ANDA 209348

ANDA APPROVAL/TENTATIVE APPROVAL

Dr. Reddy's Laboratories Inc.
U.S. Agent for Dr. Reddy's Laboratories Limited
107 College Road East
Princeton, NJ 08540
Attention: Robert Tambe
VP and Head, RA & QA - North America

Dear Robert Tambe:

This letter is in reference to your abbreviated new drug application (ANDA) received for review on July 12, 2016, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) for Lenalidomide Capsules, 2.5 mg, 5 mg, 10 mg, 15 mg, 20 mg, and 25 mg.

Reference is also made to the complete response letter issued by this office on August 12, 2020, and to any amendments thereafter.

We have completed the review of this ANDA and have concluded that adequate information has been presented to demonstrate that the drug meets the requirements for approval under the FD&C Act. We have determined your Lenalidomide Capsules, 2.5 mg, 5 mg, 10 mg, 15 mg, 20 mg, and 25 mg, to be bioequivalent and therapeutically equivalent to the reference listed drug (RLD), Revlimid Capsules, 2.5 mg, 5 mg, 10 mg, 15 mg, 20 mg, and 25 mg, of Celgene Corporation (Celgene).

However, we are unable to grant final approval to your Lenalidomide Capsules, 5 mg, 10 mg, 15 mg, and 25 mg, at this time because of the exclusivity issue noted below. Therefore, your ANDA is **approved** insofar as it pertains to Lenalidomide Capsules, 2.5 mg and 20 mg. Your Lenalidomide Capsules, 5 mg, 10 mg, 15 mg, and 25 mg are **tentatively approved**. This determination is based upon information available to the Agency at this time (e.g., information in your ANDA and the status of current good manufacturing practices (cGMPs) of the facilities used in the manufacturing and testing of the drug product). This determination is subject to change on the basis of new information that may come to our attention.

The RLD upon which you have based your ANDA, Revlimid Capsules, 2.5 mg, 5 mg, 10 mg, 15 mg, 20 mg, and 25 mg, of Celgene, is subject to periods of patent protection. The following patents and expiration dates are currently listed in the Agency's publication titled *Approved Drug Products with Therapeutic Equivalence Evaluations* (the "Orange Book"):

U.S. Patent Number	Expiration Date
7,189,740 (the '740 patent)	April 11, 2023
7,465,800 (the '800 patent)	April 27, 2027
7,468,363 (the '363 patent)	October 7, 2023
7,855,217 (the '217 patent)	November 24, 2024
7,968,569 (the '569 patent)	October 7, 2023
8,404,717 (the '717 patent)	April 11, 2023
8,492,406 (the '406 patent)	October 7, 2023
8,530,498 (the '498 patent)	May 15, 2023
8,648,095 (the '095 patent)	May 15, 2023
8,741,929 (the '929 patent)	March 8, 2028
9,056,120 (the '120 patent)	April 11, 2023
9,101,621 (the '621 patent)	May 15, 2023
9,101,622 (the '622 patent)	May 15, 2023
9,155,730 (the '730 patent)	May 15, 2023
9,393,238 (the '238 patent)	May 15, 2023

With respect to the '363, '406, '929, '730, and '238 patents, your ANDA contains statements under section 505(j)(2)(A)(viii) of the FD&C Act that these are method-of-use patents that do not claim any indication or other conditions of use for which you are seeking approval under your ANDA.

With respect to the '740, '800, '217, '569, '717, '498, '095, '120, '621 and '622 patents, your ANDA contains paragraph IV certifications under section 505(j)(2)(A)(vii)(IV) of the FD&C Act stating that the patents are invalid, unenforceable, or will not be infringed by your manufacture, use, or sale of Lenalidomide Capsules, 2.5 mg, 5 mg, 10 mg, 15 mg, 20 mg, and 25 mg, under this ANDA. You have notified the Agency that Dr. Reddy's Laboratories Limited (Dr. Reddy's) complied with the requirements of section 505(j)(2)(B) of the FD&C Act. Litigation was initiated within the statutory 45-day period against Dr. Reddy's for infringement of the '800, '217, '569, '498, '095, '621, and '622

patents in the United States District Court for the District of New Jersey [Celgene Corporation v. Dr. Reddy's Laboratories, Ltd. and Dr. Reddy's Laboratories, Inc., Civil Action No. 16-07704] and for infringement of the '740, '717, and '120 patents in the United States District Court for the District of New Jersey [Celgene Corporation v. Dr. Reddy's Laboratories, Ltd. and Dr. Reddy's Laboratories, Inc., Civil Action No. 17-05314]. You have also notified the Agency that these cases were dismissed.

