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Considerations for the CLINICAL STUDIES Section of Labeling - 2017

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Disclaimer

- The views and opinions expressed in this presentation represent those of the presenter, and do not necessarily represent an official FDA position.
- The labeling examples in this presentation are provided only to demonstrate current labeling development challenges and should not be considered FDA recommended templates.
- Reference to any marketed products is for illustrative purposes only and does not constitute endorsement by the FDA.

CLINICAL STUDIES Section - To Improve Readability, Recommend (1 of 2):

- Use one statistical population for efficacy results
- Use mean or median (not both)
- Round when displaying treatment effects in percentages (if appropriate)
- Include results in a table or text (not both)

CLINICAL STUDIES Section - To Improve Readability, Recommend (2 of 2):

- Define terms not understood
- When subsection heading(s) are used, recommend not including information between Section 14 and subsection 14.1

For Complicated CLINICAL STUDIES Sections Consider Creating an Overview Subsection[1]

14 CLINICAL STUDIES

14.1 Description of Clinical Trials

The efficacy of VOSEVI was evaluated in two Phase 3 trials in DAA-experienced subjects with genotype 1, 2, 3, 4, 5, or 6 HCV infection without cirrhosis or with compensated cirrhosis, as summarized in Table 8.

Same primary endpoint

Sustained virologic response, defined as HCV RNA less than LLOQ at 12 weeks after the cessation of treatment, was the primary endpoint in both trials.

Table 8 Trials Conducted With VOSEVI in DAA-Experienced Subjects With HCV Infection

Trial	Population	Study Arms and Comparator Groups (Number of Subjects Treated)
POLARIS-1	Genotype 1, 2, 3, 4, 5, or 6 NS5A inhibitor-experienced[a], without cirrhosis or with compensated cirrhosis	VOSEVI 12 weeks (263) Placebo 12 weeks (152)
POLARIS-4	Genotype 1, 2, 3, or 4 DAA-experienced[b] who have not received an NS5A inhibitor, without cirrhosis or with compensated cirrhosis	VOSEVI 12 weeks (182) SOF/VEL 12 weeks (151)

Derived from FDA-approved PI for VOSEVI (7/18/2017) (slightly modified for presentation purposes)

CLINICAL STUDIES Section: Subsection Titles

- Bold font[1] and Title case[2]

- Title should reflect information within subsection
  - Instead of "**14.1 Monotherapy**"
  - State "**14.1 Monotherapy Use of DRUG-X in Patients with Disease-Y**"

- Avoid conclusions about results in title
  - Avoid "**Improvement in Mayo Score at 24 Weeks in Study 1**"

[1] 21 CFR 201.57(d)(1); [2] Clinical Studies Section of Labeling Guidance

CLINICAL STUDIES Section: Subsection Titles

14 CLINICAL STUDIES

- 14.1 Unresectable or Metastatic Melanoma
- 14.2 Metastatic Non-Small Cell Lung Cancer (NSCLC)
- 14.3 Renal Cell Carcinoma
- 14.4 Classical Hodgkin Lymphoma
- 14.5 Recurrent or Metastatic Squamous Cell Carcinoma of the Head and Neck (SCCHN)
- 14.6 Urothelial Carcinoma
- 14.7 Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient (dMMR) Metastatic Colorectal Cancer

CLINICAL STUDIES Section - Titles of Tables and Figures

Should include type of data, time point, patient population, and study name:[1]

Change in Bone Mineral Density from Baseline at Month 12 in Postmenopausal Women with Osteoporosis in Study 1

Type of data

Time point

Patient population

Study name

[1] Clinical Studies Section of Labeling guidance

Recommend Including NCT# in CLINICAL STUDIES Section

14 CLINICAL STUDIES

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MONARCH 2 (NCT02107703) was a randomized, placebo-controlled, multicenter study in women with HR-positive, HER2-negative metastatic breast cancer in combination with fulvestrant in patients with disease progression following endocrine therapy who had not received chemotherapy in the metastatic setting.


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Extra Slides: Additional Labeling Considerations

PI = prescribing information

Use of "Studies" vs. "Trials" in PI

- Regulations do not define the terms "studies" and "trials" for use in labeling
- Labeling regulations use these terms inconsistently
  - Title of Section 14 must be "CLINICAL STUDIES"[1]
  - Title of one of the Adverse Reaction subsections is "Clinical Trials Experience"[2]
  - INDICATIONS AND USAGE section regulations uses both terms (e.g., "short term trial" and "adequate and well-controlled studies")[3]
- Consider using a consistent use of scientifically appropriate terminology throughout PI

[1] 21 CFR 201.56(d) and 21 CFR 201.57(c)(15); [2] 21 CFR 201.57(c)(7)(ii)(A) [3] 21 CFR 201.57(c)(2)

Use of “Subjects” vs. “Patients” in PI

- Regulations do not define the terms “subjects” and “patients” for use in labeling
- Labeling regulations use these terms inconsistently. For example, in the Geriatric Use subsection[1] of the USE IN SPECIFIC POPULATIONS section both terms are used
- Consider using a consistent use of terminology throughout PI if scientifically appropriate

[1] 21 CFR 201.57(c)(9)(v)

Appropriate Units in PI

Recommend units in labeling are understood by U.S. healthcare providers. For example:

- Instead of LDL = 4.14 mmol/L
- Use LDL = 160 mg/dL