Expanded Access to Investigational Drugs for Treatment Use: Questions and Answers

Guidance for Industry

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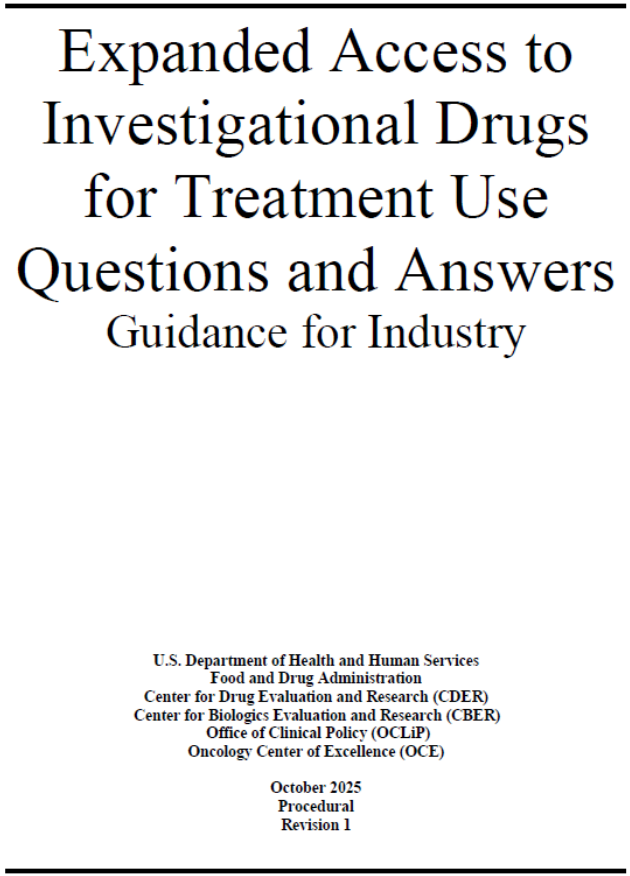


Focus of guidance:

- Explains pathways for providing investigational drugs for treatment of patients with serious or immediately life-threatening diseases when no satisfactory treatment alternatives exist
- Clarifies regulatory requirements and FDA recommendations for the Expanded Access program
- Addresses recent statutory changes and common questions

Overview

- Define expanded access
- Explain the three categories of expanded access
- Discuss submission requirements and processes
- Knowledge check
- Share key resources

What is Expanded Access (EA)?

- Use of an investigational medical product (drug, biological product, or medical device) to treat a patient with a serious or immediately life-threatening disease or condition who does not have comparable or satisfactory alternative therapies to treat the disease or condition
  - Primary purpose of use is clearly treatment
- Contrast with investigational drug in a clinical trial where the primary purpose is research
  - Systematic collection of data with the intent to analyze it to learn about the drug

Note: This presentation will focus on expanded access to drugs and biological products

Expanded Access

Compassionate Use

Preapproval Access

Regulatory Background

- FDA has a long history of facilitating EA for patients with serious or immediately life-threatening diseases who lack satisfactory therapeutic alternatives
- The 2009 EA regulations (21 CFR part 312, subpart I) consolidated and expanded the provisions for EA
  - Provide criteria for access, requirements for submission of EA requests to FDA, and applicable safeguards including informed consent, Institutional Review Board (IRB) review, and reporting requirements
- 21st Century Cures Act (2016) and FDA Reauthorization Act (FDARA (2017)) provided additional requirements for manufacturers and distributors to make their EA policy readily available to the public

Three General Categories of EA

Common Criteria for All Types of EA:*

1. Patients have serious or immediately life-threatening disease or condition
2. No comparable or satisfactory alternative therapy
3. Potential benefits must justify the potential risks of the treatment
4. Providing the product under EA will not interfere with or compromise the investigational product development program

* Additional criteria, specific to each category, must be fulfilled

Individual Patient EA

Subcategories:

- ***Individual patient expanded access for emergency***

  Used for emergency situations (e.g., a patient needs to be treated before a written submission can be made)

  - The treatment is initially requested and authorized by telephone (or other means of electronic communication)
  - A written submission is required within 15 working days of the initial authorization and IRB should be notified within 5 working days of treatment initiation

