Easy as 123:
CGT, FDA and Industry

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Celebrating 40 Years: An In-Depth Examination of the FDA Orange Book – October 28, 2020

Learning Objectives

- Describe the process for submitting a request for competitive generic therapy (CGT) designation
- Outline the criteria for designating a drug as a CGT
- Provide information on the considerations for expedited development and review of CGTs
- Answer procedural questions regarding CGT exclusivity determinations

Where did CGTs originate?

- *FDA Reauthorization Act of 2017 (FDARA)*
  - Reauthorization of the Generic Drug User Fee Amendments (GDUFA) to support timely access to high quality, affordable generic medicines
  - Section 803 of FDARA amended the Federal Food, Drug, and Cosmetic Act (FD&C Act) to add section 506H:
    - created a new pathway by which FDA may, at the request of the applicant, designate a drug with "inadequate generic competition" as a CGT
  - At the request of the applicant, FDA may also expedite the development and review of an abbreviated new drug application (ANDA) for a drug designated as a CGT
  - Section 808 of FDARA amended the FD&C Act to add CGT exclusivity and forfeiture provisions

CGT Guidance for Industry

- *Draft Guidance published February 19, 2019*
- *Final Guidance published March 16, 2020*

Considering Development of a CGT?

- Various factors may influence an applicant's decision to develop or not develop a generic medicine
  - some drugs may not attract a high level of interest if there is a limited market for those products
  - some products are more difficult to develop
- These drugs can play an important role in diagnosing, treating, and preventing various types of disease or conditions
- Incentivizing generic competition for these products can help ensure patients have access to the medicines they need

FDA Goals for CGTs

- To facilitate increased competition, FDA may take certain actions to expedite the development and review of an ANDA for a drug that is designated as a CGT
- May help to clarify the regulatory expectations for a particular drug
- Assist applicants in developing a more complete submission
- Promote a more efficient and effective ANDA review process in order to help reduce the number of review cycles necessary to obtain ANDA approval

Requesting CGT Designation

- Request submitted by an ANDA applicant
- Designation is application-specific
  - Each applicant should submit a request to FDA for designation
  - Once FDA designates a product in an applicant's ANDA as a CGT, it will remain designated as a CGT

Requesting CGT Designation

- Must be made concurrent with, or at any time prior to, the submission of an original ANDA
  - Prior to application
    - As a stand-alone request or as an accompaniment to the pre-submission facility correspondence (PFC) for an ANDA
    - If requesting pre-ANDA meeting, submit before meeting request

Requesting CGT Designation

- Must be for a drug for which there is "inadequate generic competition"
- FDA will determine whether request satisfies designation criteria within 60 days of request
  - Letter issued to applicant either granting or denying designation

Designation Criteria

- "Inadequate generic competition" for the drug:
  - at the time of the designation, not more than one approved version of that drug in the active section of the Orange Book
    - Can also mean no drugs listed in active section
    - Each strength of a drug is a distinct drug product
    - may either be the reference listed drug (RLD) or a drug approved in an ANDA referencing the same RLD as the drug for which designation as a CGT is sought

Content of Request

- Pre-assigned ANDA number
- Statement supporting request
  - Identification of drug product (application number, proprietary name, strength)
- Information supporting “inadequate generic competition”
- Submit in eCTD format through Electronic Submission Gateway (ESG) and include FDA Form 356h

Benefits of CGT Designation

- Expedite the development and review of an application
- Most applicants concerned with eligibility for CGT 180-day exclusivity
- As of Sept 2020, there have been more than 500 requests for CGT designation.
  - ~80% of requests have been granted CGT designation
  - 42 grants of CGT 180-day exclusivity

Benefits of CGT Designation

- Actions FDA may take to expedite *development*
  - Product development meetings
  - Pre-submission meetings
- Actions FDA may take to expedite *review*
  - Mid-review-cycle meetings
  - Coordinated review of CGTs
  - Strive to act on the ANDA as soon as possible, including prior to the GDUFA goal date, if possible

Factors FDA Considers for Expedited Action

- Complexity of developing ANDA for the specific drug
- Potential public health impact of the product, including severity of disease treated, size of impacted patient population, and availability of therapeutic alternatives
- Impact on FDA resources/existing workload commitments
- Whether there are unexpired patents/exclusivities for RLD

CGT Web Page

- **Competitive Generic Therapy Approvals:**
  FDA recently published a new webpage listing all approved ANDAs for products that received a CGT designation.
- Updated on a bi-weekly basis and includes information about:
  - Approved application
  - Drug product
  - Potential CGT exclusivity

