Pharmaceuticals and Medical Devices Safety Information

No. 246 May 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. 246 May 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. 196)

(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 Notification dated March 21, 2008.

<Pituitary hormone preparations>

1 Desmopressin Acetate (drug products with the indication for nocturnal enuresis)

[Brand Name] Desmopressin•Spray 10 Kyowa
(Kyowa Hakko Kogyo Co., Ltd.)

[Warning]

WARNING

There have been reports of convulsions due to serious hyponatraemia in patients treated with desmopressin acetate intranasal formulations for nocturnal enuresis. Patients and/or caregivers should be adequately informed and advised about possible water intoxication (hyponatraemia) and the need for careful control of fluid intake.

[Important Precautions] Symptoms of water intoxication may be induced during the treatment with this drug. Caution should be exercised for the following points.

(1) Avoid excessive fluid intake including that by instillation and fluid replacement.
(2) If the treatment with this drug is continued for a period of one week and more, tests of plasma osmolality and serum sodium should be conducted.
(3) Physicians should monitor patients' conditions periodically (monthly), and pay adequate attention to the symptoms that would suggest water intoxication (malaise, headache, nausea/vomiting, etc.) during the treatment with this drug.

Patients and/or caregivers should be adequately informed and advised about the following points to prevent possible water intoxication.

(1) Fluid intake should be avoided as much as possible from 2 to 3 hours before desmopressin administration (after dinner), until the next morning. In case of excessive fluid intake, avoid taking this drug. Particular care should be given to the patients with complications such as pyrexia and asthma associated with an increase in fluid intake.
(2) Be sure to urinate before bedtime. The instructed dosage should be strictly taken.
(3) If symptoms that would suggest water intoxication (malaise, headache, nausea/vomiting, etc.) occur, immediately discontinue administration and contact their physicians.
(4) If the patients are examined at another hospitals or departments, tell their physicians about taking this drug.

<Pituitary hormone preparations>

2 Desmopressin Acetate (drug products with the indication for central diabetes insipidus)

[Brand Name] Desmopressin Intranasal Kyowa, Desmopressin•Spray 2.5 Kyowa
(Kyowa Hakko Kogyo Co., Ltd.)

[Important Precautions] Patients and/or caregivers should be adequately informed and advised about the following points to prevent possible water intoxication.

(1) Instructions on the amounts of fluid intake, dosage and administration should be strictly followed.
(2) In case of excessive fluid intake, avoid taking this drug. Particular care should be given to the patients with complications such as pyrexia and asthma associated with an increase in fluid intake.
(3) If symptoms that would suggest water intoxication (malaise, headache, nausea/vomiting, etc.) occur, immediately discontinue administration and contact their physicians.
(4) If the patients are examined at another hospitals or departments, tell their physicians about taking this drug.

<Blood and body fluid agents-Miscellaneous>

3 Clopidogrel Sulfate

[Brand Name] Plavix Tablets 25 mg and 75 mg
(Sanofi-Aventis K.K)

[Adverse Reactions (clinically significant adverse reactions)] **Interstitial pneumonia:** Interstitial pneumonia may occur. Patients should be carefully monitored by chest X-rays, etc. If abnormalities are observed, administration should be discontinued, and appropriate measures should be taken.

<Acting mainly on gram-positive bacteria and gram-negative bacteria>

4 Biapenem

[Brand Name] Omegacin 0.3g for Intravenous Drip Infusion, Omegacin 0.3g Bag for Intravenous Drip Infusion
(Wyeth K.K.)

[Adverse Reactions (clinically significant adverse reactions)] **Agranulocytosis, pancytopenia, leucopenia, and thrombocytopenia:** Agranulocytosis, pancytopenia, leucopenia, and thrombocytopenia may occur. Patients should be carefully monitored through periodic blood testing etc. If abnormalities are observed, administration should be discontinued, and appropriate measures should be taken.

<Synthetic antibacterials>

5 Garenoxacin Mesilate Hydrate

[Brand Name] Geninax Tablets 200 mg
(Toyama Chemical Co., Ltd.)