The RLD upon which you have based your ANDA, Celgene's Revlimid Capsules, 2.5 mg, 5 mg, 10 mg, 15 mg, 20 mg, and 25 mg, is also subject to periods of exclusivity. With respect to the ODE-88 and ODE-131 exclusivities, the Agency has received a letter from Celgene that waives the unexpired exclusivity periods with respect to Dr. Reddy's ANDA 209348.

Upon the foregoing, your ANDA is **approved** insofar as it pertains to the 2.5 mg and 20 mg products. Your 5 mg, 10 mg, 15 mg, and 25 mg products are **tentatively approved**.

I. Approval of Lenalidomide Capsules, 2.5 mg and 20 mg

With respect to 180-day generic drug exclusivity, we note that Dr. Reddy's was the first ANDA applicant to submit a substantially complete ANDA with a paragraph IV certification for Lenalidomide Capsules, 2.5 mg and 20 mg. Therefore, with this approval, Dr. Reddy's is eligible for 180 days of generic drug exclusivity for Lenalidomide Capsules, 2.5 mg and 20 mg. FDA notes that after issuance of this approval letter, eligibility for 180-day exclusivity is subject to future events that may result in forfeiture of exclusivity under section 505(j)(5)(D) of the FD&C Act. This exclusivity, which is provided for under section 505(j)(5)(B)(iv) of the FD&C Act, will begin to run from the date of the commercial marketing identified in section 505(j)(5)(B)(iv). Please submit correspondence to this ANDA notifying the Agency within 30 days of the date of the first commercial marketing of this drug product or the RLD. If you do not notify the Agency within 30 days, the date of first commercial marketing will be deemed to be the date of the drug product's approval. See 21 CFR 314.107(c)(2).

Under section 506A of FD&C Act, certain changes in the conditions described in this ANDA require an approved supplemental application before the change may be made.

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

Section 505-1 of the FD&C Act authorizes FDA to require the submission of a risk evaluation and mitigation strategy (REMS), if FDA determines that such a strategy is necessary to ensure that the benefits of the drug outweigh the risks [section 505-1(a) of the FD&C Act]. In accordance with section 505-1(i) of the FD&C Act, a drug that is the subject of an ANDA under section 505(j) of the FD&C Act is subject to certain elements of the REMS required for the applicable listed drug.

The details of the REMS requirements were outlined in our REMS notification letter dated August 31, 2016.

Your final proposed REMS, received on April 14, 2021; is approved, and will be posted on the FDA REMS website: http://www.fda.gov/rems. Other products may be added in the future if additional NDAs or ANDAs are approved.

The PS-Lenalidomide REMS consists of Elements to Assure Safe Use (ETASU) and an implementation system.

Your REMS must be fully operational before you introduce **lenalidomide** into interstate commerce.

Your REMS, known as the PS-Lenalidomide REMS Program, is approved as a separate REMS program from that of the reference listed drug, using a different, comparable aspect of the ETASU. Pursuant to section 505-1(i)(3), FDA is requiring that this REMS Program can be used with respect to any other drug that is the subject of an application under section 505(j) or 505(b) of the FD&C Act that references the same listed drug.

Under section 505-1(g)(2)(C) of the FD&C Act, FDA can require the submission of a REMS assessment if FDA determines an assessment is needed to evaluate whether the REMS should be modified to ensure the benefits of the drug outweigh the risks or to minimize the burden on the healthcare delivery system of complying with the REMS.

FDA has determined that assessments are needed for the PS-Lenalidomide REMS program.

Additionally, the details for what should be included in your REMS assessments and the dates of the REMS assessments are listed in Appendix 1.

