public Health Service Act) [35].

Breakthrough Therapy Designation: It is intended to accelerate the development and review of drugs designed to treat serious conditions, where preliminary clinical evidence suggests the drug may offer significant improvement over existing therapies on clinically meaningful endpoints. Assessing whether the improvement is substantial requires judgment and depends on factors such as the magnitude of the treatment effect, its duration, and the significance of the observed clinical outcomes. Generally, the preliminary clinical data must demonstrate a clear and notable advantage over current treatment options [36].

Accelerated Approval: Studying a new drug often requires many years to determine if it has a meaningful impact on a patient's survival, quality of life, or daily functioning. A positive therapeutic effect that is significant within the context of a particular disease is referred to as "clinical benefit." Recognising that measuring a drug's clinical benefit may take a long time, the FDA introduced Accelerated Approval regulations in 1992. These regulations allow the approval of drugs for serious conditions that address unmet medical needs based on surrogate endpoints. By using surrogate endpoints, the FDA can expedite the approval process for such drugs [37].

Priority Review: A Priority Review designation focuses attention and resources on the evaluation of applications for drugs that, if approved, could significantly enhance the safety or effectiveness of treatment, diagnosis, or prevention of serious conditions compared to existing therapies [38].
A significant improvement may be shown through examples such as:

- Evidence of greater effectiveness in treating, preventing, or diagnosing a condition.
- Elimination or major reduction of a treatment-limiting side effect.
- Proven enhancement of patient compliance, leading to better serious health outcomes.
- Evidence of safety and efficacy in a previously underserved subpopulation [38].

Once the government declares a severe event or disease outbreak as an emergency (ex-COVID-19 pandemic), Emergency Use Authorisation comes into action, and the FDA reviews all EUA requests made by drug manufacturers and grants permission if all necessary criteria are met [39].

The FDA approval process for EUA is as follows [40].
1. Development: the vaccine manufacturer conducts research to develop a potential vaccine candidate or lead drug compound.

2. Animal Testing: the sponsor now conducts animal trials to determine the safety and effectiveness of the compound, and drug toxicity is also studied [41].

3. Investigational New Drug Application (IND): after animal research, the manufacturer gathers all data during the trial and submits an IND application to the FDA to now begin trials involving human subjects [26].

4. Clinical Trials: trials are conducted after approval to determine the efficacy of the vaccine in human participants.
5. Data Safety Monitoring Boards (DSMB): they evaluate data obtained from phase 3 clinical trial and tell the manufacturer if the criteria for clinical endpoint have been met or not; based on this data, the manufacturer decides if he wants to submit and EUA or not.

6. Review Meeting: The manufacturer arranges a review meeting with scientists and technical experts to assess whether their vaccine aligns with the FDA's safety and efficacy standards. Based on this evaluation, they decide whether to submit an emergency use authorisation application to the FDA or not [42].

7. Centre for Biologics Evaluation and Research (CBER): CBER reviews the manufacturer's EUA application to analyse the vaccine's safety and effectiveness. Additionally, the manufacturing data is carefully scrutinised to verify its alignment with the requirements for authorising the vaccine's use during an emergency.

8. FDA Approval: If the FDA determines that all safety requirements are satisfied and the vaccine demonstrates a favourable risk-benefit profile, the FDA grants authorisation for the vaccine's emergency use. The manufacturing data must confirm adherence to all quality and consistency standards. Subsequently, the FDA informs the manufacturer that their EUA has been accepted and authorised [42].

The FDA informs the manufacturer that its EUA has been accepted and authorized [43].
The differences between the processes are illustrated in (Figure 1).

