Pharmaceuticals and Medical Devices Safety Information

No. 253 December 2008

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This *Pharmaceuticals and Medical Devices Safety Information (PMDSI)* is issued based on safety information collected by the Ministry of Health, Labour and Welfare. It is intended to facilitate safer use of pharmaceuticals and medical devices by healthcare providers. PMDSI is available on the Pharmaceuticals and Medical Devices Agency website (http://www.pmda.go.jp/english/index.html) and on the MHLW website (http://www.mhlw.go.jp/, Japanese only).

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Pharmaceuticals and Medical Devices Safety Information

No. 253 December 2008

Pharmaceutical and Food Safety Bureau, Ministry of Health, Labour and Welfare, Japan

[Outline of Information]

D: Distribution of Dear Healthcare Professional Letters *P*: Revision of PRECAUTIONS *C*: Case Reports

To Pharmaceuticals and Medical Devices Safety Management Supervisor
—Please use our e-mail alert service—

Pharmaceuticals and Medical Devices Agency is providing a "Pharmaceuticals and Medical Devices Information E-mail Alert Service" (http://www.info.pmda.go.jp/info/idx-push.html, Japanese only), when important safety information regarding pharmaceuticals and medical devices including Dear Healthcare Professional Letters or Revision of PRECAUTIONS is issued. You are encouraged to register to and use the service.

Reporting of safety information such as adverse reactions to the Minister of Health, Labour and Welfare is a duty of medical and pharmaceutical providers.

If medical and pharmaceutical providers such as physicians, dentists, and pharmacists detect adverse reactions, infections associated with drugs or medical devices, or medical device adverse events, they are obligated to report them to the Minister of Health, Labour and Welfare directly or through the marketing authorisation holder. As medical and pharmaceutical providers, drug retailers with a second-class license and household distributors are also required to report safety issues related to drugs and medical devices.

1

Revision of PRECAUTIONS

(No. 202)

(1) Drugs

This section presents details of revisions to the PRECAUTIONS section of package inserts and brand names of drugs that have been revised according to the Notifications dated October 24, 2008 and November 17, 2008.

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1 <Antiparkinsonian agents>

Amantadine Hydrochloride

[Brand Name] Symmetrel Fine Granules 10%, Symmetrel Tablets 50 mg and 100 mg (Novartis Pharma K.K.), and others

[Important Precautions] Use of this drug for "Improvement of hypobulia (abulia) and decreased initiative associated with Parkinson's syndrome or late effects of cerebral infarction" Aggravation of symptoms of Parkinson's disease, neuroleptic malignant syndrome, catatonia, confusion, disorientation, deterioration of mental status, and delirium may occur when the administration of this drug is suddenly stopped. The dose should be gradually decreased for discontinuation of administration.

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2 <Miscellaneous metabolism agents>

Everolimus

[Brand Name] Certican Tablets 0.25 mg, 0.5 mg, and 0.75 mg (Novartis Pharma K.K.)

[Adverse Reactions (clinically significant adverse reactions)] **Pericardial effusion:** Pericardial effusion may occur. Patients should be carefully monitored with electrocardiogram, echocardiography, and chest X-ray examination, etc. before initiating the administration. If any abnormalities are observed, appropriate measures, such as discontinuation of administration, should be taken.

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3 <Miscellaneous metabolism agents>

Ciclosporin (oral dosage form, injectable dosage form)

[Brand Name] Sandimmun Capsules 25 mg and 50 mg, Sandimmun for Internal Use, Sandimmun Injection, Neoral 10 mg, 25 mg, and 50 mg Capsules, Neoral for Internal Use (Novartis Pharma K.K.), and others

[Important Precautions] Central nervous system disorder may occur due to hypomagnesaemia. Caution should be exercised for serum magnesium levels especially immediately after a transplant. If decrease in magnesium levels is observed, appropriate measures, such as magnesium supply, should be taken.
Blood pressure increased, which may lead to reversible posterior leukoencephalopathy syndrome and hypertensive encephalopathy, may occur. Physicians should conduct periodical blood pressure measurement. If blood pressure increased is observed, appropriate measures, such as a treatment with an antihypertensive, should be taken.

[Adverse Reactions (clinically significant adverse reactions)]

Central nervous system disorder including reversible posterior leukoencephalopathy syndrome and hypertensive encephalopathy: Central nervous system disorder such as reversible posterior leukoencephalopathy syndrome and hypertensive encephalopathy may occur. If symptoms such as generalised convulsion, consciousness disturbed, disorientation, confusion, motor paralysis, cerebellar ataxia, visual disturbance, papilloedema, and sleep loss are observed, imaging diagnosis with CT and MRI should be performed, and administration should be decreased or discontinued, and appropriate measures, such as a control of blood pressure and administration of anticonvulsant, should be taken.