If the assessment instruments and methodology for your REMS assessments are not included in the REMS supporting document, or if you propose changes to the submitted assessment instruments or methodology, you should update the REMS supporting document to include specific assessment instrument and methodology information at least 90 days before the assessments will be conducted. Updates to the REMS supporting document may be included in a new document that references previous REMS supporting document submission(s) for unchanged portions. Alternatively, updates may be made by modifying the complete previous REMS supporting document, with all changes marked and highlighted. Prominently identify the submission containing the assessment instruments and methodology with the following wording in bold capital letters at the top of the first page of the submission:

> **ANDA 209348 REMS CORRESPONDENCE**
> (insert concise description of content in bold capital letters, e.g.,
> **UPDATE TO REMS SUPPORTING DOCUMENT - ASSESSMENT METHODOLOGY**

We remind you that you must include an adequate rationale to support a proposed REMS modification for the addition, modification, or removal of any goal or element of the REMS, as described in section 505-1(g)(4) of the FD&C Act.

We also remind you that section 505-1(f)(8) of the FD&C Act prohibits holders of an approved covered application from using any element to assure safe use to block or delay approval of an application under section 505(b)(2) or (j). A violation of this provision in 505-1(f) could result in enforcement action.

Prominently identify any submission containing a REMS assessment or proposed modifications of the REMS with the following wording in bold capital letters at the top of the first page of the submission as appropriate:

ANDA 209348 REMS ASSESSMENT

or

NEW SUPPLEMENT FOR ANDA 209348/S-000
CHANGES BEING EFFECTED IN 30 DAYS
PROPOSED MINOR REMS MODIFICATION

or

NEW SUPPLEMENT FOR ANDA 209348/S-000
PRIOR APPROVAL SUPPLEMENT
PROPOSED MAJOR REMS MODIFICATION

or

NEW SUPPLEMENT FOR ANDA 209348/S-000
PRIOR APPROVAL SUPPLEMENT
PROPOSED REMS MODIFICATIONS DUE TO SAFETY LABELING CHANGES SUBMITTED IN SUPPLEMENT XXX

Should you choose to submit a REMS revision, prominently identify the submission containing the REMS revisions with the following wording in bold capital letters at the top of the first page of the submission:

REMS REVISION FOR ANDA 209348

To facilitate review of your submission, we request that you submit your proposed modified REMS and other REMS-related materials in Microsoft Word format. If certain documents, such as enrollment forms, are only in PDF format, they may be submitted as such, but the preference is to include as many as possible in Word format.

SUBMISSION OF REMS DOCUMENT IN SPL FORMAT

In addition to submitting the proposed REMS as described above, you can also submit the REMS document in Structured Product Labeling (SPL) format. If you intend to submit the REMS document in SPL format, include the SPL file with your proposed REMS submission.

For more information on submitting REMS in SPL format, please email REMSWebsite@fda.hhs.gov.

REPORTING REQUIREMENTS

Postmarketing reporting requirements for this ANDA are set forth in 21 CFR 314.80-81 and 314.98 and at section 506I of the FD&C Act. The Agency should be advised of any change in the marketing status of this drug or if this drug will not be available for sale after approval. In particular, under section 506I(b) of the FD&C Act, you are required to notify the Agency in writing within 180 days from the date of this letter if this drug will not be available for sale within 180 days from the date of approval. As part of such written notification, you must include (1) the identity of the drug by established name and proprietary name (if any); (2) the ANDA number; (3) the strength of the drug; (4) the date on which the drug will be available for sale, if known; and (5) the reason for not marketing the drug after approval.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling materials prior to publication or dissemination. Please note that these submissions are voluntary. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert (PI), Medication Guide, and patient PI (as applicable) to:

OPDP Regulatory Project Manager
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion
5901-B Ammendale Road
Beltsville, MD 20705

Alternatively, you may submit a request for advisory comments electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft Guidance for Industry (available at: https://www.fda.gov/media/128163/download)

You must also submit final promotional materials and package insert(s), accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR

314.81(b)(3)(i)]. Form FDA 2253 is available at https://www.fda.gov/media/73013/download. Information and Instructions for completing the form can be found at https://www.fda.gov/media/132152/download. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/opdp-ectd.