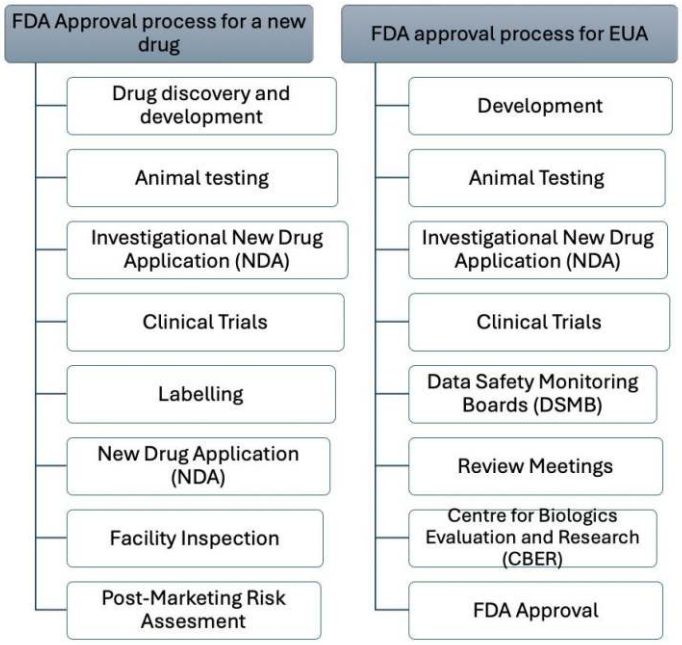

Figure 1: Comparison of regular FDA drug approval process with the FDA approval process for EUA

Aim of EUA within FDA: the main objective for issuance of EUA by the FDA is to protect public health during a medical or biological emergency, and to make sure safe and effective alternatives are available during emergency situations [44].

- Medical countermeasures are available to help facilitate their development.
- Safeguarding public health by guaranteeing the security, reliability, soundness and integrity of regulated medical products.
- Being more prepared when dealing with an emergency.
- Ensuring supply chain integrity during an emergency [44].

The time period of a standard FDA approval compared to a EUA:
In the last few years FDA has approved various vaccines for the treatment of flu, from the application of an IND to conducting a Phase I trial to submitting an NDA for approval of the vaccine; the whole process takes about 8-9 years, after which the manufacturer can finally market their product [45]. During the COVID-19 outbreak, Pfizer-Bio N-Tech were the initial ones to submit a EUA for their COVID-19 vaccine; the vaccine was clinically developed for six months prior to submitting a EUA, the FDA granted the EUA in under a month, and full approval was given within a mere 8 months [46].

Approval of drug/vaccine during emergencies by Different Countries

1. European Union and its Conditional Marketing Authorization:

Directive 2001/83/EC overviews all regulatory pathways in The European Union and provides several routes for the marketing approval of new medicinal products. The four main pathways for approval of new drugs in the EU are

- **Centralised Procedure**: EMA reviews a single application, and the European Commission grants EU-wide authorisation.
- **Decentralised Procedure**: A single application is submitted to multiple EU countries, with one leading the assessment. Each country issues its own authorisation upon approval.
- **Mutual Recognition Procedure**: An existing national authorisation in one EU country is used as the basis for approvals in others.
- **National Procedure**: For medicines intended for one country only, the application is submitted through that country's national process [47].

All drugs in the EU undergo the centralized authorisation procedure. To enable the use of certain drugs in emergency situations, facilitated pathways are available within this procedure.

Conditional Marketing Authorisation: Conditional marketing authorisation under EC No 507/2006 is granted for medicines to treat, prevent or diagnose severe or uncommon rare diseases or use certain drugs during public health emergencies such as pandemics. Application is granted based on less comprehensive pharmaceutical and clinical data; orphan medicines are also included under conditional marketing authorisation [48].

A Conditional Marketing Authorisation (CMA) has a validity of one year and can be renewed on a yearly basis. This designation serves as an expedited pathway for the approval of drugs. The CMA holder must conduct all required research within a stipulated timeframe to verify the safety and risk of the drug/vaccine. The CMA application should comprise the specified details, along with clinical effectiveness [48][49].

- The number of people to whom the drug/vaccine is to be given.
- The pharmaceutical quality and purity data
- Data related to the manufacturing of batches
- Compliance with international requirements for animal testing and the conduct of clinical trials.
- Types of immune response

Marketing Authorisation under Exceptional Circumstances: Under Article 14(8) of Regulation (EC) No 726/2004, In exceptional circumstances where full data are unavailable, the EMA can grant marketing authorisation if the applicant provides justified and verifiable evidence. This approval is maintained through yearly review of the conditions, with guidance issued by the EMA on the process [50].

Accelerated Assessment: under this Article 14 (9) of Regulation (EC) No 726/2004, Accelerated assessment of a marketing authorisation application may be requested when a medicinal product demonstrates significant public health relevance and therapeutic innovation. When these conditions are satisfied, the evaluation timeline is reduced from 210 days to 150 days [50].

Priority Medicines (PRIME) Scheme: Launched in 2016 under Article 14(9), PRIME supports the development of medicines addressing unmet medical needs or offering significant advantages over existing therapies. It fosters early interaction, scientific advice, and accelerated assessment [51][52].

