

EXCLUSIVITY SUMMARY

NDA # 206089

SUPPL #

HFD #

Trade Name Jatenzo

Generic Name Testosterone undecanoate (oral)

Applicant Name Clarus Therapeutics

Approval Date, If Known March 27, 2019

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, and all efficacy supplements. Complete PARTS II and III of this Exclusivity Summary only if you answer "yes" to one or more of the following questions about the submission.

a) Is it a 505(b)(1), 505(b)(2) or efficacy supplement?

YES NO

If yes, what type? Specify 505(b)(1), 505(b)(2), SE1, SE2, SE3, SE4, SE5, SE6, SE7, SE8

505(b)(2)

b) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "no.")

YES NO

If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

N/A

If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:

N/A

c) Did the applicant request exclusivity?

YES NO

If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

3 years

d) Has pediatric exclusivity been granted for this Active Moiety?

YES NO

If the answer to the above question in YES, is this approval a result of the studies submitted in response to the Pediatric Written Request?

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS AT THE END OF THIS DOCUMENT.

2. Is this drug product or indication a DESI upgrade?

YES NO

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8 (even if a study was required for the upgrade).

PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES

(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES NO

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s). **See information listed at the end of this document**

NDA#

NDA#

NDA#

2. Combination product.

If the product contains more than one active moiety(as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)

YES NO

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA#

NDA#

NDA#

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8. (Caution: The questions in part II of the summary should only be answered "NO" for original approvals of new molecular entities.)
IF "YES," GO TO PART III.

PART III THREE-YEAR EXCLUSIVITY FOR NDAs AND SUPPLEMENTS

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2 was "yes."

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a)

is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation.

YES NO

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

(a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?

YES NO

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval AND GO DIRECTLY TO SIGNATURE BLOCK ON PAGE 8:

(b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application?

YES NO

(1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO.

YES NO

If yes, explain:

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness of this drug product?

YES NO

If yes, explain:

- (c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

Study CLAR-15012

Studies comparing two products with the same ingredient(s) are considered to be bioavailability studies for the purpose of this section.

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1 YES NO

Investigation #2 YES NO

If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

b) For each investigation identified as "essential to the approval", does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1 YES NO

Investigation #2 YES NO

If you have answered "yes" for one or more investigation, identify the NDA in which a similar investigation was relied on:

c) If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):

Study CLAR-15012

4. To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.

a) For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

Investigation #1
IND # 078104 YES ! NO
! Explain:

Investigation #2
IND # YES ! NO
! Explain:

(b) For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study?

Investigation #1
YES ! NO
Explain: ! Explain:

Investigation #2

YES

Explain:

!

!

! NO

! Explain:

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES

NO

If yes, explain:

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Name of person completing form: Jeannie Roule
Title: Senior Regulatory Health Project Manager
Date: March 27, 2019

Name of Division Director signing form: Hylton V. Joffe
Title: Director

Form OGD-011347; Revised 05/10/2004; formatted 2/15/05; removed hidden data 8/22/12

A083976 TESTRED
A080767 METHYLTESTOSTERONE
A084310 METHYLTESTOSTERONE
A086450 ANDROID 10
A087147 ANDROID 25
N020489 ANDRODERM
N021015 ANDROGEL 1%
N022309 ANDROGEL 1.62%
N022219 AVEED
N205488 NATESTO
N021454 TESTIM
A080911 TESTOPEL
N022504 AXIRON
N021463 FORTESTA
N202763 TESTOSTERONE GEL
N209863 XYOSTED
N203098 TESTOSTERONE GEL
N021543 STRIANT
A090387 TESTOSTERONE
CYPIONATE
A090387 TESTOSTERONE
CYPIONATE
A040530 TESTOSTERONE
CYPIONATE
A085635 DEPO-TESTOSTERONE
A085635 DEPO-TESTOSTERONE
A040615 TESTOSTERONE
CYPIONATE
A040615 TESTOSTERONE
CYPIONATE
A040652 TESTOSTERONE
CYPIONATE
A086030 TESTOSTERONE
CYPIONATE
N009165 DELATESTRYL
A040575 TESTOSTERONE
ENANTHATE
A040647 TESTOSTERONE
ENANTHATE
A085598 TESTOSTERONE
ENANTHATE

