U.S. FOOD & DRUG ADMINISTRATION

Memorandum

DATE: November 9, 2020

TO: Rosa Sherafat-Kazemzadeh, MD,
CBER/OTAT/DCEPT

Candace Jarvis
CBER/OTAT/DRPM/RPMBII

FROM: Michael Brony, Pharm.D.
CBER/OCBQ/DCM/APLB

THROUGH: Lisa L. Stockbridge, Ph.D.
CBER/OCBQ/DCM/APLB

SUBJECT: Labeling Review
STRATAGRAFT [Skin Tissue]
BLA-125730/0
Sponsor: Stratatech Corp.

Background: The sponsor submitted:

__x__ New Approval
_____ Changes Being Effected (CBE) supplement
_____ Prior Approval Supplement (PAS) Amendment
_____ Major Amendment

Submission contains:
__X__ Prescribing Information (PI)
_____ Patient Package Insert (PPI)
__X__ Package and/or container labels
_____ Other (Medication Guide)

Submission Date: June 5, 2020
Action Due Date: February 2, 2021

APLB Comments/Recommendations

Stratatech Corp. submitted a Biologics License Application (BLA) for STRATAGRAFT [Skin Tissue], indicated for treatment of adult patients with deep partial thickness thermal burns, containing intact dermal elements for which surgical intervention is clinically indicated.

APLB has reviewed the draft PI and labels from a promotional and comprehension perspective and offer the following comments:

GENERAL COMMENTS

- Use command language wherever possible (e.g. DOSAGE AND ADMINISTRATION).
- Avoid vague terms with no established definitions or quantification.
    - Mild, moderate, severe
    - Well-tolerated
    - Rare
    - Use caution
- Avoid research terminology (e.g., Phase 1, 2, 3, pivotal), as not all end users are academic researchers. Simply describe the clinically significant data regarding safety and effectiveness.
- Only use bolding on headings and statements as required by the regulations. Overuse of bolding minimizes its importance. Subsection headings use title case and are not bolded.
- Remove all annotations and references to modules.
- The term “regenerative” appears throughout the PI. Is this a valid claim? If not, please delete all references to regeneration as this seems promotional.
- The proprietary name should be presented in all capital letters. Tall man lettering is discouraged and will not carry-over through all SPL stylesheets.
- Please replace the term, “Skin Tissue”, with the appropriate proper name.

HIGHLIGHTS

- Revise the indication to follow the regulatory format:

    [TRADENAME] is a [product class name] that is indicated for [indication(s)].

- Revise the DOSAGE AND ADMINISTRATION section to be in active voice. Specifically, you state:

    Tissues may be trimmed to accommodate the size and shape of the wound bed.

Revise to state:

Trim tissue to accommodate the size and shape of the wound bed.

- Ensure that the WARNINGS AND PRECAUTIONS reflect section 5 WARNINGS AND PRECAUTIONS of the FULL PRESCRIBING INFORMATION.

- In the ADVERSE REACTIONS section, delete the following sentence:

All adverse events related to StrataGraft skin tissue were mild or moderate in severity.

This sentence is promotional.

- Since this is a new application, please remove *Revised: [date].*

FULL PRESCRIBING INFORMATION: CONTENTS

Delete the period after the number 3 for DOSAGE FORMS AND STRENGTHS.

FULL PRESCRIBING INFORMATION (FPI)

2 DOSAGE AND ADMINISTRATION

- Immediately following the heading, DOSAGE AND ADMINISTRATION, please include the bolded, sentence case statement "**For topical application use only.**"

- For consistency with similar biologic product labeling, please organize this section into two or three subsections:

2.1 Dose
2.2 Administration

or

2.1 Dose
2.2 Preparation
2.3 Administration

- For readability and comprehension, revise this section to active voice. Provide clear and concise directions. Eliminate statements that are purely practice of medicine or attempts to limit the use of this product, which is not being provided under limited distribution.

- **Wound Preparation**

  Revise to state, "*Ensure clinically appropriate wound bed preparation (excise/debridement) prior to application*."

- Overuse of bolding minimizes its importance. Subsection headings use title case and are not bolded. We recommend, perhaps, underlining these subsections.

  STEP 4

  Revise to state, "*Place the StrataGraft Product Dish containing the tissue on a flat surface outside of the sterile field (Illustration K).*"

  Step 8

  Revise to state, "*Use Hold Solution, sterile 0.9% normal saline, or lactated Ringer's solution to moisten the mesher/tissue board as needed to prevent adhesion and maintain moisture."*

- **StrataGraft skin tissue Placement, Anchoring, and Dressing**

  STEP 1

  Revise to state, "*Use adhesive to anchor StrataGraft skin tissue*."

  Revise to state, "*Place the meshed StrataGraft skin tissue with the dermal (shiny) side down in contact with the patient's prepared wound bed. Ensure the epidermal (matte) side is facing up*."

  Note

  Revise to state, "*Ensure that StrataGraft skin tissue has contact across the entire surface of the wound bed*."

5 WARNINGS AND PRECAUTIONS

- List risks in decreasing order of severity and public health significance.

- The information in subsection **5.1 Infected Wounds and Unexcised Eschar**, appears to be practice of medicine and is not necessary. We recommend deleting this information.

6 ADVERSE REACTIONS

- Directly beneath the section heading restate the most common adverse reactions, along with a cut-off frequency, that is found in the HIGHLIGHTS.

- The statement, *"All adverse reactions were mild or moderate in severity*," is promotional and should be deleted.

8 USE IN SPECIFIC POPULATIONS

Revise the language used in subsection 8.4 to reflect the following required format:

> "The safety and effectiveness of [TRADENAME] have been established in the age groups X to Y [note any limitations]."

11 DESCRIPTION

Follow 21 CFR §201.57(c)(12) when revising this section. It should include the following

- Proprietary and proper name
- Pharmacologic or therapeutic class of the drug
- Type of dosage form and routes of administration
- Qualitative and/or quantitative ingredient information
    - Injectable products must include both qualitative (list of ingredients) and quantitative (amount) information (also see 21 CFR §610.60 and §610.61)
    - Injectable products must list inactive ingredients, except those to adjust pH
    - List inactive ingredients in alphabetical order

12 CLINICAL PHARMACOLOGY

Subsection 12.1 Mechanism of Action is promotional in tone. This subsection should summarize established mechanism(s) of action in humans and avoid speculation on mechanisms of action, as the latter is considered promotional.

13 NONCLINICAL TOXICOLOGY

The statement, "*The cellular components of StrataGraft skin tissue have been extensively tested for tumorgenicity*" is promotional in tone and should be revised. Please provide specifics about the data.

14 CLINICAL STUDIES

Do not bold headings for sub-subsections. Use italics and/or underlining if a sub-subsection heading is necessary.

PACKAGE/CONTAINER LABELS

General

- The proper name goes above the tradename, symmetrically arranged with respect to other printing on the label.

- The proper name should be printed in letters that are at least half as large as the letters of the proprietary name (21 CFR 201.10(g)(1) and (2); 202.1(b)(1) and (2)).

- The proprietary name and the proper name may not be separated by placement of intervening matter that, in any way, would detract, obfuscate, or de-emphasize the established name of the product, or obscure the relationship between the proprietary name and the proper name.

If you have any questions regarding this review please contact Michael Brony, Pharm.D. at 240-402-8898.