European Medicines Agency (EMA) allows for the development of medicines that treat unmet medical needs or the use of certain medications during emergencies under the Conditional Marketing Authorisation (CMA) application [53]. Conditional marketing authorisation is granted for medicines to treat, prevent or diagnose severe or uncommon rare diseases or use certain drugs during public health emergencies such as pandemics. Application is granted based on less comprehensive pharmaceutical and clinical data; orphan medicines are also included under conditional marketing authorisation [54].

During the COVID-19 pandemic, the USFDA and EMA worked differently in approving new indications of existing treatments. The USFDA was quick in approving remdesivir compared to the EMA, which took a longer time [55]. This was due to the EU's conditional marketing which excludes new indications of previously approved medicines [56]. Both the US and EU utilized their emergency pathways to give patients timely and effective treatments while maintaining strict quality and efficacy requirements. It was also noticed that EMA was more stringent than the USFDA in granting MA, some drugs that were approved by the USFDA were not accepted by the EMA [55].

2. Japan and its Special Approval for Emergency (SAE):

The Pharmaceutical and Medical Device Agency (PMDA) is the regulatory authority that approves new pharmaceuticals or medical devices in Japan. Japan allows for emergency use of pharmaceuticals under "special approval" called Special Approval for Emergency (SAE) under article 14-3 of the Pharmaceutical and Medical Devices Act if the following criteria are met [57].

- There is an immediate need for the drug to mitigate the transmission of a disease or illness that significantly impacts the well-being of the people in Japan.
- No other countermeasures or remedies are available.
- The drug's quality is on par with that of medications available in Japan.
- The drug must be approved for marketing in said countries – the United States, UK, Canada, Germany, and France [58].
- The steps for obtaining a Special Approval for Emergency (SAE) are as follows.
- The Cabinet Order must designate a medicinal product under SAE
- An application is filed for any product meeting the criteria under SAE.
- PMDA then proceeds to prepare a report in a very short time, which will be discussed by the Pharmaceutical Affairs and Food Sanitation Council (MHLW).
- The council, after discussion, recommends either approval or disapproval, Once approval is granted, the product obtains marketing authorisation under SAE [59].

The whole process of approval of a new indication/product under SAE happens in a very short period when compared to a regular authorisation. Due to shorter approval processes, the medicinal products under SAE undergo additional pharmacovigilance. The Minister may revoke the approval if the emergency conditions no longer exist or if the revocation is required to safeguard public health.

During the COVID-19 pandemic, Japanese authorities used their special pathway to grant SAE to remdesivir after EUA was granted to it in the USA. Before approving the SAE clinical trials of remdesivir efficacy in covid patients was conducted on small Japanese patient populations. After satisfactory results from the clinical trial, PMDA granted SAE to remdesivir on May 7th 2020 [60].
In February 2021, Pfizer's COVID-19 vaccine also received Special Approval for Emergency (SAE) in Japan. This approval was consistent with the framework outlined in the *Principles* for the Evaluation of Vaccines against the Novel Coronavirus *SARS-CoV-2* [61]. With this emergency authorisation, Japanese citizens began receiving vaccinations, starting with prioritised groups, to protect against SARS-CoV-2. Remdesivir and Pfizer COVID-19 vaccine were the only two indications that were granted SAE in Japan [61].
Till date, only four drugs have been approved under this special marketing authorisation pathway in Japan as shown in (table 1).

Table 1: approved drugs in Japan under SAE

S.No	Brand name	Generic name	Duration of the SAE
1.	Arepanrix	Influenza A (H1N1) Vaccine	Oct. 16 2009 – Mar.2011
2.	Influenza HA vaccine H1N1 (Novartis)	Influenza A (H1N1) Vaccine	Jan 20 2010 – Mar.2011
3.	Veklury	Remdesivir	May 7 2020 – Jan 2021
4.	Comirnaty (Pfizer)	Tozinameran (mRNA vaccine)	Feb 2021 – ongoing

In May 2022, Japan revised its Pharmaceutical and Medical Device Act to introduce a new “Emergency Approval System” known as Kin-kyu-sho-ninSeido (緊急承認制度). Theobjective of this revision was to establish a pathway for promptly authorising new pharmaceutical products, medical devices, and medical products during an emergency to prevent the spread of health hazards in scenarios such as the outbreak of diseases that could significantly impact the lives and well-being of Japanese citizens. The main advantage of this new system is that the sponsor can file for an emergency approval in Japan without depending on any EUA from Western countries. Additionally, PMDA can waive of GCP and GMP inspections if all data required is not available to allow for a quicker regulatory review response during an emergency. After the emergency is lifted, the sponsor needs to submit all the waived data, This revision was made to make sure therapeutic drugs and vaccines are delivered to Japanese people at the same time as Western countries in case of future emergencies and pandemics [62].
In May 2022, Japan revised its Pharmaceutical and Medical Device Act to introduce a new "Emergency Approval System" (緊急承認制度, Kin-kyu-sho-ninSeido). This system allows for the expedited approval of pharmaceuticals, medical devices, and regenerative medical products during public health emergencies, enabling quicker access to essential treatments when urgent needs arise [62]. The regulatory pathway is summarised in (figure 2).

