Summary of Investigation Results
Gilteritinib fumarate

January 21, 2020

Non-proprietary name
Gilteritinib fumarate

Branded name (Marketing authorization holder)
Xospata Tablets 40 mg (Astellas Pharma Inc.)

Indications
Relapsed or refractory acute myeloid leukemia (AML) with a FLT3 mutation

Summary of consideration
The necessity of adding “differentiation syndrome” to the package insert was discussed.

Investigation results and background of the revision
Based on the results of their investigation of the currently available evidence and in consultation with expert advisors, MHLW/PMDA concluded that revision of the package insert at this time was not necessary considering the following:
1. Unlike the differentiation therapy for acute promyelocytic leukemia (APL), it is not clear whether gilteritinib fumarate induces leukemia cell differentiation or not.
2. Neither a clear definition nor diagnostic criteria are currently available of the “differentiation syndrome” as generally called specifically induced by gilteritinib fumarate.
3. Events that may be present in APL differentiation syndrome induced by differentiation therapy (such as renal disorder, pericardial effusion, and dyspnoea) have been already alerted in the current package insert of gilteritinib fumarate or for those not alerted, no
cases that support revision of the package insert at this time have been identified for any specific event.

**Number of cases and patient mortalities reported in Japan during the previous 3 fiscal years**

A total of 10 cases involving differentiation syndrome have been reported to date (A causal relationship with the drug and event could not be established in any of these cases.) No patient mortalities have been reported to date.

(Japanese market launch: December 2018)