

## Summary of Investigation Results

### Ferric carboxymaltose, saccharated ferric oxide, and ferric derisomaltose

Non-proprietary name Brand name	Non-proprietary name	Brand name (marketing authorization holder)
	(1) Ferric carboxymaltose (2) Saccharated ferric oxide (3) Ferric derisomaltose	(1) Ferinject solution for injection/infusion 500mg (Zeria Pharmaceutical Co., Ltd.) (2) Fesin Intravenous Injection 40 mg (Nichi-Iko Pharmaceutical Co., Ltd.) (3) MonoVer for I.V. Injection 500 mg, 1000 mg (Nippon Shinyaku Co., Ltd.)
Japanese market launch	(1) Ferinject solution for injection/infusion 500mg: September 2020 (2) Fesin Intravenous Injection 40 mg: October 1961 (3) MonoVer for I.V. Injection 500 mg, 1000 mg: March 2023	
Indications	Iron deficiency anemia	
Summary of revisions	<p>(1)</p> <p>1. Precautions concerning "Hypophosphataemia, osteomalacia" should be added to the 8. IMPORTANT PRECAUTIONS section.</p> <p>2. "Hypophosphataemia, osteomalacia" should be added to the 11.1 Clinically Significant Adverse Reactions section in the 11. ADVERSE REACTIONS.</p> <p>(2)</p> <p>1. Precautions concerning "Hypophosphataemia, osteomalacia" should be added to the 8. IMPORTANT PRECAUTIONS section.</p> <p>2. The section of the 11.1.2 Osteomalacia in the 11.1 Clinically Significant Adverse Reactions in the 11. ADVERSE REACTIONS should be changed to "Hypophosphataemia, osteomalacia".</p> <p>(3)</p> <p>The necessity of adding precautions concerning "Hypophosphataemia, osteomalacia" to the 8. IMPORTANT PRECAUTIONS section and adding "Hypophosphatemia, osteomalacia" to the 11.1 Clinically Significant Adverse Reactions section in the 11. ADVERSE REACTIONS was evaluated.</p>	
Investigation results and background of the revision	Cases involving hypophosphataemia and osteomalacia were evaluated. Cases in which a causal relationship between ferric carboxymaltose or saccharated ferric oxide and hypophosphataemia or osteomalacia 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	

	<p>PRECAUTIONS, the MHLW/PMDA concluded that revision of PRECAUTIONS was necessary. On the other hand, for ferric derisomaltose, factors such as the accumulation status of cases in Japan and results of clinical studies at the time of application for approval were also considered, and as a result of consultation with expert advisors, the MHLW/PMDA concluded that revision of PRECAUTIONS was unnecessary at present.</p>
<p>Reference: Number of cases involving hypophosphataemia and osteomalacia reported in Japan</p>	<p>&lt; Hypophosphataemia &gt;<sup>*1</sup></p> <p>(1) A total of 61 cases have been reported to date (including 2 cases in which a causal relationship between the drug and the event was reasonably possible). No deaths have been reported to date.</p> <p>(2) A total of 56 cases<sup>*3</sup> have been reported to date. No deaths have been reported to date.</p> <p>(3) A total of 1 case<sup>*3</sup> has been reported to date. No deaths have been reported to date.</p> <p>&lt; Osteomalacia &gt;<sup>*2</sup></p> <p>(1) A total of 8 cases have been reported to date (including 2 cases in which a causal relationship between the drug and the event was reasonably possible). No deaths have been reported to date.</p> <p>(2) A total of 35 cases<sup>*3</sup> have been reported to date. No deaths have been reported to date.</p> <p>(3) A total of 0 cases have been reported to date.</p>

<sup>1</sup>: Cases collected in the PMDA's safety database for drugs

(Among cases reported with MedDRA PTs "Hypophosphataemia" or "Blood phosphorus decreased", the cases with events assessed as Grade 3 or higher according to CTCAE (ver. 6.0) were retrieved) and the cases submitted by the company.

<sup>2</sup>: Cases collected in the PMDA's safety database for drugs (cases reported with MedDRA PTs "Osteomalacia" or "Hypophosphataemic osteomalacia" are retrieved) and cases submitted by the company.

<sup>3</sup>: As this was an expected event, the possibility of a causal relationship between the drug and the event was not evaluated.

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).