Pharmaceuticals and Medical Devices Safety Information

No. 248 July 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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This translation of the original Japanese text is for information purpose only (in the event of inconsistency, the Japanese text shall prevail).

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No. 248 July 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

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. 198)

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 May 30 and June 16, 2008.

1 <Antiarrhythmic agents> Bepridil Hydrochloride

[Brand Name] Bepricor Tablets 50 mg and 100 mg (Schering-plough K.K.)

[Important Precautions] Interstitial pneumonia may occur during administration of this product (often within the first 4 months after the initiation of administration), leading to fatal conditions in some cases. Clinical symptoms should be closely monitored. Examinations such as a chest X-ray should be periodically performed.

[Adverse Reactions (clinically significant adverse reactions)]

QT prolongation, ventricular tachycardia (including Torsades de pointes), ventricular fibrillation, sinus arrest, atrioventricular block: QT prolongation, ventricular tachycardia (including Torsades de pointes), ventricular fibrillation, sinus arrest, atrioventricular block, Adams-Stokes syndrome may occur. An electrocardiogram should be performed periodically and on an as needed basis. If abnormal changes or symptoms are observed, administration should be discontinued and appropriate measures, such as intravenous administration of lidocaine, magnesium sulfate, isoproterenol, defibrillation and pacing, should be taken.

Interstitial pneumonia: Interstitial pneumonia, in some cases resulting in fatal outcomes, may occur. If pyrexia, cough, dyspnoea or abnormal chest sound (crepitations) etc. are noted, administration should be immediately discontinued, examinations such as a chest X-ray should be promptly conducted and appropriate measures such as administration of adrenal corticosteroids should be taken.

2 <Antineoplastics-Plant extract preparations> Irinotecan Hydrochloride

[Brand Name] CAMPTO 40 mg and 100 mg for I.V. infusion (Yakult Honsha Co., Ltd.)
TOPOTECIN INJECTION (Daiichi Sankyo Co., Ltd.)

[Important Precautions] The active metabolite SN-38 of irinotecan is metabolized predominantly by UDP-glucuronosyltransferase (UGT). It has been reported that patients known to be homogenous (UGT1A1＊6/＊6 or UGT1A1＊28/＊28) or heterozygous (UGT1A1＊6/＊28) in allele UGT1A1＊6, UGT1A1＊28 of UGT, may be at increased risk for serious adverse reactions (especially neutropenia,) caused by lower gluconization of UGT1A1 and slower metabolism of SN-38. Extreme caution should be exercised when administering in such patients.

2

List of products subject to Early Post-marketing Phase Vigilance

(As of July 1, 2008)

Nonproprietary name Brand name	Name of the marketing authorisation holder	Date of EPPV initiation
Dienogest Dinagest Tab. 1 mg	Mochida Pharmaceutical Co., Ltd.	January 21, 2008
Loratadine Claritin Dry Syrup 1%	Schering-Plough K.K.	January 21, 2008
Gadoxetate Sodium EOB·Primovist Inj. Syringe	Bayer Yakuhin, Ltd.	January 25, 2008
Cinacalcet Hydrochloride Regpara Tablets 25 mg and 75 mg	Kirin Pharma Company, Limited	January 25, 2008
Montelukast Sodium Kipres Tablets 10*[1]	Kyorin Pharmaceutical Co., Ltd.	January 25, 2008
Montelukast Sodium Singulair Tablets 10 mg*[1]	Banyu Pharmaceutical Co., Ltd.	January 25, 2008
Sorafenib Tosilate Nexavar 200 mg	Bayer Yakuhin, Ltd.	February 25, 2008
Galsulfase (Genetical recombination) Naglazyme for Intravenous Infusion 5 mg	AnGens MG, Inc.	April 14, 2008
Tocilizumab (Genetical recombination) Actemra 200 for Intravenous Infusion*[2]	Chugai Pharmaceutical Co., Ltd.	April 16, 2008
Sildenafil Citrate Revatio Tablets 20 mg	Pfizer Japan Inc.	April 18, 2008
Naratriptan Hydrochloride Amerge Tablets 2.5 mg	GlaxoSmithKline K.K.	April 18, 2008
Montelukast Sodium Kipres Tablets 5 mg	Kyorin Pharmaceutical Co., Ltd.	April 18, 2008
Montelukast Sodium Singulair Tablets 5 mg	Banyu Pharmaceutical Co., Ltd.	April 18, 2008
Zinc Acetate Dihydrate Nobelzin Capsules 25 mg and 50 mg	Nobelpharma Co., Ltd.	April 22, 2008
Blonanserin Lonasen Tablets 2 mg and 4 mg, Lonasen Powder 2%	Dainippon Sumitomo Pharma Co., Ltd.	April 22, 2008

Enoxaparin Sodium Clexane for Subcutaneous Injection Kit 2000 IU	Sanofi-Aventis K.K.	April 24, 2008
Varenicline Tartrate Champix Tablets 0.5 mg and 1 mg	Pfizer Japan Inc.	May 8, 2008
— Artcereb Irrigation and Perfusion Solution for Cerebrospinal Surgery	Otsuka Pharmaceutical Factory, Inc.	May 12, 2008
Thrombomodulin Alfa (Genetical recombination) Recomodulin Inj. 12800	Asahi Kasei Pharma Corporation	May 12, 2008
Human Serum Albumin (Genetical recombination) Medway Injection 25% and 5%	Mitsubishi Tanabe Pharma Corporation	May 19, 2008
Tacrolimus Hydrate Talymus Ophthalmic Suspension 0.1%	Senju Pharmaceutical Co.,Ltd.	May 20, 2008
Fondaparinux Sodium Arixtra Injection 1.5 mg and 2.5 mg *3	GlaxoSmithKline K.K.	May 20, 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

*1: An additional indication for “rhinitis allergic”
*2: Additional indications for “rheumatoid arthritis (including prevention for structural damage of joints), polyarticular-course juvenile idiopathic arthritis, and systemic-onset juvenile idiopathic arthritis”
*3: An additional indication for “prophylaxis of vein thromboembolism in patients undergoing abdominal surgery who are at risk for venous thromboembolism”