[Adverse Reactions (clinically significant adverse reactions)] **Hypoglycaemia:** Hypoglycaemia may occur (particularly in the elderly and patients with diabetes mellitus). Patients should be carefully monitored. If abnormalities are observed, administration should be discontinued, and appropriate measures should be taken.

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(2) Medical Devices

This section presents details of revisions to the PRECAUTIONS section of package inserts of medical devices that have been revised according to the Notification dated February 27, 2008.

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1 Coronary Drug-Eluting Stent

① [Brand Name] Cypher Stent
(Johnson & Johnson K.K.)

[Warning]

WARNING

2) Compared to non-drug coated bare metal stents, the Cypher Stent requires a longer administration period of clopidogrel sulfate products or ticlopidine hydrochloride products as antiplatelet therapy following the stent placement. Use of this stent with clopidogrel sulfate products or ticlopidine hydrochloride products increases risks of bleeding and serious adverse reactions. Physicians should be encouraged to carefully select appropriate patients before using this stent by balancing risks and benefits for each patient. In the selection of patients, the location of the target lesion (blood vessel), reference vessel diameter, lesion length and its characteristics, and the size of the myocardial area exposed to the risk of acute or subacute thrombosis should be considered.

3) Before use of the Cypher Stent, physicians should adequately advise the patients of the risks associated with the antiplatelet therapy following the stent placement as well as the characteristics of the stent (risks and benefits) and ensure that the patient is fully aware of the information given before using. Physicians should adequately instruct the patients to contact the physician if ischemic symptoms such as chest pain appear after the stent placement. In particular, physicians should inform the patient of the possible occurrence of life-threatening serious adverse reactions associated with the administration of ticlopidine hydrochloride products, and give the following instructions. These instructions should also be considered at the administration of clopidogrel sulfate products.
   - ① In principle, the patient should consult a physician once every 2 weeks since periodical blood test is required for the first 2 months after the initiation of administration.
   - ② The patient should contact a physician, etc. immediately if symptoms that suggest any adverse reactions occur.

4) In using the Cypher Stent, proper antiplatelet and anticoagulant therapy as well as the periodical follow-up after the stent placement should be conducted. For antiplatelet therapy, in particular, caution should be exercised for the following points.
   - ① Premedicate the patient adequately beforehand so that full effect will be achieved at the time of stent placement.
   - ② Indefinite aspirin therapy and a postoperative regimen of clopidogrel sulfate products or ticlopidine hydrochloride products for a period of 3 months are recommended for the patients with the Cypher Stent placement. However, since late stent thrombosis developed over 1 year after stent placement has been reported, considerations to extend the administration period should be made depending on the conditions of the patients while observing the risks of adverse reactions such as bleeding.
   - ③ Safety of the Cypher Stent with antiplatelet therapy less than 2 months has not been established.
   - ④ Antiplatelet therapy/anticoagulant therapy following the stent placement with the Cypher Stent may result in bleeding/haematoma. Patients should be instructed to contact a physician if abnormal bleeding occurs. Patients should also be instructed to inform their physicians of their use of antiplatelet drugs if they receive medical consultation at other hospitals (departments).

⑤ The package inserts of antiplatelet drugs should surely be referred for each concomitant use.

Clinically significant adverse reactions such as thrombotic thrombocytopenic purpura (TTP), agranulocytosis, and serious liver disorder etc. may occur following administration of ticlopidine hydrochloride products. These symptoms have been reported to occur most commonly within 2 months after the initiation of administration, leading to fatal outcome in some cases. Physicians should prescribe the drug for 2 weeks at one time during the first 2 months after the initiation of the administration as a general rule and pay adequate attention to the following points. Also at the administration of clopidogrel sulfate products, attention should be paid to these points.

① For at least 2 months after initiating administration, physicians should be particularly alerted to the emergence of initial symptoms of the above mentioned adverse reactions. In principle, blood count (including differential leukocyte count) and hepatic function tests should be performed once every 2 weeks. If these adverse reactions are observed, administration should be discontinued and appropriate measures should be taken. Physicians should conduct periodical blood test during the treatment period with the product and be alerted to these adverse reactions.

② If thrombotic thrombocytopenic purpura (TTP), agranulocytosis, and liver disorder etc. are suspected from the conditions of the patient on medication with the product, physicians should conduct haemogram or liver function tests as necessary and take appropriate measures.

