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September 27, 2019

Kristina Gregory
3025 Chemical Road
Plymouth Meeting, PA 19462
USA

Dear Ms. Gregory,

Please consider the following information.

Response(s):

- DARZALEX - NCCN Compendium Communication - CASSIOPEIA Approval - September 2019

I look forward to working with you as you consider the enclosed information. The information provided is not intended as an endorsement of any usage not contained in the Prescribing Information. For complete information, please refer to the full Prescribing Information, including the following sections: INDICATIONS AND USAGE, DOSAGE AND ADMINISTRATION, CONTRAINDICATIONS, WARNINGS AND PRECAUTIONS, and ADVERSE REACTIONS.

If you require further information, please feel free to contact me via the Janssen Medical Information Center at 1-800-JANSSEN (1-800-526-7736).

Sincerely,





Cynthia Toso, PharmD
Associate Director
Medical Information

Inquiry #:01509138

Enclosure(s)/Electronic Link(s):

- DARZALEX® (daratumumab) Prescribing Information at https://imedicalknowledge.veevavault.com/ui/approved_viewer?token=7994-dc33e1e3-dde0-4c18-b1e3-a3a79c07d600

Need Help? If you have any additional questions, please contact us via:

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DARZALEX® (daratumumab)
NCCN Compendium Communication – Product Update September 2019

September 27, 2019

Name: Cindy Toso, PharmD
Company/Organization: Janssen Biotech, Inc.
Address: 850 Ridgeview Drive Horsham, PA 19044
Phone: 215.325.4244
E-mail: ctoso@its.jnj.com
Date of request: September 27, 2019
NCCN Guidelines® Panel: Multiple Myeloma

Dear NCCN,

As a follow-up to our Janssen Biotech, Inc. submission on June 13, 2019, I respectfully request the NCCN Guidelines® Multiple Myeloma Panel review the enclosed FDA approved labeling for DARZALEX® (daratumumab), revised September 2019, and the provided summary of key changes.¹

Specific Change Requested: Recommend the inclusion of DARZALEX® in combination with bortezomib, thalidomide, and dexamethasone (D-VTd) for the treatment of patients with newly diagnosed multiple myeloma who are transplant eligible with a Category 1 evidence level rating. In addition, please align all related content currently in the NCCN Guidelines® Version 1.2020, NCCN Compendium®, NCCN Templates® and any other NCCN® publications or platforms with the current version of the DARZALEX® Prescribing Information, noting pertinent efficacy and safety updates related to the inclusion of CASSIOPEIA study data. Key changes to the DARZALEX® Prescribing Information are summarized on pages 3 and 4 of this communication.

FDA Clearance: On September 26, 2019, the FDA approved DARZALEX® for the treatment of adult patients with multiple myeloma in combination with bortezomib, thalidomide, and dexamethasone in newly diagnosed patients who are eligible for autologous stem cell transplant.¹

- This is in addition to previous FDA approved indications for DARZALEX® for the treatment of multiple myeloma: (1) in combination with lenalidomide and dexamethasone in newly diagnosed patients who are ineligible for autologous stem cell transplant and in patients with relapsed or refractory multiple myeloma who have received at least one prior therapy, (2) in combination with bortezomib, melphalan and prednisone in newly diagnosed patients who are ineligible for autologous stem cell transplant, (3) in combination with bortezomib and dexamethasone in patients who have received at least one prior therapy, (4) in combination with pomalidomide and dexamethasone in patients who have received at least two prior therapies including lenalidomide and a proteasome inhibitor (PI), and (5) as monotherapy, in patients who have received at least three prior lines of therapy including a PI and an immunomodulatory agent or who are double-refractory to a PI and an immunomodulatory agent.¹

Rationale: The FDA has approved DARZALEX® for the treatment of adult patients with multiple myeloma in combination with bortezomib, thalidomide, and dexamethasone in newly diagnosed patients who are eligible for autologous stem cell transplant. Complete efficacy and safety results have been published in *The Lancet* and the study publication was provided in our previous submission on June 13, 2019.²

Sincerely,

Cindy Toso, PharmD

Associate Director, Payer & Health Systems, Medical Information & Knowledge Integration
Janssen Scientific Affairs, LLC

REFERENCES

1. DARZALEX (daratumumab) [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc.; https://imedicalknowledge.veevavault.com/ui/approved_viewer?token=7994-da4865e5-0aec-46f4-9b62-41c098e1edfa
2. Moreau P, Attal M, Hulin C, et al. Bortezomib, thalidomide, and dexamethasone with or without daratumumab before and after autologous stem-cell transplantation for newly diagnosed multiple myeloma (CASSIOPEIA): a randomised, open-label, phase 3 study. [published online ahead of print June 2, 2019]. *Lancet*. doi:10.1016/S0140- 6736(19)31240-1.