- ***Individual patient expanded access for non-emergency***

  Used when patient does not need be to treated before written submission can be made

  - A written submission to FDA and IRB approval is required prior to treatment initiation

Intermediate-Size Patient Population

- For treatment of more than one patient, but generally fewer patients than are treated under a treatment IND or protocol
- Used to consolidate access to an investigational drug for multiple patients with the same disease or condition
- Can be used when the drug is
  - not being developed for marketing for the same indication as the expanded access use, or
  - being developed but the patients requesting access are unable to participate in the trial (e.g., have a different stage of disease than the one being studied)

Treatment IND and Protocol

- For providing access to large (widespread) populations
- Only used when the drug is being investigated in a controlled clinical trial under an IND to support a marketing application for the same use

OR

If all clinical trials of the drug are complete and the sponsor is actively pursuing marketing approval of the drug for the expanded access use

Two Paths for Regulatory Submission

Expanded Access IND	Expanded Access Protocol
• A new IND submission • Separate and distinct from any existing INDs • Can be submitted by a patient's physician or the pharmaceutical company or drug manufacturer	• Submitted as a protocol amendment to an existing IND • Generally used when the sponsor of an existing IND (typically the pharmaceutical company or drug manufacturer) is sponsoring the EA use

Who can Submit EA Requests to FDA?

- **Pharmaceutical company or manufacturer:** Submits an EA IND, if there is no IND in place, or a protocol to its existing IND (sponsor)
  - The patient's physician acts as the investigator

- **Licensed Physician:** Submits a new EA IND and acts as the sponsor-investigator

Submission Process: Forms and app

Form FDA 3926

- Streamlined form for EA
- For licensed physicians only
- Can only be used to submit individual patient IND (including emergency use)

Form FDA 1571

- Standard IND form
- Required for the commercial sponsors submitting:
  - An individual patient IND or protocol (including emergency use)
  - Intermediate-size patient population IND/protocol
  - Treatment IND/protocol
- May be used:
  - By licensed physicians
  - For individual patient IND/protocol (including emergency use)

eRequest app

- Web application
- For licensed physicians only
- Can only be used to submit individual patient expanded access IND in non-emergency settings
- Compatible with multiple devices

