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Summary of Investigation Results
Bisphosphonates
(preparations indicated for osteoporosis)

January 17, 2023

Non-proprietary name

See attachment.

Brand name (marketing authorization holder)

See attachment.

Japanese market launch

See attachment.

Indications

See attachment.

Summary of revisions

The results of a database study conducted in Japan should be added to the PRECAUTIONS CONCERNING PATIENTS WITH SPECIFIC BACKGROUNDS or Careful Administration section showing that among patients with renal impairment who used bisphosphonates for osteoporosis, particularly in those with severe renal impairment, an increased incidence of hypocalcaemia has been observed.

Investigation results and background of the revision

Based on the summary of the survey results using MID-NET® (Appendix), MHLW/PMDA determined that the incidence of hypocalcaemia may be increased when bisphosphonates are used in patients with osteoporosis complicated by renal impairment, especially in those with severe renal impairment, in consideration of the following:

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- In this study, a similar trend to the overall population was observed in the age category of patients under 65 years old, suggesting that an increased risk of hypocalcaemia is likely to be affected by the severity of renal impairment, regardless of age.
- In the analysis by ingredient, alendronate sodium hydrate, minodronic acid hydrate, and risedronate sodium all indicated similar trends to bisphosphonates as a whole, suggesting that the risk of hypocalcaemia in patients with renal impairment is common to all bisphosphonates.

As a result of consultation with expert advisors regarding the appropriateness of the above-mentioned PMDA's opinion and the necessity of revising the Precautions based on the opinion, MHLW/PMDA concluded that revision of Precautions for bisphosphonates indicated for osteoporosis was necessary.

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).

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Attachment

No.	Non-proprietary name	Brand name	Marketing authorization holder	Japanese market launch	Indications
a.	Alendronate sodium hydrate	a-1. Fosamac Tablets 5, 35 mg, and the others	Organon K.K., and the others	Tablets 5: August 2001 Tablets 35 mg: September 2006 Oral Jelly: March 2013 Bag for I.V. Infusion: May 2012	Osteoporosis
		a-2. Bonalon Tablet 5 mg, 35 mg, Bonalon Oral Jelly 35 mg, Bonalon Bag for I.V. Infusion 900 μg, and the others	Teijin Pharma Limited., and the others		
b.	Ibandronate sodium hydrate	b. Bonviva Tablets 100 mg, Bonviva Syringes for Intravenous Injection 1 mg, and the others	Chugai Pharmaceutical Co., Ltd., and the others	Tablets: April 2016 Syringes: August 2013	Osteoporosis
c.	Minodronic acid hydrate	c-1. Recalbon Tablets 1 mg, 50 mg, and the others	Ono Pharmaceutical Co., Ltd., and the others	Tablets 1 mg: April 2009 Tablets 50 mg: September 2011	Osteoporosis
		c-2. Bonoteo Tablets 1 mg, 50 mg, and the others	Astellas Pharma Inc., and the others		
d.	Sodium risedronate hydrate	d-1. Actonel Tablets 2.5 mg, 17.5 mg, 75 mg, and the others	EA Pharma Co., Ltd., and the others	Tablets 2.5 mg: May 2002 Tablets 17.5 mg: June 2007 Tablets 75 mg: February 2013	<Tablets 2.5 mg, 75 mg> Osteoporosis <Tablets 17.5 mg>
		d-2. Benet Tablets 2.5 mg, 17.5	Takeda Pharmaceutical		

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No.	Non-proprietary name	Brand name	Marketing authorization holder	Japanese market launch	Indications
		mg, 75 mg, and the others	Company Limited., and the others		・Osteoporosis ・Paget's disease of bone
e.	Etidronate disodium	e. Didronel Tablets 200	Sumitomo Pharma Co., Ltd.	November 1990	・Osteoporosis ・Prevention of heterotopic ossification in the early or advanced stages in the following conditions Post-spinal cord injury or post-hip arthroplasty ・Paget's disease of bone
f.	Zoledronic acid hydrate (indicated for osteoporosis)	f. Reclast for i.v. infusion 5 mg	Asahi Kasei Pharma Corporation	November 2016	Osteoporosis

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