The early marketing approval process is as follows:

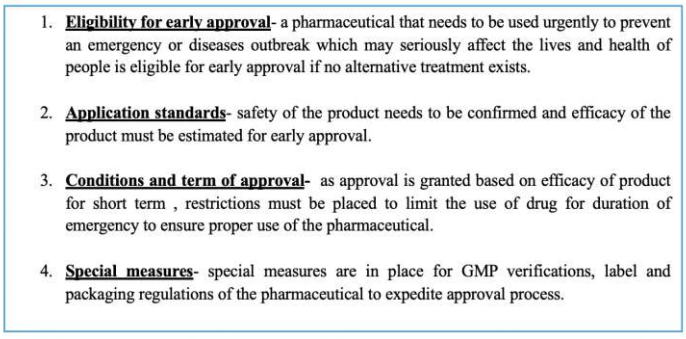
1. **Eligibility for early approval**- a pharmaceutical that needs to be used urgently to prevent an emergency or diseases outbreak which may seriously affect the lives and health of people is eligible for early approval if no alternative treatment exists.
2. **Application standards**- safety of the product needs to be confirmed and efficacy of the product must be estimated for early approval.
3. **Conditions and term of approval**- as approval is granted based on efficacy of product for short term , restrictions must be placed to limit the use of drug for duration of emergency to ensure proper use of the pharmaceutical.
4. **Special measures**- special measures are in place for GMP verifications, label and packaging regulations of the pharmaceutical to expedite approval process.

Figure 2: early marketing approval process

3. Canada'sInterim Order Pathway

In emergencies such as disease outbreaks and pandemics, Canada uses an Interim Order mechanism to authorise the use of medicinal products (drugs and vaccines) [63]. Covid -19 pandemic posed a severe risk to the health and safety of Canadian citizens, Health Canada facilitated a number of interim orders in accordance with section 30.1 of the *Food and Drugs Act* to streamline access to drugs, medical devices and foods for special needs [64].
Canada's interim order is a type of temporary regulation put in place for medicinal products used in treating the outbreak. It enables the sponsors in obtaining expedited authorization in sale, import and marketing of drugs used to treat COVID-19 [65].
There are three distinct pathways under the Interim Order:

- A flexible application pathway for COVID-19 drugs, with fewer requirements and earlier filing compared to Part C, Division 8 of the FDR.
- A shortened pathway for COVID-19 drugs approved by foreign regulatory authorities, limited to drugs listed by the Minister for the COVID-19 pandemic.
- A mechanism allowing the Minister to expand COVID-19 indications for authorised drugs under the FDR, without requiring a manufacturer's application, provided evidence shows the benefits outweigh the risks [64][65].

During the COVID-19 pandemic, Health Canada issued Interim Orders for vaccines like Pfizer-BioNTech and Moderna, allowing their use while ongoing studies provided further data. In 2020 and 2021, the Minister of Health issued Interim Orders (IOs) granting Health Canada additional authority to address shortages exacerbated by the COVID-19 pandemic [66].
These included:

- Interim Order Respecting Drug Shortages (Safeguarding the Drug Supply), issued on November 27, 2020 [64].
- Interim Order No. 2 Respecting Drugs, Medical Devices, and Foods for Special Dietary Purposes, issued on March 1, 2021 [67].

These amendments were made to ensure that negative outcomes such as delayed or cancelled treatments, disruptions in treatments of patients in need, hoarding or rationing of drugs and medical devices, and invalidity of alternate treatments do not occur in case of future disease outbreaks and pandemics [68].

4. Australia and its emergency pathways:

Australia's health governing body, Therapeutic Goods Administration (TGA), has two established pathways for rapid approval of therapeutic indications and lifesaving drugs. The main aim of these two pathways is to make essential medicines available to people sooner than the usual regulatory process [69].