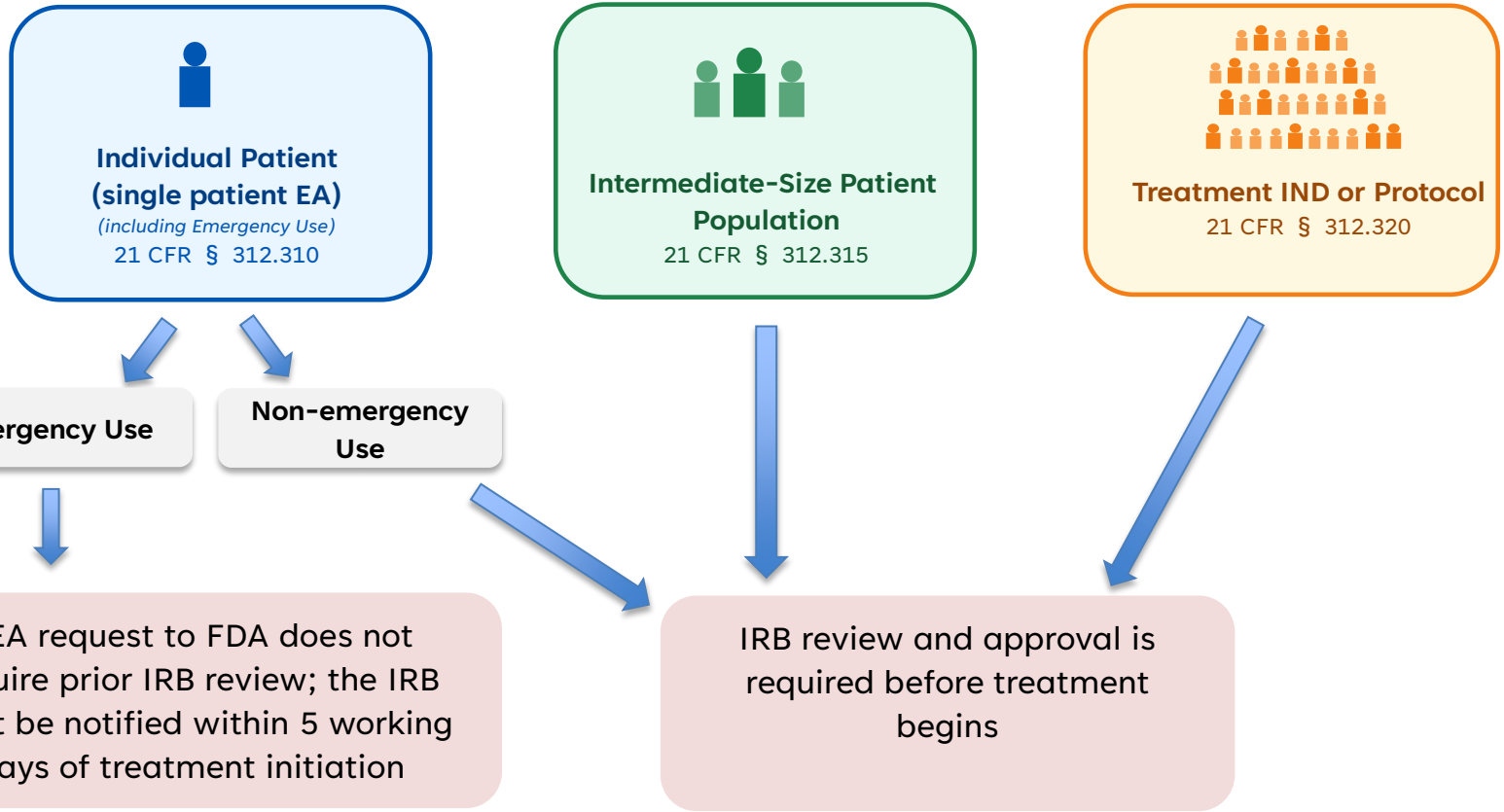
Submission Process: Core Information

- Submissions must include all information required by § 312.305(b)
- Submissions must include any additional information required for the specific category of access requested by the sponsor
- Sponsor-investigators (e.g., physicians) should obtain a ‘Letter of Authorization’ from the drug manufacturer

Submission Process: IRB Review

- IRB review and approval is required before treatment with the investigational drug may begin (21 CFR part 56), unless it is for emergency use
  - Regardless of whether the submission is a new IND or a protocol to an existing IND (21 CFR § 312.305(c)(4))
- The IRB reviews the expanded access use at a convened meeting at which a majority of the members are present (full IRB review) (21 CFR § 56.108(c))
- The IRB's primary purpose is to ensure the rights and welfare of human subjects are protected

