This English version is intended to be a reference material for the convenience of users. In the event of inconsistency between the Japanese original and this English translation, the former shall prevail.

Summary of Investigation Results

Denosumab (genetical recombination) (120 mg product)

March 19, 2019

Non-proprietary name

Denosumab (genetical recombination) (120 mg product)

Branded name (Marketing authorization holder)

Ranmark Subcutaneous Injection 120 mg (Daiichi Sankyo Co., Ltd.)

Indications

Bone lesion associated with multiple myeloma or with bone metastasis of solid carcinoma

Bone giant cell tumour

Summary of revisions

1. “Hypercalcaemia after discontinuation of denosumab treatment” should be added to the Clinically Significant Adverse Reactions section.
2. “Multiple vertebral fractures after discontinuation of denosumab treatment” should be added to the Clinically Significant Adverse Reactions section.

Investigation results and background of the revision

1. Cases of hypercalcaemia after discontinuation of denosumab treatment have been reported overseas (including cases reported during the previous 3 fiscal years). MHLW/PMDA concluded that revision of the package insert was necessary based on the results of their investigation of the currently available evidence and in consultation with expert advisors.
2. Results of a clinical study (D-CARE study) showed some cases of multiple vertebral fractures in the denosumab group after discontinuation of the treatment, whereas no

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cases were found in the placebo group. MHLW/PMDA concluded that revision of the package insert was necessary based on the results of their investigation of the currently available evidence and in consultation with expert advisors.

Number of adverse reactions and patient mortalities reported in Japan during the previous 3 fiscal years

1. 1 case involving hypercalcaemia after discontinuation of denosumab treatment has been reported to date (a causal relationship with the product could not be established in this case.) No patient mortalities have been reported to date.
2. No cases involving multiple vertebral fractures after discontinuation of denosumab treatment have been reported to date.