CGT Approvals Web Page

Competitive Generic Therapy Approvals

	RLD Name and NDA Number	ANDA Number	ANDA Applicant	Active Ingredient Name, Dosage Form, Strength	Date of Approval	Eligible for CGT Exclusivity	CGT Exclusivity Forfeiture	Date of First Commercial Marketing of CGT with Exclusivity
31	Depen, NDA 19854	211497	Teva Pharmaceuticals USA, Inc.	Penicillamine Tablets USP, 250mg	2/13/2020	Yes		
30	Mestinon, NDA 15193	212702	Amneal	Pyridostigmine Bromide Oral Syrup, USP 60 mg/5 mL	1/10/2020	No	N/A	N/A
29	Valium, NDA 016087	211998	Beloteca, Inc.	Diazepam Injection USP, 50 mg/10 mL (5 mg/mL)	12/26/2019	Yes		
28	Proglycem Oral Suspension, NDA 017453	211050	e5 Pharma, LLC	Diazoxide Oral Suspension USP, 50 mg/mL,	12/20/2019	Yes	No	12/20/2019
27	Triamcinolone Acetonide, ANDA 089595	212384	Encube	Triamcinolone Acetonide Ointment USP, 0.05%	11/29/2019	Yes	No	12/2/2019
26	Amicar, NDA 15197	212492	Amneal	Aminocaproic Acid Tablets USP, 500 mg	11/27/2019	Yes	No	12/3/2019

How is CGT exclusivity different from 180-day patent challenge exclusivity?

Hatch-Waxman 180-day Exclusivity	CGT Exclusivity
➢ Eligibility based on applicant qualifying as First Applicant	➢ Eligibility partially based on being a First Approved Applicant
➢ Eligibility possible after original submission (i.e., can be based on PIV certifications submitted after original ANDA submission)	➢ Eligibility not possible after original submission (i.e., must request CGT designation at or before this point to potentially qualify for exclusivity)*
➢ Blocks subsequent applicants both prior to and during first 180 days of commercial marketing	➢ Blocks other applicants only after marketing commencement
➢ Subject to multiple complex forfeiture provisions	➢ Subject to a single simple forfeiture provision
	*Refuse to Receive exception

How is CGT exclusivity similar to 180-day patent challenge exclusivity?

Hatch-Waxman 180-day Exclusivity	CGT Exclusivity
✓ Can be relinquished or selectively waived	✓ Can be relinquished or selectively waived
✓ Triggered by First Commercial Marketing	✓ Triggered by First Commercial Marketing
✓ Can be shared (common)	✓ Can be shared (uncommon)
✓ Exclusivity period runs continuously once triggered	✓ Exclusivity period runs continuously once triggered

Exclusivity Criteria

- To be eligible for CGT exclusivity, the ANDA applicant must qualify as a *"first approved applicant,"* meaning the applicant has submitted an application that:
  - Is for a CGT that is approved on the first day on which any ANDA for such CGT is approved
  - Is not eligible for 180-day patent challenge exclusivity for the drug that is the subject of the ANDA for the CGT
  - Is not a drug for which all drug versions have forfeited eligibility for 180-day patent challenge exclusivity

Exclusivity Criteria

- For purposes of the exclusivity provisions, a *"competitive generic therapy"* is defined as:
  - A drug that is designated as a CGT ***and***
  - For which there are no unexpired patents or exclusivities in the Orange Book at the time of submission of the ANDA for the CGT
- This is different than how CGT is defined for purposes of the designation provisions
  - A drug may be designated as a CGT, but will be ineligible for CGT exclusivity if there are unexpired patents/exclusivity in the Orange Book at the time the original ANDA is submitted

How can an applicant forfeit CGT exclusivity ?

- Special Forfeiture Rule for CGT at 505(j)(5)(D)(iv):

Exclusivity shall be forfeited by a first approved applicant if the applicant fails to market the competitive generic therapy within 75 days after the date on which the approval of the first approved applicant's application for the competitive generic therapy is made effective.

- Forfeiture of CGT is straightforward - forfeiture takes place when marketing of the CGT drug product(s) does not commence within 75 days after the date of approval.

How can an applicant trigger CGT exclusivity?

- First approved applicant must commence commercial marketing within the 75-day period beginning on the day after approval in order to trigger CGT exclusivity.
- FDA is not generally aware of when an applicant commences commercial marketing.
- Applicants should inform FDA once marketing has commenced in order for subsequent approvals to be halted by this exclusivity.
  - Submit correspondence to your ANDA
  - Email the Patent and Exclusivity Team: CDER-OGDPET@fda.hhs.gov
- OGD will continue to approve other ANDAs for the drug product if notice of marketing has not been received.

Challenge Question #1

All of the following are reasons a CGT-designated ANDA would not qualify for CGT 180-day exclusivity except (one correct answer)?

A. Was not the first approved CGT designated ANDA

B. There were unexpired patents for the RLD at the time the ANDA was submitted

C. On the date the ANDA was approved there was now adequate generic competition

D. The CGT designated drug product had previously been subject to forfeiture of patent challenge 180-day exclusivity

Challenge Question #2

When may I request CGT Designation:

A. With a prior approval supplement

B. Prior to submission of an original ANDA

C. Prior to approval of an original ANDA

D. With an amendment of an ANDA

Resources

- Guidance - https://www.fda.gov/media/136063/download
- Public docket - FDA-2019-D-0065
- List of all CGT approvals - https://www.fda.gov/drugs/generic-drugs/competitive-generic-therapy-approvals

Summary

- CGT designations can be requested for drugs with “inadequate generic competition”
- Make the request before, or at the time of, submitting an original ANDA
- To trigger CGT exclusivity and halt other approvals, promptly inform the Agency when you’ve commenced marketing

Questions?

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