Timing for IRB Review and Approval

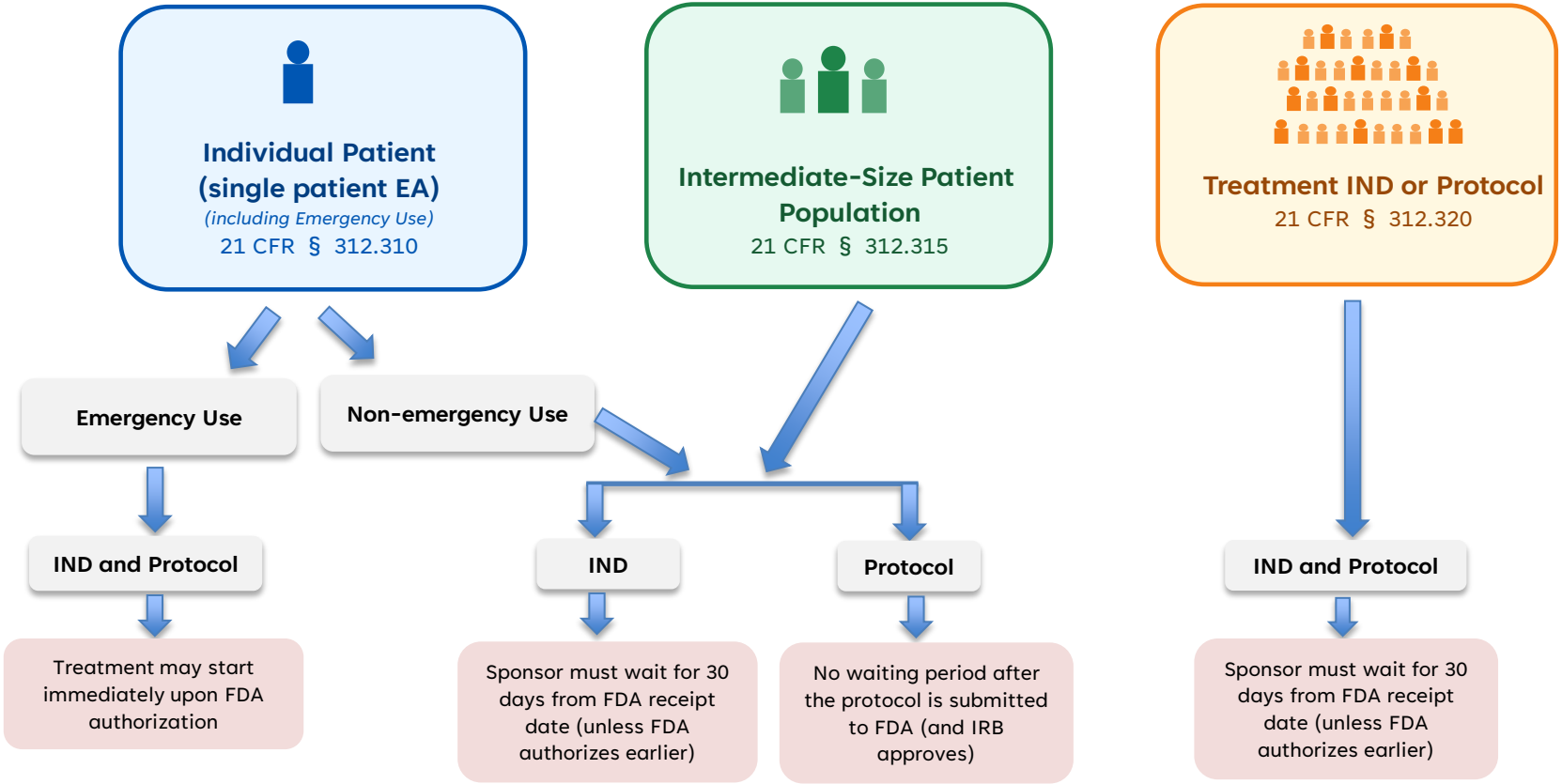


Waiver of the Requirement for Full IRB Review and Approval

- Upon request, FDA intends to allow for waivers of the requirement for review and approval at a convened full IRB meeting for individual patient non-emergency EA requests
  - The IRB chairperson or another designated IRB member provides concurrence
- A waiver is appropriate for:
  - initial submission
  - any amendments to the IND
  - continuing review
- A waiver can be requested by checking the box 10b of Form FDA 3926 or by a written request

Submission Process:

Waiting Period Before Treatment May Begin



Submission Process: Ongoing Responsibilities for Active EA IND and Protocols

- IND safety reporting (§ 312.32)
- Submit annual report (when the treatment continues for a year or more)
- Submit a written summary of the results of the expanded access use, including adverse events, at the conclusion of treatment for individual patient EA
- Maintain drug disposition records
- Seek withdrawal of an EA IND, with inclusion of a final report, when the treatment ends

Informed Consent

- Informed consent is required (as described in 21 CFR part 50) for expanded access, unless one of the exceptions found in part 50 applies
- The consent form must contain information to enable the patient to make an informed decision about receiving experimental treatment (21 CFR § 50.20 and § 50.25)
- Sponsors are not required to include informed consent as part of an EA submission, unless FDA requests
- The guidance includes a template for developing informed consent for individual patient INDs

Expanded Access Policy: Public Availability

- Manufacturers or distributors of investigational drugs must make their policies for evaluating and responding to EA requests readily available to the public
- Timeline for posting: **Earlier** of the following dates:
  - At the first initiation of a phase 2 or phase 3 study
  - 15 days after the drug receives a designation as a breakthrough therapy, fast track product, or regenerative advanced therapy

Expanded Access Policy: Public Availability (Cont'd)

The publicly available policy must include:

- Contact information
- Procedures for submission of EA requests
- General criteria for evaluation and responses to the requests
- Acknowledgment timeframe
- Hyperlink or other reference to the clinical trial record in ClinicalTrials.gov

Note: Posting does not guarantee access

Where Can The Public Find Information About EA Policy?

