

Briefing on Proposed Draft Official Monograph “Eribulin Mesilate”

September 2019

Pharmaceuticals and Medical Devices Agency

Office of Review Management

Before publication of a proposed new official monograph draft “Eribulin Mesilate” for public consultation, the following information is provided for your review.

From the point of view of quality assurance, requirements that should be noted on manufacturing processes, if appropriate in addition to the specifications, are shown in the heading “Manufacture” in the Japanese Pharmacopoeia (JP) monograph (JP General Notice 12).

Because eribulin mesilate has 19 chiral carbons and complex structures, it is difficult to control all potential stereochemical isomers derived from these chiral carbons only by the final specification of API. Therefore, this monograph draft has stipulated the requirements on related substances including main potential stereochemical isomers as specifications of the starting materials and intermediates in the upstream process. These requirements have been shown in the heading “Manufacture”. Although eribulin mesilate is synthesized from the starting materials via many chemical reaction processes, this monograph has clarified the control strategy of the isomers derived from 19 chiral carbons by setting the specifications of the starting materials and control requirements of the intermediates.

As this monograph has described “When manufactured without reaction using the compounds 1 and 2, perform the control based on the control mentioned above.” in the heading “Manufacture”, the use of starting materials are not limited to Compound 1 and Compound 2 which are described in this monograph. However, in such case, please note that users for marketing this API in Japan should request the revision of this monograph so that the alternative control strategy can be applicable to eribulin mesilate. The alternative control strategy must be reviewed by the JP Expert Committee in the point of view of equivalency with that in this monograph.