GDUFA III DMF Review Prior to ANDA Submission: Eligibility Criteria for the ANDA Submissions

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SBIA DMF Workshop: GDUFA III Enhancements and Structured Data Submissions – November 30, 2022

Learning Objectives

- Identify when the holder of a DMF can submit a request for assessment 6 months prior to the submission date for an original ANDA, ANDA amendment responding to a Complete Response Letter (CRL), or ANDA amendment seeking approval of a previously tentatively approved application
  - Identify the five categories outlined in the GDUFA III Commitment Letter for DMF review prior to ANDA submission
  - Recognize when the criteria for each category is met

Overview: Criteria for DMF Review Prior to ANDA Submission

- All patents and exclusivities will expire within 12 months of the planned submission date;
- The submission is for a drug product for which there are not more than three approved drug products, and for which there are no blocking patents or exclusivities;
- The submission is for a drug product that could help mitigate or resolve a drug shortage and prevent future shortages;
- The submission is for a drug product that could help address a public health emergency; *or*
- The submission is for a drug product for which there is only one approved drug product listed in the Prescription Drug Product List of the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations (Orange Book) and that drug product is approved under an ANDA.

All patents and exclusivities will expire within 12 months of the planned submission date

- All unexpired NDA patents and/or exclusivities must expire within 12 months of the planned submission date for the original ANDA, ANDA amendment containing a response to a CRL, or ANDA amendment seeking final approval of a tentatively approved ANDA
  - Note: the other four categories of ANDA submissions that can qualify a DMF for review prior to ANDA submission are similar to prioritization factors reflected in the Manual of Policy and Procedures (MAPP) 5240.3 Rev. 6, *Prioritization of the Review of Original ANDAs, Amendments, and Supplements,* but this category does not have a parallel prioritization factor in that MAPP

Not More Than Three Approved Applications

- Submissions for drug products for which there are not more than three approved drug products listed in the Orange Book and for which there are no blocking patents or exclusivities listed for the reference listed drug (RLD), and the ANDA applicant is not seeking approval for less than all the conditions of use in the RLD labeling. In other words, if there are fewer than four approved therapeutically equivalent drug products, including the RLD, listed in the Orange Book, and if there are no blocking patents or unexpired exclusivities for the RLD in the Orange Book, and the applicant is not seeking to "carve-out" any conditions of use, it can qualify under this category.
- Approved drug products include both the NDA and ANDAs:
  - Approved ANDAs listed in the inactive section of the Orange Book are considered approved drug products unless the ANDA has been withdrawn with a notice in the Federal Register.
  - 505(b)(2) NDAs listed in the active section of the Orange Book and designated therapeutically equivalent to the RLD are also counted for purposes of determining whether there are fewer than four approved therapeutically equivalent drug products.

Locating NDA Patents/Exclusivities in the Orange Book

- NDA Orange Book Listing: click on highlighted number

RX	BREXPIPRAZOLE	REXULTI	N205422	TABLET	ORAL	0.25MG	AB	RLD
RX	BREXPIPRAZOLE	REXULTI	N205422	TABLET	ORAL	0.5MG	AB	RLD
RX	BREXPIPRAZOLE	REXULTI	N205422	TABLET	ORAL	1MG	AB	RLD
RX	BREXPIPRAZOLE	REXULTI	N205422	TABLET	ORAL	2MG	AB	RLD
RX	BREXPIPRAZOLE	REXULTI	N205422	TABLET	ORAL	3MG	AB	RLD
RX	BREXPIPRAZOLE	REXULTI	N205422	TABLET	ORAL	4MG	AB	RLD

- Click on highlighted “Patent and Exclusivity Information”

REXULTI (BREXPIPRAZOLE)
0.25MG
Marketing Status: Prescription

Active Ingredient: BREXPIPRAZOLE
Proprietary Name: REXULTI
Dosage Form; Route of Administration: TABLET; ORAL
Strength: 0.25MG
Reference Listed Drug: Yes
Reference Standard: No
TE Code: AB
Application Number: N205422
Product Number: 001
Approval Date: Jul 10, 2015
Applicant Holder Full Name: OTSUKA PHARMACEUTICAL CO LTD
Marketing Status: Prescription
Patent and Exclusivity Information

Locating NDA Patents/Exclusivities in the Orange Book (continued)