Examples:

- Website of the relevant pharmaceutical company or drug manufacturer
- Other publicly available websites
  - Company Directory Webpage of the Reagan-Udall Foundation's Expanded Access Navigator website
  - ClinicalTrials.gov (under certain circumstances)

Can FDA Require a Sponsor to Provide Expanded Access to Its Drug?

- No. A sponsor provides expanded access to its drug voluntarily.

- Posting of EA policy on sponsors' website does not guarantee access.

Project Facilitate

Assisting Healthcare Providers with Expanded Access Requests for Investigational Oncology Products

Oncology Center of Excellence

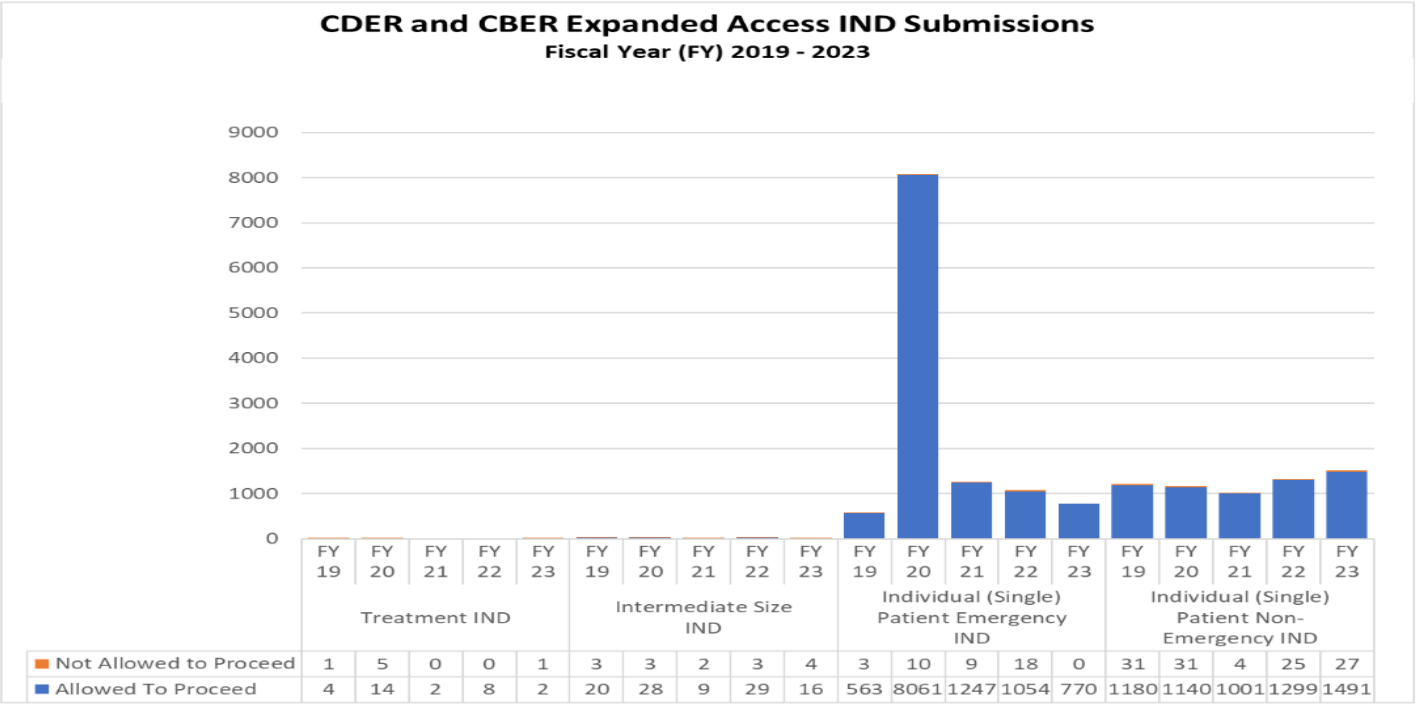
- Who We Are - Oncology Center of Excellence
- Project Patient Voice
- **Cancer Community Resources**
- **OCE Annual Reports**

