CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

208745Orig1s000

CHEMISTRY REVIEW(S)

Memorandum

DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

Date: **January 11, 2017**
From: **Hitesh Shroff, Ph.D.**
Application Technical Lead, Branch V
Division of New Drug Products II
Office of New Drug Products

Through: **Moo-Jhong Rhee, Ph.D.**
Chief, Branch V
Division of New Drug Products II
Office of New Drug Products

To: **CMC Review #1 of NDA 208745**

Subject: Final Recommendation for NDA 208745

At the time when the CMC Review #1 was completed on October 6, 2016, it had noted the following pending issues:

- The label/labeling issues were not resolved.
- Final "Acceptable" recommendation from the Office of Process and Facilities was not issued.

Because of these deficiencies, the NDA was not recommended for approval from the OPQ perspective.

On October 11, 2016, the applicant submitted revised labeling. The CMC sections of the labeling were reviewed and found acceptable (**Attachment -1**).

On December 5, 2016, the Office of Process and Facilities issued the overall "Approval" recommendation for the facilities involved in this NDA (**Attachment – 2**).

Recommendation:
This NDA is now recommended for Approval from the OPQ perspective.

Application Technical Lead's Assessment and Signature

The NDA is recommended for Approval from quality perspective.

Hitesh Shroff, Ph.D.
Application Technical Lead, Branch V
Division of New Drug Products II

Hitesh N. Shroff -S
Digitally signed by Hitesh N. Shroff -S
DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, 0.9.2342.19200300.100.1.1=20[illegible]00348333, cn=Hitesh N. Shroff

Attachment 1:

Labeling:

Memorandum DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

Date: **October 18, 2016**

From: **Moo-Jhong Rhee, Ph.D.**
Chief, Branch V
Division of New Drug Products II
Office of New drug Products

Moojhong Rhee -S

Digitally signed by Moojhong Rhee -S
DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, cn=Moojhong Rhee -S, 0.9.2342.19200300.100.1.1=1300041261
Date: 2016.10.18 10:13:49 -04'00'

To: **Labeling Review #1 of NDA 208745**

Subject: **Final Recommendation**

The Labeling review #1 has noted the following two pending issues:

1. Manufacturer information [e.g., name and location of business (street address, city, state and zip code)] is required in labeling and should be located after **section 17,** Patient counseling information
2. "Do not remove the desiccant packet from the bottle" should be added in **section 16,** How Supplied/Storage and Handling.

And because of these deficiencies, in the Labeling Review #1, this NDA was not recommended for approval from the labeling perspective.

On October 11, 2016, the applicant amended the labeling and the above issues are satisfactorily resolved (see the **Attachment**).

Recommendation:

This NDA is **now** recommended for approval from the labeling perspective.

Attachment:

16 HOW SUPPLIED/STORAGE AND HANDLING

TRULANCE tablets are packaged in an aluminum foil unit dose blister pack of 30 in a child-resistant pack or in a white, opaque, high-density polyethylene round bottle with a screw-top polypropylene child-resistant cap and heat-activated induction seal. Each bottle container-closure system also contains a desiccant and a polyester coil.

TRULANCE 3 mg tablets are white to off-white, plain and round, debossed with "SP" on one side and "3" for 3 mg on the other side and supplied as:

NDC Number	Size
70194-203-30	Bottle of 30
70194-003-30	Aluminum foil unit dose blister pack of 30 in a child-resistant pack

Store at room temperature, 20 to 25°C (68 to 77°F); excursions permitted to 15 to 30°C (59 to 86°F) [see USP Controlled Room Temperature].

Keep TRULANCE in a dry place. Protect from moisture. For bottles, keep TRULANCE in the original bottle. Do not remove desiccant from the bottle. Do not subdivide or repackage.

PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Medication Guide).

Advise Patients:

Diarrhea

- To stop TRULANCE and contact their healthcare provider if they experience severe diarrhea *[see Warnings and Precautions (5.2)]*.

Accidental Ingestion

- Accidental ingestion of TRULANCE in children, especially in children less than 6 years of age, may result in severe diarrhea and dehydration. Instruct patients to take steps to store TRULANCE securely and out of reach of children and to dispose of unused TRULANCE *[see Contraindications (4), Warnings and Precautions (b) (4) 5.2)]*.