DARZALEX® (daratumumab)
Compendia Communication – September 2019 USPI New Indication Update

SUMMARY

- The DARZALEX Prescribing Information was revised in September 2019.¹ In addition to the HIGHLIGHTS OF PRESCRIBING INFORMATION, the following sections of the Prescribing Information were revised:
 - Section 1: INDICATIONS AND USAGE
 - Section 2: DOSAGE AND ADMINISTRATION
 - Section 6: ADVERSE REACTIONS
 - Section 8: USE IN SPECIFIC POPULATIONS
 - Section 14: CLINICAL STUDIES
 - PATIENT INFORMATION
- This update incorporates a new indication for combination therapy with bortezomib, thalidomide, and dexamethasone for patients with newly diagnosed multiple myeloma eligible for autologous stem cell transplant (ASCT) and data from the related registrational study (CASSIOPEIA).
- For complete documentation of all changes please see the full DARZALEX Prescribing Information.
- Please ensure monograph alignment with the current DARZALEX Full Prescribing Information Version September 2019.

DARZALEX PRESCRIBING INFORMATION SEPTEMBER 2019 KEY CHANGES

INDICATIONS AND USAGE

- New indication for combination therapy with bortezomib, thalidomide, and dexamethasone for patients with newly diagnosed multiple myeloma eligible for ASCT added.

DOSAGE AND ADMINISTRATION

- Section 2.1 Recommended Dose and Schedule
 - New indication dosing incorporated for combination therapy with bortezomib, thalidomide, and dexamethasone for patients with newly diagnosed multiple myeloma eligible for ASCT.
 - Tables renumbered.

ADVERSE REACTIONS

- Section 6.1: Clinical Trials Experience
 - Second paragraph describing safety data updated.
 - Exposure data updated to 2066 patients with multiple myeloma including 1910 patients who received DARZALEX in combination with background regimens and 156 patients who received DARZALEX as monotherapy.
 - "Combination Treatment with Bortezomib, Thalidomide, and Dexamethasone (DVTd)" section added under "Newly Diagnosed Multiple Myeloma Eligible for Autologous Stem Cell Transplant" heading.
 - "Adverse Reactions Reported in ≥ 10% of Patients and With at Least a 5% Greater Frequency in the DVTd Arm in CASSIOPEIA" table added under "Combination Treatment with Bortezomib, Thalidomide, and Dexamethasone (DVTd)" heading.
 - "Treatment-Emergent Hematology Laboratory Abnormalities in CASSIOPEIA" table added under "Combination Treatment with Bortezomib, Thalidomide, and Dexamethasone (DVTd)" heading.
 - Tables renumbered.
 - Language describing clinical trials updated.

- "Infusion Reactions" section patient numbers, onset times, and language updated.
- Fourth paragraph added in "Infusion Reactions" section describing incidence upon re-initiation of DARZALEX after dose interruption in the setting of ASCT (Study CASSIOPEIA).
- "Infections" section percentages updated for DVTd and VTd in newly diagnosed patient studies.

USE IN SPECIFIC POPULATIONS

- Section 8.5 Geriatric Use
 - Patient numbers and percentages updated.

CLINICAL STUDIES

- Subsection added summarizing data from registrational study (CASSIOPEIA) supporting new indication for combination therapy with bortezomib, thalidomide, and dexamethasone for patients with newly diagnosed multiple myeloma eligible for ASCT.
 - 14.1 Newly Diagnosed Multiple Myeloma: Combination Treatment with Bortezomib, Thalidomide and Dexamethasone in Patients Eligible for Autologous Stem Cell Transplant
- Tables and figures renumbered throughout.
- "Efficacy Results from CASSIOPEIA at Day 100 Post-Transplant" table added under "Combination Treatment with Bortezomib, Thalidomide and Dexamethasone in Patients Eligible for Autologous Stem Cell Transplant" section.
- Language added describing efficacy results evaluated by stringent Complete Response (sCR) rate at day 100 post-transplant, Complete Response Rate (CR) at day 100 post-transplant, and Progression-Free Survival.
- "Kaplan-Meier Curve of PFS in CASSIOPEIA" added including language describing that treatment with DVTd resulted in a reduction in the risk of progression or death by 53% compared to VTd alone.

PATIENT INFORMATION

- Updated to include new indication for combination therapy with bortezomib, thalidomide, and dexamethasone for patients with newly diagnosed multiple myeloma eligible for autologous stem cell transplant (ASCT).

REFERENCE

1. DARZALEX (daratumumab) [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc.; https://imedicalknowledge.veevavault.com/ui/approved_viewer?token=7994-da4865e5-0aec-46f4-9b62-41c098e1edfa