<Hormones-Miscellaneous>

4 Insulin Kit, Insulin Cartridge With a Part of Structure of Insulin Pen

[Brand Name]

Lantus Inj. SoloStar (sanofi-aventis K.K)
Humulin R Kit, Humulin N Kit, Humulin 3/7 Kit, Humalog Kit, Humalog Mix 25 Kit, Humalog Mix 50 Kit, Humalog N Kit, Humalog MirioPen, Humalog Mix 25 MirioPen, Humalog Mix 50 MirioPen, Humalog N MirioPen (Eli Lilly Japan K.K.)
InnoLet R for injection, InnoLet 10R, 20R, 30R, 40R, and 50R for injection, InnoLet N for injection, NovoRapid FlexPen, NovoRapid 30 Mix FlexPen, Novolin R FlexPen, Novolin 10R, 20R, 30R, 40R, and 50R FlexPen, Novolin N FlexPen, Levemir FlexPen (Novo Nordisk Pharma Ltd.)
Lantus Inj. OptiClik, Lantus Inj. Cart (sanofi-aventis K.K)
NovoRapid Penfill, NovoRapid 30 Mix Penfill, Penfill R, Penfill 10R and 20R 300, Penfill 30R, 40R, and 50R, Penfill N, Levemir Penfill (Novo Nordisk Pharma Ltd.)

[Precautions in Use]

This product should be used with Type A needles certified by JIS (Japanese Industrial Standards) T 3226-2. [This product is assured of compatibility with ○○○○.]
Instruct patients how to deal with events such as leakage occurring when a Type A needle was attached to this product. (eg. exchange for a new needle, etc.).

Note) The statement in [ ] is not essential but, if written, a brand name of Type A needle certified by JIS T 3226-2 should be filled in the part ○○○○.

(2) Medical Devices

This section presents details of revisions to the PRECAUTIONS section of package inserts and brand names of medical devices that have been revised according to the Notification dated November 17, 2008.

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1 Insulin Pen

[Brand Name]

OptiClik, and others (sanofi-aventis K.K)
HumaPen LUXURA (Eli Lilly Japan K.K.)
NovoPen 300, and others (Novo Nordisk Pharma Ltd.)

[Important Precautions]

This product should be used with Type A needles certified by JIS T 3226-2.
[This product is assured of compatibility with ○○○○.]
Instruct patients how to deal with events such as leakage occurring when a Type A needle was attached to this product. (eg. exchange for a new needle, etc.).

Note) The statement in [ ] is not essential but, if written, a brand name of Type A needle certified by JIS T 3226-2 should be filled in the part ○○○○.

2

List of products subject to Early Post-marketing Phase Vigilance

(As of December 1, 2008)

Nonproprietary name Brand name	Name of the marketing authorisation holder	Date of EPPV initiation
Tocilizumab (Genetical recombination) Actemra for Intravenous Infusion 200 mg[*1]	Chugai Pharmaceutical Co., Ltd.	April 16, 2008
Sitafloxacin Hydrate Gracevit Tablets 50 mg, Gracevit Fine Granules 10%	Daiichi Sankyo Co., Ltd.	June 2, 2008
Sunitinib Malate Sutent Capsule 12.5 mg	Pfizer Japan Inc.	June 13, 2008
Tocilizumab (Genetical recombination) Actemra for Intravenous Infusion 80 mg and 400 mg	Chugai Pharmaceutical Co., Ltd.	June 13, 2008
Deferasirox Exjade Dispersible Tablets 125 mg and 500 mg	Novartis Pharma K.K.	June 16, 2008
Adalimumab (Genetical recombination) Humira Subcutaneous Injection 40 mg Syringe 0.8 mL	Abbott Japan Co., Ltd.	June 18, 2008
Irbesartan Avapro Tablets 50 mg and 100 mg	Dainippon Sumitomo Pharma Co., Ltd.	July 1, 2008
Irbesartan Irbetan Tablets 50 mg and 100 mg	Shionogi & Co., Ltd.	July 1, 2008
Famciclovir Famvir Tab. 250 mg	Asahi Kasei Pharma Corporation	July 1, 2008
Raltegravir Potassium Isentress Tablets 400 mg	Banyu Pharmaceutical Co., Ltd.	July 7, 2008
Norethisterone/Ethinylestradiol Lunabell Tablets	Nobelpharma Co., Ltd.	July 8, 2008
Argatroban Hydrate Slonnon HI Injection 10 mg/2 mL[*2]	Daiichi Sankyo Co., Ltd.	July 16, 2008
Argatroban Hydrate Novastan HI inj. 10 mg/2 mL[*2]	Mitsubishi Tanabe Pharma Corporation	July 16, 2008
Sapropterin Hydrochloride Biopten Granules 2.5%[*3]	Asubio Pharma Co., Ltd.	July 16, 2008
Sodium Risedronate Hydrate Actonel Tab. 17.5 mg[*4]	Ajinomoto Co., Inc.	July 16, 2008
Sodium Risedronate Hydrate Benet Tablets 17.5 mg[*4]	Takeda Pharmaceutical Company Limited	July 16, 2008
Diazoxide Aroglycem Capsules 25 mg	Schering-Plough K.K.	July 22, 2008