- NDA Orange Book Patent and Exclusivity Listings

Patent and Exclusivity for: N205422

Product 001
BREXPIPRAZOLE (REXULTI) TABLET 0.25MG

Patent Data

Product No	Patent No	Patent Expiration	Drug Substance	Drug Product	Patent Use Code	Delist Requested	Submission Date
001	7888362	04/12/2026	DS			Y	07/17/2015
001	8349840	04/12/2026		DP	U-1529		07/17/2015
001	8618109	04/12/2026			U-543 U-3281		07/17/2015
001	9839637	04/12/2026		DP	U-543 U-1529 U-3281		01/09/2018
001	10307419	10/12/2032		DP			06/14/2019
001	RE48059	12/23/2028	DS				07/20/2020

Exclusivity Data

Product No	Exclusivity Code	Exclusivity Expiration
001	NPP	12/27/2024

Not More Than Three Approved Applications

Active Section of Orange Book

RX	CHLORDIAZEPOXIDE HYDROCHLORIDE	CHLORDIAZEPOXIDE HYDROCHLORIDE	A084768	CAPSULE	ORAL	5MG	AB		
RX	CHLORDIAZEPOXIDE HYDROCHLORIDE	CHLORDIAZEPOXIDE HYDROCHLORIDE	A084878	CAPSULE	ORAL	5MG	AB		
RX	CHLORDIAZEPOXIDE HYDROCHLORIDE	CHLORDIAZEPOXIDE HYDROCHLORIDE	A083116	CAPSULE	ORAL	10MG	AB		
RX	CHLORDIAZEPOXIDE HYDROCHLORIDE	CHLORDIAZEPOXIDE HYDROCHLORIDE	A084041	CAPSULE	ORAL	10MG	AB		
RX	CHLORDIAZEPOXIDE HYDROCHLORIDE	CHLORDIAZEPOXIDE HYDROCHLORIDE	A084769	CAPSULE	ORAL	25MG	AB		
RX	CHLORDIAZEPOXIDE HYDROCHLORIDE	CHLORDIAZEPOXIDE HYDROCHLORIDE	A084879	CAPSULE	ORAL	25MG	AB		
RX	CHLORDIAZEPOXIDE HYDROCHLORIDE	LIBRIUM	A085481	CAPSULE	ORAL	5MG	AB	RLD	
RX	CHLORDIAZEPOXIDE HYDROCHLORIDE	LIBRIUM	A085472	CAPSULE	ORAL	10MG	AB	RLD	
RX	CHLORDIAZEPOXIDE HYDROCHLORIDE	LIBRIUM	A085475	CAPSULE	ORAL	25MG	AB	RLD	

Inactive Section

DISCN	CHLORDIAZEPOXIDE HYDROCHLORIDE	CHLORDIAZEPOXIDE HYDROCHLORIDE	A084644	CAPSULE	ORAL	5MG
DISCN	CHLORDIAZEPOXIDE HYDROCHLORIDE	CHLORDIAZEPOXIDE HYDROCHLORIDE	A088129	CAPSULE	ORAL	5MG
DISCN	CHLORDIAZEPOXIDE HYDROCHLORIDE	CHLORDIAZEPOXIDE HYDROCHLORIDE	A086383	CAPSULE	ORAL	5MG
DISCN	CHLORDIAZEPOXIDE HYDROCHLORIDE	CHLORDIAZEPOXIDE HYDROCHLORIDE	A085014	CAPSULE	ORAL	5MG
DISCN	CHLORDIAZEPOXIDE HYDROCHLORIDE	CHLORDIAZEPOXIDE HYDROCHLORIDE	A087524	CAPSULE	ORAL	10MG
DISCN	CHLORDIAZEPOXIDE HYDROCHLORIDE	CHLORDIAZEPOXIDE HYDROCHLORIDE	A085339	CAPSULE	ORAL	10MG
DISCN	CHLORDIAZEPOXIDE HYDROCHLORIDE	CHLORDIAZEPOXIDE HYDROCHLORIDE	A085113	CAPSULE	ORAL	10MG
DISCN	CHLORDIAZEPOXIDE HYDROCHLORIDE	CHLORDIAZEPOXIDE HYDROCHLORIDE	A083742	CAPSULE	ORAL	10MG
DISCN	CHLORDIAZEPOXIDE HYDROCHLORIDE	CHLORDIAZEPOXIDE HYDROCHLORIDE	A085119	CAPSULE	ORAL	10MG
DISCN	CHLORDIAZEPOXIDE HYDROCHLORIDE	CHLORDIAZEPOXIDE HYDROCHLORIDE	A086876	CAPSULE	ORAL	10MG
DISCN	CHLORDIAZEPOXIDE HYDROCHLORIDE	CHLORDIAZEPOXIDE HYDROCHLORIDE	A087037	CAPSULE	ORAL	10MG
DISCN	CHLORDIAZEPOXIDE HYDROCHLORIDE	CHLORDIAZEPOXIDE HYDROCHLORIDE	A086217	CAPSULE	ORAL	10MG
DISCN	CHLORDIAZEPOXIDE HYDROCHLORIDE	CHLORDIAZEPOXIDE HYDROCHLORIDE	A084601	CAPSULE	ORAL	10MG
DISCN	CHLORDIAZEPOXIDE HYDROCHLORIDE	CHLORDIAZEPOXIDE HYDROCHLORIDE	A084598	CAPSULE	ORAL	10MG

