August 5th, 2020

Stephen Hahn, M.D.
Commissioner
Food and Drug Administration
U.S. Department of Health and Human Services
10903 New Hampshire Avenue
Silver Spring, MD 20993

Dear Commissioner Hahn,

Thank you for taking the time to consider our Citizen's Petition regarding a determination on class labeling for all currently approved Hedgehog inhibitors.

As dermatologists who specialize in cutaneous oncology and have conducted studies with hedgehog inhibitors, we recognize the advantages treatment with Hedgehog inhibitors provide patients with advanced basal cell carcinoma. However, we are concerned about the inconsistencies between the labels of the currently approved Hedgehog inhibitors. Vismodegib (Erivedge®, Genentech, South San Francisco, CA) received its FDA approval in 2012; since then, two additional Hedgehog inhibitors have been approved—sonidegib (Odomzo®, Sun Pharmaceutical Industries, Inc., Cranbury, NJ) and glasdegib (Daurismo™, Pfizer, Inc., New York, NY). The label for vismodegib acknowledges the high rate of muscle spasms but does not include monitoring requirements for creatinine kinase. The labels for sonidegib and glasdegib include information related to creatinine kinase monitoring due to additional information that became available post-approval for vismodegib.

In clinical practice, we have seen patients taking vismodegib and sonidegib experience muscle spasms and increased creatinine kinase levels. This is consistent with the published data

that supports a similar safety profile for all approved Hedgehog inhibitors. Based on our real-world experience, as well as the similar mechanism of action, all currently approved Hedgehog inhibitors should have the same warning regarding musculoskeletal adverse events and creatinine kinase level monitoring in their prescribing information.

The FDA has the authority to require additional measures and monitoring for class labeling when the agency "becomes aware of new safety information and makes a determination that such a strategy is necessary to ensure that the benefits of the drug outweigh the risks of the drug." Based on the information in the Citizen's Petition, we believe the same musculoskeletal and creatinine kinase level monitoring in the label for sonidegib and glasdegib should be included on the label for vismodegib.

Thank you for your time and consideration of our Citizen's Petition.

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