ANNUAL FACILITY FEES

The Generic Drug User Fee Amendments of 2012 (GDUFA) (Public Law 112-144, Title III) established certain provisions[1] with respect to self-identification of facilities and payment of annual facility fees. Your ANDA identifies at least one facility that is subject to the self-identification requirement and payment of an annual facility fee. Self-identification must occur by June 1st of each year for the next fiscal year. Facility fees must be paid each year by the date specified in the *Federal Register* notice announcing facility fee amounts.

All finished dosage forms or active pharmaceutical ingredients manufactured in a facility that has not met its obligations to self-identify or to pay fees when they are due will be deemed misbranded. This means that it will be a violation of federal law to ship these products in interstate commerce or to import them into the United States. Such violations can result in prosecution of those responsible, injunctions, or seizures of misbranded products. Products misbranded because of failure to self-identify or pay facility fees are subject to being denied entry into the United States.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit, using the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm, that is identical in content to the approved labeling (including the package insert, and any patient package insert and/or Medication Guide that may be required). Information on submitting SPL files using eLIST may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As" at https://www.fda.gov/media/71211/download. The SPL will be accessible via publicly available labeling repositories.

We remind you that you must continually monitor available labeling resources such as DRUGS@FDA for changes to your reference listed drug's labels and labeling and make any necessary revisions to your labels and labeling. More information on post-approval labeling changes may be found in the guidance for industry titled "Changes to an Approved NDA or ANDA" at https://www.fda.gov/media/71846/download.

II. Tentative Approval of Lenalidomide Capsules, 5 mg, 10 mg, 15 mg, and 25 mg

We are unable to grant final approval to your Lenalidomide Capsules, 5 mg, 10 mg, 15 mg, and 25 mg, at this time. Prior to the submission of your ANDA, another applicant or applicants submitted a substantially complete ANDA providing for Lenalidomide Capsules, 5 mg, 10 mg, 15 mg, and 25 mg, and containing a paragraph IV certification. Your ANDA for these strengths will be eligible for final approval on the date that is 180 days after the commercial marketing date identified in section 505(j)(5)(B)(iv) of the FD&C Act.

Our decision to tentatively approve your Lenalidomide Capsules, 5 mg, 10 mg, 15 mg, and 25 mg, is based upon information currently available to the Agency (i.e., data in your ANDA and the status of current good manufacturing practice (cGMP) of the facilities used in the manufacture and testing of the drug product). This decision is subject to change on the basis of new information that may come to our attention.

RESUBMISSION

To request final approval, please submit an amendment titled "FINAL APPROVAL REQUESTED" with enough time to permit FDA review prior to the date you believe that your ANDA will be eligible for final approval. A request for final approval that contains no new data, information, or other changes to the ANDA generally requires a period of 3 months for Agency review. Accordingly, such a request for final approval should be submitted no later than 3 months prior to the date on which you seek approval. A request for final approval that contains substantive changes to this ANDA or changes in the status of the manufacturing and testing facilities' compliance with cGMPs will be classified and reviewed according to OGD policy in effect at the time of receipt. Applicants should review available agency guidance for industry related to amendments under the generic drug user fee program to determine the duration of Agency review needed to review the changes submitted. As part of this consideration, applicants should monitor any changes to the RLD that occur after tentative approval, including changes in labeling, patent or exclusivity information, or marketing status. The submission of multiple amendments prior to final approval may also result in a delay in the issuance of the final approval letter.

The amendment requesting final approval should provide the legal/regulatory basis for your request for final approval and should include a copy of a court decision, settlement or licensing agreement, or other information described in 21 CFR 314.107, as appropriate. It should also identify changes, if any, in the conditions under which the ANDA was tentatively approved, i.e., updated information such as final-printed labeling, chemistry, manufacturing, and controls data as appropriate. This amendment should be submitted even if none of these changes were made, and it should be designated clearly in your cover letter as a "MINOR/MAJOR AMENDMENT TO ORIGINAL #2 – FINAL APPROVAL REQUESTED."

In addition to the amendment requested above, the Agency may request, at any time prior to the date of final approval, that you submit an additional amendment containing information as specified by the Agency. Failure to submit either or, if requested, both types of amendments described above may result in a delay in the issuance of the final approval letter.