The two pathways are

1. The Priority Review pathway: a pathway which aims to complete the evaluation of an application in 150 working days, when compared to 255 days standard approval process.

In priority review complete dossier of data regarding the medicinal product must be submitted to the TGA. If the review is successful, then the drug application is granted full registration on the Australian Register of Therapeutic Goods [70].

2. The Provisional Approval Pathway: when compared with the priority review pathway provisional approval pathway enables a time-limited registration of a drug based on phase II preliminary trial data. If approved under this pathway, the drug is available for two years, and the sponsor can further apply for extensions up to 6 years. Here, phase III safety, efficacy and quality data must be submitted by the sponsor. As the application is accepted before the completion of the trial, the medicine is brought sooner into the market [71].

The provisional approval pathway is granted for the following medicines:

- A new prescription medicine that includes

a. A chemical, biological, or radiopharmaceutical active ingredient not previously listed in the Australian Register of Therapeutic Goods (ARTG), or

b. A fixed combination of active ingredients where at least one is not previously listed in the ARTG.

- A registered prescription medicine with a new indication where

a. It has the same active ingredient(s) as another medicine already listed in the ARTG,

b. But it is approved for a different indication than the other medicine [72].

Drugs approved under provisional approval pathway by the TGA during COVID-19 are listed in (table 2) [73].

Table 2: drugs approved by TGA for covid-19 under provisional approval pathway

S.No	Sponsor	name	Approval Date
1.	AstraZeneca	tixagevimab and cilgavimab	A. 24 February 2022 B.12 December 2022
2.	Merck Sharp & Dohme (Australia) Pty Ltd	Molnupiravir	18 January 2022
3.	Pfizer Australia Pty Ltd	nirmatrelvir+ritonavir (PAXLOVID)	18 January 2022 26 August 2024
4.	Celltrion Healthcare Australia Pty Ltd	regdanvimab (REGKIRONA)	6 December 2021
5.	Roche Products Pty Ltd	tocilizumab (ACTEMRA)	1 December 2021
6.	Roche Products Pty Ltd	casirivimab + imdevimab (RONAPREVE)	15 October 2021
7.	GlaxoSmithKline Australia Pty Ltd	Sotrovimab (XEVUDY)	20 August 2021
8.	Gilead Sciences Pty Ltd	remdesivir (VEKLURY)	A. 10 July 2020 B. 6 May 2022

5. India:

Central Drug Standard Control Organisation (CDSCO) under the Ministry of Health and Family Welfare, Government of India, holds the regulatory jurisdiction that approves new pharmaceutical drugs, cosmetics, vaccines, biologics, and medical devices in India [74].

During emergency situations such as a pandemic, India does not have a particular regulatory approval process; the "New Drug and Clinical Trial Rules 2019" serves as the primary regulatory framework for authorisation of new drugs and vaccines [75]. The Ministry of Health and Family Welfare allows for the use of vaccines in emergency situations in India that have gained authorisation by the US FDA (EUA), European Medicines Agency (CMA), or PMDA in Japan [77].

The manufacturer must adhere to the following guidelines to manufacture its vaccine in India during an emergency:

- The application must comply with the Drugs and Cosmetics Act, 1940.
- The application for emergency use must be submitted through the SUGAM online portal and must provide all data regarding the drug product, chemistry, manufacturing control data, certificate of analysis, preclinical and clinical data, regulatory approval in other countries, certificate of pharmaceutical product (COPP), and proposed labelling requirements.
- CDSCO processes such applications with the highest priority through an accelerated process.
- CDSCO carefully examines all safety-related information presented by the applicant, and on satisfactory assessment review, will sanction the use of the vaccine.
- The manufacturer needs to conduct a bridging trial within the specified timeline and submit all data generated to CDSCO.
- The DCGI now reviews the permission granted for restricted use during emergencies [76][77].

This pathway was utilised during the COVID-19 pandemic for vaccines like Covaxin, which were granted EUA based on interim clinical trial data.

CONCLUSION

With the increase in the occurrence of health crises in the last few years, Emergency Use Authorisation acts as an essential pathway that helps reduce the burden on public health workers, safeguards the health of the public by providing alternatives, and provides an exemption to drug manufacturers to market new drugs/vaccines. It makes sure that medicines with intended quality and safety are manufactured to fulfil treatment demands during emergencies specially when off-label use of medicines for unapproved drugs soared during the COVID-19 pandemic. Therefore, it became essential for regulatory authorities worldwide to promptly authorise COVID-19 medicines to ensure safe and effective treatments.

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