Submissions Related to Drug Shortages

- Submissions that could help mitigate or resolve a drug shortage and prevent future shortages, including submissions related to products that are listed on FDA's Drug Shortage List at the time of the submission.

Submissions Related to Public Health Emergencies

- Submissions for drug products that either could help address a public health emergency (PHE) declared by the Secretary of the U.S. Department of Health and Human Services under section 319 of the Public Health Service Act (42 U.S.C. 247d) or anticipated under the same criteria as apply to such a declaration.
  - For example, COVID-19, Opioid Crisis
- In determining which products could help address a PHE, FDA generally uses information from a variety of sources to determine which products are needed the most.

Submissions for “sole source” Drug Products

- Submissions for drug products for which (1) there is only one approved drug product listed in the Active Section of the Orange Book and that product is approved under an ANDA (i.e., the RLD is in the ”Discontinued Section” and there is not more than one ANDA in the “Active Section”); (2) the approved ANDA for the drug product listed in the Active Section was not approved pursuant to a suitability petition; (3) there are no blocking patents or exclusivities for the RLD; and (4) the submission does not qualify for prioritization under any other factor listed in MAPP 5240.3 (the prioritization MAPP).
  - Although submissions for which the sole source product is a petitioned ANDA would not qualify a DMF for review prior to submission under this category, such submissions could potentially meet the criteria for the not more than three approved applications category

ANDA Approved Under a Suitability Petition

- NDA Drug Product

DISCN	CHLORZOXAZONE	PARAFON FORTE DSC	N011529	TABLET	ORAL	500MG **Federal Register determination that product was not discontinued or withdrawn for safety or effectiveness reasons**		RLD

- ANDA Drug Products – ANDA strength not available under the approved NDA

RX	CHLORZOXAZONE	CHLORZOXAZONE	A212053	TABLET	ORAL	375MG	AB
RX	CHLORZOXAZONE	CHLORZOXAZONE	A211849	TABLET	ORAL	375MG	AB
RX	CHLORZOXAZONE	CHLORZOXAZONE	A040861	TABLET	ORAL	375MG	AB
RX	CHLORZOXAZONE	CHLORZOXAZONE	A212253	TABLET	ORAL	375MG	AB
RX	CHLORZOXAZONE	CHLORZOXAZONE	A212743	TABLET	ORAL	375MG	AB
RX	CHLORZOXAZONE	CHLORZOXAZONE	A213126	TABLET	ORAL	375MG	AB
RX	CHLORZOXAZONE	CHLORZOXAZONE	A212898	TABLET	ORAL	375MG	AB

Resources

- See Section III.A. of the draft guidance, *Review of Drug Master Files in Advance of Certain ANDA Submissions Under GDUFA*:
  - https://www.fda.gov/regulatory-information/search-fda-guidance-documents/review-drug-master-files-advance-certain-anda-submissions-under-gdufa
- FDA Drug Shortages:
  - https://www.accessdata.fda.gov/scripts/drugshortages/default.cfm
- GDUFA III Commitment Letter, Section VI. E.:
  - https://www.fda.gov/media/153631/download
- Orange Book:
  - https://www.accessdata.fda.gov/scripts/cder/ob/index.cfm
- Manual of Policy and Procedures 5240.3 Rev. 6, *Prioritization of the Review of Original ANDAs, Amendments, and Supplements:*
  - https://www.fda.gov/media/89061/download

Challenge Question #1

If the RLD is listed in the inactive section of the Orange Book, and there is one approved petitioned ANDA for the drug in the active section of the Orange Book, a DMF could qualify for review prior to the planned submission of an ANDA under the sole-source category.

A. True

B. False

Challenge Question #2

If there are no approved generic applications in the Orange Book, and there is an unexpired exclusivity listed for the RLD but the ANDA applicant is seeking to “carve out” the condition of use covered by this exclusivity, a DMF could qualify for review prior to the planned submission of the ANDA under the not more than three approved drug products category.

A. True

B. False


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