This drug product may not be marketed without final Agency approval under section 505(j) of the FD&C Act. The introduction or delivery for introduction into interstate commerce of this drug product before the final approval date is prohibited under section 301 of the FD&C Act. Also, until the Agency issues the final approval letter, this drug product will not be deemed approved for marketing under section 505(j) of the FD&C Act, and will not be listed in the Orange Book.

ANNUAL FACILITY FEES

The Generic Drug User Fee Amendments of 2012 (GDUFA) (Public Law 112-144, Title III) established certain provisions[1] with respect to self-identification of facilities and payment of annual facility fees. Your ANDA identifies at least one facility that is subject to the self-identification requirement and payment of an annual facility fee. Self-identification must occur by June 1st of each year for the next fiscal year. Facility fees must be paid each year by the date specified in the *Federal Register* notice announcing facility fee amounts.

All finished dosage forms or active pharmaceutical ingredients manufactured in a facility that has not met its obligations to self-identify or to pay fees when they are due will be deemed misbranded. This means that it will be a violation of federal law to ship these products in interstate commerce or to import them into the United States. Such violations can result in prosecution of those responsible, injunctions, or seizures of misbranded products. Products misbranded because of failure to self-identify or pay facility fees are subject to being denied entry into the United States.

In addition, we note that GDUFA requires that certain non-manufacturing sites and organizations listed in generic drug submissions comply with the self-identification requirement. The failure of any facility, site, or organization to comply with its obligation to self-identify and/or to pay fees when due may raise significant concerns about that site or organization and is a factor that may increase the likelihood of a site inspection prior to approval. FDA does not expect to give priority to completion of inspections that are required simply because facilities, sites, or organizations fail to comply with the law requiring self-identification or fee payment.

For further information on the status of this ANDA or upon submitting an amendment to the ANDA, please contact Zera Kwende, Regulatory Project Manager, at (301) 796 - 3556.

Sincerely yours,

{See appended electronic signature page}

For Edward M. Sherwood
Director
Office of Regulatory Operations
Office of Generic Drugs
Center for Drug Evaluation and Research

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[1] Some of these provisions were amended by the Generic Drug User Fee Amendments of 2017 (GDUFA II) (Public Law 115-52, Title III).

APPENDIX 1

REMS Assessment Plan

PS-Lenalidomide REMS Sponsors will submit PS-Lenalidomide REMS assessments to the FDA annually from the date of initial approval of the PS-Lenalidomide REMS. To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment should conclude no earlier than 60 days before the submission date for that REMS assessment. The PS-Lenalidomide REMS Sponsors will submit each REMS assessment so that it will be received by the FDA on or before the due date.

For each annual PS-lenalidomide REMS assessment report, the following information will be provided. A tabular format will be utilized when appropriate.

The PS-Lenalidomide Shared System REMS Assessment Plan will include, but is not limited to, the following information:

Program Implementation and Operations

1. REMS Program Implementation (1-year assessment only)
    a. Date of first commercial distribution of first generic lenalidomide
    b. Date when the PS-Lenalidomide REMS website became live and fully operational
    c. Date when healthcare providers could become certified
    d. Date when pharmacies could become certified
    e. Date when patients could become enrolled
    f. Date when the REMS Coordinating Center was established and fully operational

2. REMS Certification and Enrollment Statistics (per current and previous two reporting periods and cumulatively)
    a. Certification of healthcare providers (HCPs)
        i. Number of new certifications of HCPs, indicating whether previously certified or not, stratified by professional designation (i.e. MD, DO, PA, NP), and geographic region (defined by US Census).
        ii. Number of active HCPs (have prescribed lenalidomide at least once during the reporting period) stratified by professional designation (i.e. MD, DO, PA, NP), and geographic region (defined by US Census).
    b. Certification of pharmacies
        i. Number of new certified pharmacies stratified by geographic region (defined by US Census).
        ii. Number of active certified pharmacies (have filled or ordered at least one prescription for lenalidomide during the reporting period) stratified by geographic region (defined by US Census).

c. Patient enrollment
    i. Number of new patients enrolled stratified by age, gender, diagnosis, and patient reproductive status (i.e. females of reproductive potential (FRP) and females of non-reproductive potential (FNRP).
    ii. Number of active patients (have received at least one shipment of lenalidomide during the reporting period) stratified by age gender, diagnosis, and patient reproductive status (i.e. females of reproductive potential (FRP) and females of non-reproductive potential (FNRP).

