



NDA 216195

COMPLETE RESPONSE

Xspray Pharma AB
c/o Lachman Consultant Services Inc.
Attention: Jennifer Leaming, MSRA, RAC
US Agent; Principal Consultant
1600 Stewart Avenue, Suite 604
Westbury, NY 11590

Dear Jennifer Leaming:

Please refer to your new drug application (NDA) (b) (4)
(b) (4) for (b) (4) (dasatinib) tablets.

We acknowledge receipt of your amendment dated (b) (4) which constituted a complete response to our July 25, 2024, action letter.

We have completed our review of this application, as amended, and have determined that we cannot approve this application in its present form. We have described our reasons for this action below and, where possible, our recommendations to address these issues.

CLINICAL

The proposed risk mitigation strategies of the minor numerical adjustments to the original strengths and your nomenclature proposal to include (b) (4)
(b) (4) are not acceptable to allow for the safe use of (b) (4) for the proposed indications.

As discussed at the (b) (4) the proposed numerical adjustment of strengths (b) (4)
(b) (4) alone cannot sufficiently mitigate the risk of medication errors. At that time, we encouraged consideration of the proposed slight change in strength (as a mitigation strategy to eliminate the direct numerical overlap in strength between (b) (4) and the proposed (b) (4) be used in tandem with a nomenclature strategy.

As stated in our CR letter dated July 25, 2024, label comprehension studies that evaluated adding the descriptor (b) (4) after (b) (4) (dasatinib tablets)" failed, and there is no evidence that your newly proposed nomenclature would result in different findings. Furthermore, we are concerned that your proposed nonproprietary

name (b) (4) is similar to nomenclature policy for biological products licensed (b) (4)

Thus, we are concerned that your proposed nomenclature would create confusion and would not have the intended effect of mitigating the risk of medication errors associated with switching between your proposed dasatinib product and an approved dasatinib product and safe treatment initiation with your proposed dasatinib product.

Below are two possible actions that you may consider to place your application in condition for approval:

1. You may consider conducting new labeling comprehension studies with the currently proposed numerical adjustment of strengths (b) (4) and modified labeling (including a boxed warning and additional information in dosage and administration) to determine if these strategies are able to mitigate the risks of medication errors.
2. You also may consider reformulating your product so that there will be either:
 - a. identical strengths that are mg-to-mg equivalent to the listed drug relied upon, or
 - b. greater differences between the proposed (b) (4) strengths from (b) (4) (e.g., instead of (b) (4) where the slight difference in numerical strength may not prevent inadvertent wrong substitution with (b) (4) (b) (4) You could do this by reformulating (b) (4) so its strengths would result in numerically nonoverlapping or not close to overlapping strengths of the listed drug relied upon.

If you choose to reformulate your product under option a or b above, you will need to conduct studies with the new strengths to show their equivalence to the listed drug relied upon.

We recommend that you request a meeting with the Agency to discuss your plans on reformulation, the design of any new label comprehension studies, or another proposed approach that would allow for the safe use of (b) (4) for the proposed indications.

PRODUCT QUALITY

(b) (4)

¹ When final, this guidance will reflect FDA's current thinking on this topic.

(b) (4)

FACILITY INSPECTIONS

- (2) Following a CGMP inspection and pre-approval inspection of (b) (4) (b) (4) listed in this application, FDA conveyed deficiencies to the representative of the facility. Satisfactory responses from the facility are needed before this application can be approved. The facility's satisfactory responses are dependent on FDA's determination that the facility has come into compliance with CGMP and may require re-inspection of the facility. Satisfactory outcomes of both the PAI and the CGMP inspections will be needed prior to an approval of the application. As the applicant, we do not expect a response to this facility-related deficiency when responding to any other deficiencies cited in this or other information request or discipline review letters. Instead, please work with the facility, as applicable, in resolving the related deficiencies.

PRESCRIBING INFORMATION

- (3) We reserve comment on the proposed labeling until the application is otherwise adequate. We encourage you to review the labeling review resources on the Prescription Drug Labeling Resources² and Pregnancy and Lactation Labeling Final Rule³ websites, including regulations and related guidance documents and the Selected Requirements for Prescribing Information (SRPI) – a checklist of important format items from labeling regulations and guidances.

² <https://www.fda.gov/drugs/laws-acts-and-rules/prescription-drug-labeling-resources>

³ <https://www.fda.gov/drugs/labeling-information-drug-products/pregnancy-and-lactation-labeling-drugs-final-rule>

If you revise labeling, use the SRPI checklist to ensure that the Prescribing Information conforms with format items in regulations and guidances. Your response must include updated content of labeling [21 CFR 314.50(l)(1)(i) in structured product labeling (SPL) format as described at FDA.gov.⁴

CARTON AND CONTAINER LABELING

- (4) We reserve comment on the proposed labeling until the application is otherwise adequate.

PROPRIETARY NAME

Please refer to our correspondence dated, (b) (4), which addresses the proposed proprietary name, (b) (4). This name was found conditionally acceptable pending approval of the application in the current review cycle. Please resubmit the proposed proprietary name when you respond to all of the application deficiencies that have been identified in this letter.

SAFETY UPDATE

When you respond to the above deficiencies, include a safety update as described at 21 CFR 314.50(d)(5)(vi)(b). The safety update should include data from all nonclinical and clinical studies/trials of the drug under consideration regardless of indication, dosage form, or dose level.

- (1) Describe in detail any significant changes or findings in the safety profile.
- (2) When assembling the sections describing discontinuations due to adverse events, serious adverse events, and common adverse events, incorporate new safety data as follows:
 - Present new safety data from the studies/clinical trials for the proposed indication using the same format as in the original submission.
 - Present tabulations of the new safety data combined with the original application data.
 - Include tables that compare frequencies of adverse events in the original application with the retabulated frequencies described in the bullet above.

⁴ <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>

- For indications other than the proposed indication, provide separate tables for the frequencies of adverse events occurring in clinical trials.
- (3) Present a retabulation of the reasons for premature trial discontinuation by incorporating the drop-outs from the newly completed trials. Describe any new trends or patterns identified.
 - (4) Provide case report forms and narrative summaries for each subject who died during a clinical trial or who did not complete a trial because of an adverse event. In addition, provide narrative summaries for serious adverse events.
 - (5) Describe any information that suggests a substantial change in the incidence of common, but less serious, adverse events between the new data and the original application data.
 - (6) Provide updated exposure information for the clinical studies/trials (e.g., number of subjects, person time).
 - (7) Provide a summary of worldwide experience on the safety of this drug. Include an updated estimate of use for drug marketed in other countries.
 - (8) Provide English translations of current approved foreign labeling not previously submitted.

OTHER

Within one year after the date of this letter, you are required to resubmit or take other actions available under 21 CFR 314.110. If you do not take one of these actions, we may consider your lack of response a request to withdraw the application under 21 CFR 314.65. You may also request an extension of time in which to resubmit the application.

A resubmission must fully address all the deficiencies listed in this letter and should be clearly marked with "**RESUBMISSION**" in large font, bolded type at the beginning of the cover letter of the submission. The cover letter should clearly state that you consider this resubmission a complete response to the deficiencies outlined in this letter. A partial response to this letter will not be processed as a resubmission and will not start a new review cycle.

You may request a meeting or teleconference with us to discuss what steps you need to take before the application may be approved. If you wish to have such a meeting, submit your meeting request as described in the draft guidance for industry *Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products*.

The product may not be legally marketed until you have been notified in writing that this application is approved.

If you have any questions, email (b) (4)

Sincerely,

{See appended electronic signature page}

(b) (4)

Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

(b) (4)

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