



Summary of Investigation Results

Andexanet alfa (genetical recombination)

March 28, 2024

Non-proprietary name

Andexanet alfa (genetical recombination)

Brand name (marketing authorization holder)

Ondexxya for Intravenous Injection 200 mg (AstraZeneca K.K.)

Japanese market launch

May 2022

Indications

The reversal of the anticoagulant effect of a direct-acting factor Xa inhibitor (apixaban, rivaroxaban, or edoxaban tosilate hydrate) in patients experiencing life-threatening or uncontrolled bleeding

Summary of revisions

1. A cautionary statement regarding heparin resistance should be added to the IMPORTANT PRECAUTIONS section.
2. The Precautions for Co-administration (This drug should be administered with caution when co-administered with the following.) section should be newly added to the INTERACTIONS section, and “unfractionated heparin, low-molecular-weight heparin” should be added.
3. Language concerning heparin resistance in the Information Based on Clinical Use section of OTHER PRECAUTIONS should be deleted.

Investigation results and background of the revision

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Cases involving heparin resistance were evaluated. Cases for which a causal relationship between andexanet alfa (genetical recombination) and heparin resistance was reasonably possible have been reported. As a result of consultation with expert advisors regarding the causality assessment of the cases and the necessity of revision of PRECAUTIONS, the MHLW/PMDA concluded that revision of PRECAUTIONS was necessary.

Reference: Number of cases* and patient mortalities involving heparin resistance reported in Japan

A total of 15 cases have been reported to date (including 10 cases for which a causal relationship between the drug and event was reasonably possible).

A total of 4 patient mortalities have been reported to date. (A causal relationship between the drug and deaths subsequent to the event could not be established for any of these cases.)

*: The following cases were retrieved from the cases collected in the PMDA's database for adverse drug reactions, etc. report: Cases reported as an adverse drug reaction named "heparin resistance (PT)"; among the cases in which both andexanet alfa (genetical recombination) and heparin were administered to the same patient, cases occurred including episodes in the clinical course for which the possibility of heparin resistance could not be ruled out.

The expert advisors present at the Expert Discussion regarding the current investigation were nominated based on their conflict of interest declarations concerning the relevant products, pursuant to the "Rules for Convening Expert Discussions, etc., by the Pharmaceuticals and Medical Devices Agency" (PMDA Administrative Rule No. 20-8, dated December 25, 2008).