3. Utilization Data (per current and previous two reporting periods and cumulatively)
    a. Number and percentage of unique patients who received lenalidomide, new and total, stratified by patient type grouped by the following age ranges:
        i) < 6
        ii) 6 - < 18
        iii) 18 - 49
        iv) 50+
    b. Number and percentage of prescriptions (new and refills) dispensed for FRPs and FNRPs stratified by:
        i) Healthcare provider specialty
        ii) Reproductive Status (FRP or FNRP)
        iii) Patient age as outlined in 3.a above

4. Compliance with the PS-lenalidomide REMS (per current and previous two reporting periods and cumulatively; where applicable)
    a. Provide a report of audit activities for stakeholders (pharmacies, distributors, and the REMS Coordinating Center)
    b. Provide a copy of the non-compliance plan to include the following:
        i. Criteria for non-compliance
        ii. Actions taken to address non-compliance for each event identified
        iii. Criteria for de-certification
    c. Provide a copy of the audit plan.
    d. Report of audit findings.
        i. The number of audits expected, and the number of audits conducted
        ii. The number and type of deficiencies noted
            1. Number that successfully completed a corrective and preventative action (CAPA) plan within 30 days of receipt of CAPA
            2. Describe actions taken for any that did not complete the CAPA within 30 days of receipt of CAPA
            3. Include a unique ID for each stakeholder that had deviations to track deviations over time
        iii. Documentation of completion of training for relevant staff
        iv. The existence of documented processes and procedure for complying with the REMS

v. A comparison of the findings to findings of previous audits and assess whether any trends are noted

e. Non-compliance events: for each event provide the following:
   i. Source of the report
   ii. Description of the event
   iii. Cause of the event
   iv. Corrective actions taken
   v. Event:
      1. Number of lenalidomide prescriptions dispensed that were written by non-certified prescribers
      2. Number of lenalidomide prescriptions dispensed by non-certified pharmacies
      3. Number of lenalidomide prescriptions dispensed to de-enrolled or non-enrolled patients
      4. Number of times a lenalidomide prescription was dispensed without obtaining a confirmation number
      5. Number of prescriptions dispensed of greater than a 28 days' supply
      6. Number of shipments sent to non-certified pharmacies, sources of the reports, and actions taken to prevent future occurrences
      7. Number of prescribers and pharmacies who were de-certified (suspended or deactivated) for non-compliance and reasons for de-certification

5. REMS Infrastructure and Performance (per current and previous two reporting periods and cumulatively; where applicable)
   a. REMS Coordinating Center
      i) Number of contacts by stakeholder type (patients, healthcare providers, pharmacies, wholesaler(s)/distributor(s), other)
      ii) Summary of reasons for calls (e.g., enrollment question, location of a pharmacy) and by reporter (authorized representative, pharmacy, healthcare provider, patient, other)
      iii) Summary of frequently asked questions (FAQ) by stakeholder type
      iv) Summary report of REMS-related problems identified and resulting corrective actions
   b. REMS Website
      i) Number of visits and unique visits to the REMS website
      ii) Number of REMS materials downloaded or printed for each material

Health Outcomes and/or Surrogates of Health Outcomes

6. Pregnancy Metrics (per reporting period and cumulatively)
   a. Number of pregnancies reported stratified by the source of the report (spontaneous report, reported via the REMS program, etc.)
   b. Pregnancy rate

c. A summary of both US and worldwide pregnancy cases, including but not limited to the following information:
    i. Event identification number
    ii. Age of the patient
    iii. Contraceptive methods used
    iv. Outcome of each pregnancy
    v. Weeks gestation at termination if pregnancy is terminated
d. Follow-up of outstanding pregnancy reports
e. Root cause analysis of each reported pregnancy
f. Link to most recent Periodic Safety Update Report (PSUR) or Periodic Benefit-Risk Evaluation Report (PBRER) that provides information on worldwide pregnancies. Discussion of any new information provided in the PSUR or PBRER regarding pregnancy.