Addendum

To: NDA 206089, Jatenzo (testosterone undecanoate) capsule

From: Jeannie Roule

Signatory Authority: Hylton V. Joffe, M.D., M.M.Sc.
Director
Division of Bone, Reproductive and Urologic Products

Date: July 31, 2019

Re: Addendum to Exclusivity Summary for NDA 206089

This addendum is intended to supplement the explanation of the recommendation of the Division of Bone, Reproductive, and Urologic Products contained in the Exclusivity Summary for NDA 206089, dated March 27, 2019, that FDA consider Study CLAR-15012 a clinical study, other than a bioavailability (BA) study.

The Jatenzo clinical development program took more than 10 years to complete, and included phase 1, 2 and 3 studies. These studies involved extensive efficacy and safety testing. The program included a Phase 3, long-term safety extension study of up to 1 year's duration. CLAR-15012 was the third phase 3 efficacy and safety study for Jatenzo and was a clinical investigation that established the clinical safety and efficacy of Jatenzo, an oral testosterone product.

The primary objective of phase 3 clinical studies for new testosterone replacement therapies is to assess the safety and efficacy of these therapies when used for chronic testosterone replacement. For these studies, the primary efficacy endpoint is the proportion of treated subjects with a total testosterone (T) C_{avg} (time-averaged concentration) within the normal range after dose titration is complete and after a period of time on a stable dose. Success requires that at least 75% of subjects have a C_{avg} within the normal range, with the lower limit of the corresponding 95% confidence interval at least 65%.

This addendum explains that Study CLAR-15012 was a clinical study, other than a BA study because:

- The study used the standard primary efficacy endpoint described above to confirm the efficacy of Jatenzo as testosterone replacement therapy.
- Was a four-month, at-home, efficacy and safety study that included routine and special safety testing, including periodic 24-hour ambulatory blood pressure monitoring (ABPM) in most subjects and Cosyntropin (ACTH) stimulation testing in a subgroup of subjects.
- The determination is consistent with FDA's decision to recognize exclusivity for other testosterone replacement therapies that have received exclusivity in the past based on the same general study design (a phase 3 study with a primary efficacy endpoint of the proportion of treated subjects with a T C_{avg} within the normal range after dose titration was complete).
- CLAR-15012 was not intended to determine bioavailability as that had already been determined in previous phase 1 BA studies. The Applicant could not have conducted an additional BA study(ies) as a substitute for this four-month, at-home, safety and efficacy, dose-titration study.

- Although the Applicant may have described the study as a “PK efficacy” trial publicly, this has no bearing on whether study CLAR-15012 is a BA study or a clinical investigation.
- The description of Study CLAR-15012 in the 2nd Cycle Clinical Review as a “PK (efficacy)” study was subsequently corrected in the Final Cycle CDTL Review¹ in which the study was accurately described and identified as a clinical study.

¹ NDA 206089, Cross-Discipline Team Leader Memo (March 26, 2019), available at: https://darrts.fda.gov/darrts/faces/ViewDocument?documentId=090140af804e72c0&_afRedirect=383530386360122. The CDTL Memo notes that efficacy was measured using “FDA’s standard TRT benefit parameters (essentially, testosterone pharmacokinetic [PK] data).” Id. at 2. For the reasons described above, this parameter was a measure of Jatenzo’s efficacy, and the description as “PK data” should not be understood to mean that CLAR-15012 was viewed as a bioavailability study within the meaning of 21 CFR 314.108.

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/

JEANNIE M ROULE
08/06/2019 08:20:26 AM

HYLTON V JOFFE
08/06/2019 09:18:03 AM