Yttrium (^{90}Y) Ibritumomab Tiuxetan (Genetical recombination) Zevalin yttrium (^{90}Y) injection	Bayer Yakuhin, Ltd.	August 4, 2008
Indium (^{111}In) Ibritumomab Tiuxetan (Genetical recombination) Zevalin indium (^{111}In) injection	Bayer Yakuhin, Ltd.	August 4, 2008
Levobupivacaine Hydrochloride POPSCAINE 0.75% inj. 75 mg/10 mL, POPSCAINE 0.75% inj. 150 mg/20 mL, POPSCAINE 0.25% inj. 25 mg/10 mL, POPSCAINE 0.25% inj. bag 250 mg/100 mL, POPSCAINE 0.75% inj. syringe 75 mg/10 mL, POPSCAINE 0.25% inj. syringe 25 mg/10 mL	Maruishi Pharmaceutical Co., Ltd.	August 5, 2008
Estradiol Julina Tablets 0.5 mg	Bayer Yakuhin, Ltd.	September 16, 2008
Mometasone Furoate Hydrate Nasonex Nasal Solution 50 μg 56 metered spray	Schering-Plough K.K.	September 16, 2008
Cetuximab (Genetical recombination) Erbitux Injection 100 mg	Merck Serono Co., Ltd.	September 19, 2008
Tazobactam·Piperacillin Hydrate ZOSYN	Taiho Pharmaceutical Co., Ltd.	October 1, 2008
Neostigmine Methylsulfate·Atropine Sulfate Hydrate Atvago Reverse Intravenous Injection Syringe 3 mL and 6 mL	Terumo Corporation	October 1, 2008
Ramosetron Hydrochloride Irribow Tablets 2.5 μg and 5 μg	Astellas Pharma Inc.	October 7, 2008
Rifabutin MYCOBUTIN Capsules 150 mg	Pfizer Japan Inc.	October 7, 2008
Pegaptanib Sodium MACUGEN IVT Inj. KIT 0.3 mg	Pfizer Japan Inc.	October 14, 2008
Interferon Alfa (NAMALWA) Sumiferon 300 and 600, Sumiferon DS 300 and 600[*5]	Dainippon Sumitomo Pharma Co., Ltd.	October 16, 2008
Estradiol Julina Tablets 0.5 mg[*6]	Bayer Yakuhin, Ltd.	October 16, 2008
Freeze-dried Polyethylene Glycol Treated Human Normal Immunoglobulin kenketu glovenin-I-NICHIYAKU[*7]	Nihon Pharmaceutical Co., Ltd.	October 16, 2008
Ciclosporin Neoral Oral Solution, Neoral Capsules 10 mg, 25 mg, and 50 mg[*8]	Novartis Pharma K.K.	October 16, 2008
Somatropin (Genetical Recombination) Genotropin 5.3 mg, Genotropin MiniQuick s.c. inj. 0.6 mg, 1.0 mg, 1.4 mg, Genotropin Inj. 12 mg[*9]	Pfizer Japan Inc.	October 16, 2008
Bepridil Hydrochloride Hydrate Bepricor Tablets 50 mg and 100 mg[*10]	Schering-Plough K.K.	October 16, 2008
Adapalene Differin Gel 0.1%	Galderma Pharma S.A.	October 21, 2008
Tacrolimus Hydrate Graceptor Capsules 0.5 mg, 1 mg, and 5 mg	Astellas Pharma Inc.	October 28, 2008

Anti-human Thymocyte Immunoglobulin, Rabbit Thymoglobuline for Intravenous Infusion 25 mg	Genzyme Japan K.K.	November 28, 2008

*1: Additional indications for "rheumatoid arthritis (including prevention for structural damage of joints), polyarticular-course juvenile idiopathic arthritis, and systemic-onset juvenile idiopathic arthritis"

*2: An additional indication for "prophylaxis of thrombosis in patients with heparin-induced thrombocytopenia (HIT) type II"

*3: An additional indication for "reducing blood phenylalanine levels in patients with hyperphenylalaninemia (tetrahydrobiopterin-responsive hyperphenylalaninemia) due to tetrahydrobiopterin-responsive phenylalanine hydroxylase deficiency"

*4: An additional indication for "Paget disease of bone"

*5: An additional indication for "the improvement of viremia in compensated cirrhosis type C (except in the patients with HCV serogroup 1 and high blood HCV-RNA level)"

*6: An additional indication for "osteoporosis postmenopausal"

*7: An additional indication for "pemphigus (only for cases not adequately responsive to corticosteroids)"

*8: An additional indication for "dermatitis atopic (patients who are not adequately responsive to conventional therapies)"

*9: An additional indication for "SGA (Small-for-Gestational Age) dwarfism without epiphyseal closure"

*10: An additional indication for "sustained arterial fibrillation when other antiarrhythmic agents cannot be used or are ineffective"