Safe-Use Behaviors

7. Change in Reproductive Status as reported via the required prescriber survey (per current and previous two reporting periods and cumulatively)
    a. Number of status changes to a female of reproductive potential, including:
        i. Number of times lenalidomide was dispensed prior to the patient getting her first pregnancy test following the status change, any resulting adverse events, and corrective actions
    b. Number of status changes to a female of non-reproductive potential, including rationale for the change as indicated on the survey.
        i. Number of female patients for whom pregnancy testing can be discontinued because the patient has had a natural menopause for at least 24 consecutive months, a hysterectomy, and/or bilateral oophorectomy

8. Documentation of safe-use conditions (per current and previous two reporting periods and cumulatively, where applicable)

    Based on information collected from the mandatory surveys (used to document safe-use conditions) provide information that could represent potential fetal exposure or that might result in a delay or interruption in treatment.
    Provide the following in a tabular format:
    a. The total number of authorization numbers issued and the total number of authorization numbers flagged
    b. The number and proportion of failed authorizations intended for an FRP due to responses in the mandatory surveys related to pregnancy testing that did not meet the REMS requirements
    c. The number and proportion of failed authorizations that caused a delay in treatment initiation or a gap in therapy for patients due to REMS processes related to the mandatory surveys compared to the total authorization numbers. Include the time to resolution of failed authorizations in days (mean, minimum, maximum) for the reporting period and for each previous reporting period. Include the number of patients with a delay in treatment or a gap in therapy due to REMS processes related to the mandatory surveys.

Knowledge

9. Inform prescribers, patients, and pharmacists on the serious risks and safe-use conditions for lenalidomide (per current and previous two reporting periods and cumulatively, where applicable)
    a. Ensure that lenalidomide will only be dispensed to patients enrolled in the PS-Lenalidomide REMS program with evidence or other documentation of safe-use conditions
        i. Number of patient surveys that met the REMS requirements relating to knowledge compared to the total number of patient surveys submitted per patient risk category
        ii. Number of patient surveys that did not meet the REMS requirements related to knowledge as compared to the total number of patient surveys submitted per patient risk category. Include the time to resolution in days (mean, minimum, maximum) for the reporting period and for each previous reporting period. Include outreach strategies taken by the REMS Coordinating Center to resolve unacceptable safe-use survey responses.
    b. Ensure healthcare providers counsel patients on the benefits and risks of lenalidomide therapy, including risks described in the boxed warnings
        i. Number of prescriber surveys that met the REMS requirements reported per risk category
        ii. Number of prescriber surveys that did not meet the REMS requirements reported per risk category. Include the time to resolution in days (mean, minimum, maximum) for the reporting period and for each previous reporting period. Include outreach strategies taken by the REMS Coordinating Center to resolve unacceptable safe-use survey responses.
    c. Educate pharmacies on the risks and safe-use conditions of lenalidomide
        i. Total number of pharmacy certification quizzes administered
        ii. Number of pharmacies with a passing rate/total number of certified pharmacies on the last day of the reporting period

10. PS-Lenalidomide REMS Knowledge, Attitudes, and Behavior Survey (KAB) (beginning with the 1-year assessment report and annually thereafter with each assessment report)

    The first KAB assessment of prescribers and patients will be completed for inclusion in the 1-year FDA Assessment Report, and will be repeated annually. The KAB surveys will assess the following:
    a. Patient understanding of:
        i. The serious risks associated with the use of lenalidomide
        ii. The importance of regular pregnancy testing as described in the **Patient Guide**
    b. Prescriber understanding of:
        i. The serious risks associated with the use of lenalidomide

ii. The requirements for monitoring reproductive status and pregnancy status described in the **Prescriber Guide**
iii. The need to counsel patients about the risks associated with the use of lenalidomide and the need for monitoring as described in the **Prescriber Guide**

c. Pharmacist understanding of:
i. The serious risks associated with the use of lenalidomide
ii. The training and dispensing procedures for lenalidomide as described in the Pharmacy Guide
iii. The need to counsel patients on the benefits and risks of lenalidomide using the Education and Counseling Checklist for Pharmacies

11. The requirements for assessments of an approved REMS under section 505-1(g)(3) include, with respect to each goal included in the strategy, an assessment of the extent to which the approved strategy, including each element of the strategy, is meeting the goal or whether one or more such goals or such elements should be modified.

Sarah Kurtz

Digitally signed by Sarah Kurtz
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