Administration and Handling Instructions

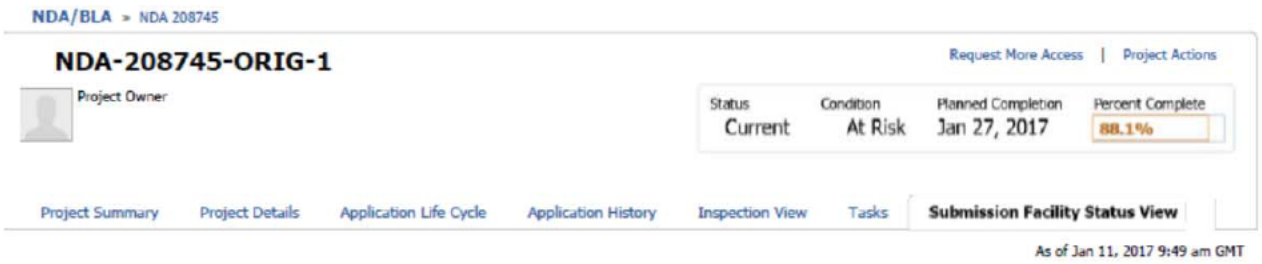
- To take TRULANCE once daily with or without food *[see Dosage and Administration (2)]*.
- If a dose is missed, skip the missed dose and take the next dose at the regular time. Do not take two doses at the same time.
- To swallow TRULANCE tablets whole.
- If adult patients have swallowing difficulties, TRULANCE tablets can be crushed and administered orally in either applesauce or with (b) (4) water or administered with water via a nasogastric or gastric feeding tube, as described in the Medication Guide.
- To keep TRULANCE in a dry place. Protect from moisture. For bottles, keep TRULANCE in the original bottle. Do not remove desiccant from the bottle. Do not subdivide or repackage. Remove and discard polyester coil after opening. Keep bottles closed tightly *[see How Supplied/Storage and Handling (16)]*.

TRULANCE™ is a trademark of Synergy Pharmaceuticals Inc.

Manufactured for:
Synergy Pharmaceuticals Inc.
420 Lexington Avenue, Suite 2012

Attachment 2:

Facilities:



Submission Overall Manufacturing Facility Status

Overall Status	Completion Date	Submission Status	Project Name
Approve	12/5/2016	Pending	NDA-208745-ORIG-1

Submission Manufacturing Facilities

Facility Status	Completion Date	Project Name	FEI	DUNS	Facility ID	Facility Name	Profile Code	As
Approve Facility	11/22/2016	NDA-208745-ORIG-1				(b) (4	(b) (4)	PEN
Approve Facility	10/2/2016	NDA-208745-ORIG-1						PEN
No Further Evaluation	10/2/2016	NDA-208745-ORIG-1					CTL CONTROL TESTING LABORATOR...	PEN
Approve Facility	10/2/2016	NDA-208745-ORIG-1					CTL CONTROL TESTING LABORATOR...	PEN
Approve Facility	10/2/2016	NDA-208745-ORIG-1					CTL CONTROL TESTING LABORATOR...	PEN
Approve Facility	10/2/2016	NDA-208745-ORIG-1					CTL CONTROL TESTING LABORATOR...	PEN
Approve Facility	10/2/2016	NDA-208745-ORIG-1					(b) (4)	PEN
Approve Facility	10/2/2016	NDA-208745-ORIG-1					CTL CONTROL TESTING LABORATOR...	PEN
Cancelled	5/8/2016	NDA-208745-ORIG-1					CTX CONTROL TESTING LABORATOR...	PEN
Approve Facility	3/8/2016	NDA-208745-ORIG-1					(b) (4)	PEN
Approve Facility	3/8/2016	NDA-208745-ORIG-1					TCM TABLETS, PROMPT RELEASE	PEN
Cancelled	3/8/2016	NDA-208745-ORIG-1					CTX CONTROL TESTING LABORATOR...	PEN
Cancelled	2/15/2016	NDA-208745-ORIG-1					CTX CONTROL TESTING LABORATOR...	PEN
Cancelled	2/15/2016	NDA-208745-ORIG-1					(b) (4)	PEN
Cancelled	2/2/2016	NDA-208745-ORIG-1					CTL CONTROL TESTING LABORATOR...	PEN

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