Oncology Center of Excellence **Project Facilitate** is a single point of contact call and information center created to help oncology healthcare providers or regulatory professionals submit an Expanded Access Request (also referred to as: Compassionate Use, Emergency IND, Single-Patient IND, or Pre-Approval) for an individual patient with cancer through FDA's Expanded Access Program.

Project Facilitate

How many Expanded Access Requests Are Authorized by FDA?

Combined CDER and CBER Expanded Access Submissions and Protocols (2019–2023)



	FY 19	FY 20	FY 21	FY 22	FY 23	FY 19	FY 20	FY 21	FY 22	FY 23	FY 19	FY 20	FY 21	FY 22	FY 23	FY 19	FY 20	FY 21	FY 22	FY 23
	Treatment IND					Intermediate Size IND					Individual (Single) Patient Emergency IND					Individual (Single) Patient Non-Emergency IND				
Not Allowed to Proceed	1	5	0	0	1	3	3	2	3	4	3	10	9	18	0	31	31	4	25	27
Allowed To Proceed	4	14	2	8	2	20	28	9	29	16	563	8061	1247	1054	770	1180	1140	1001	1299	1491

FDA Expanded Access Program Data

Knowledge Check

Question 1

For a non-emergency individual patient EA IND, when can treatment typically begin?

a) Immediately

b) Within 15 working days

c) After 30 days, unless notified earlier by the FDA

Knowledge Check 2

Question 2

For individual patient emergency INDs, by when must sponsors notify IRB about the emergency use?

a) Before the treatment begins

b) Within 5 working days of emergency use

c) Within 15 days of emergency use

Knowledge Check 3

Question 3

What is one piece of information that a public expanded access policy must include?

a) The price of the drug

b) A list of all previously treated patients

c) Contact information for the manufacturer

Knowledge Check 4

Question 4

A pharmaceutical company can be compelled by the FDA to provide expanded access to its investigational drug.

a. True

b. False

Resources

- Guidance Expanded Access to Investigational Drugs for Treatment Use: Questions and Answers (2025)
- Guidance Institutional Review Board (IRB) Review of Individual Patient Expanded Access Submissions for Investigational Drugs and Biological Products (2023)
- FDA's Expanded Access webpage with information for patients, physicians, industry, IRBs
- Example template for Informed Consent for Individual Patient IND
- Example of wording for letter requesting authorization to use alternative IRB review procedure
- Example of wording for Letter of Authorization (LOA) for individual patient expanded access IND
- Charging for Investigational Drugs Under an IND: Questions and Answers (2024)

Expanded Access Webpage

Expanded Access

- Expanded Access
- Information for Patients
- Information for Physicians
- Information for Industry
- Information for Institutional Review Boards (IRBs)
- How to Submit a Request (Forms)
- Keywords, Definitions, and Resources
- Submission Data
- Contact Information

Español

Sometimes called “compassionate use”, expanded access is a potential pathway for a patient with a serious or immediately life-threatening disease or condition to gain access to an investigational medical product (drug, biologic, or medical device) for treatment outside of clinical trials when no comparable or satisfactory alternative therapy options are available.

Expanded access may be appropriate when all the following apply:

- Patient has a serious or immediately life-threatening disease or condition.
- There is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition.
- Patient enrollment in a clinical trial is not possible.
- Potential patient benefit justifies the potential risks of treatment.
- Providing the investigational medical product will not interfere with investigational trials that could support a medical product’s development or marketing approval for the treatment indication.

Investigational drugs, biologics or medical devices have not yet been approved or cleared by FDA and FDA has not found these products to be safe and effective for their specific use. Furthermore, the investigational medical product may, or may not, be effective in the treatment of the condition, and use of the product may cause unexpected serious side effects.

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