[Precautions]

(Number of reported cases of thrombosis for this stent in Japan collected in accordance with the conditions for approval was added.)

[Clinical Data]

(Results of clinical experience study in Japan and the latest data from results of foreign clinical trials for this stent were added. The study and clinical trials were conducted in accordance with the conditions for approval.)

② [Brand Name]

TAXUS Express2 Stent
(Boston Scientific Japan K.K.)

[Warning]

WARNING

2) Long-term prognosis for the period exceeding 1 year after the stent placement has not been sufficiently observed in Japanese healthcare environment at this point. Compared to non-drug coated bare metal stents, the TAXUS Express2 Stent requires a longer administration period of clopidogrel sulfate products or ticlopidine hydrochloride products as antiplatelet therapy following the stent placement. Use of this stent with clopidogrel sulfate products or ticlopidine hydrochloride products increases risks of bleeding and serious adverse reactions. Physicians should be encouraged to carefully select appropriate patients before using this stent by balancing risks and benefits for each patient. In the selection of patients, the location of the target lesion (blood vessel), reference vessel diameter, lesion length and its characteristics, and the size of the myocardial area exposed to the risk of acute or subacute thrombosis should be considered.

3) Before use of the TAXUS Express2 Stent, physicians should adequately advise the patients of the risks associated with the antiplatelet therapy following the stent placement as well as the characteristics of the stent (risks and benefits) and ensure that the patient is fully aware of the information given before using. Physicians should adequately instruct the patients to contact the physician if ischemic symptoms such as chest pain appear after the stent placement. In particular, physicians should inform the patient of the possible occurrence of life-threatening serious adverse reactions associated with the administration of ticlopidine hydrochloride products, and give the following instructions. These instructions should

also be considered at the administration of clopidogrel sulfate products.

① In principle, the patient should consult a physician once every 2 weeks since periodical blood test is required for the first 2 months after the initiation of administration.

② The patient should contact a physician, etc. immediately if symptoms that suggest any adverse reactions occur.

4) In using the TAXUS Express2 Stent, proper antiplatelet and anticoagulant therapy as well as periodical follow-up after the stent placement should be conducted. For antiplatelet therapy, in particular, caution should be exercised for the following points.

① Premedicate the patient adequately beforehand so that full effect will be achieved at the time of stent placement.

② Indefinite aspirin therapy and a postoperative regimen of clopidogrel sulfate products or ticlopidine hydrochloride products for a period of at least 6 months are recommended for the patients with the TAXUS Express2 Stent placement. However, since late stent thrombosis developed over 1 year after stent placement has been reported, considerations to extend the administration period should be made depending on the conditions of the patients while observing the risks of adverse reactions such as bleeding.

③ Safety of the TAXUS Express2 Stent with antiplatelet therapy less than 6 months has not been established. Moreover, the frequency and time of occurrence of thrombosis has not been determined in large-scale clinical studies in Japanese patients treated concurrently with the TAXUS Express2 Stent and clopidogrel sulfate products or ticlopidine hydrochloride products.

④ Antiplatelet therapy/anticoagulant therapy following the stent placement with the TAXUS Express2 Stent may result in bleeding/ haematoma. Patients should be instructed to contact a physician if abnormal bleeding occurs. Patients should also be instructed to inform their physicians of their use of antiplatelet drugs if they receive medical consultation at other hospitals (departments).

⑤ The package inserts of antiplatelet drugs should surely be referred for each concomitant use.

Clinically significant adverse reactions such as thrombotic thrombocytopenic purpura (TTP), agranulocytosis, and serious liver disorder etc. may occur following administration of ticlopidine hydrochloride products. These symptoms have been reported to occur most commonly within 2 months after the initiation of administration, leading to fatal outcome in some cases. Physicians should prescribe the drug for 2 weeks at one time during the first 2 months after the initiation of the administration as a general rule and pay adequate attention to the following points. Also at the administration of clopidogrel sulfate products, attention should be paid to these points.

① For at least 2 months after initiating administration, physicians should be particularly alerted to the emergence of initial symptoms of the above mentioned adverse reactions. In principle, blood count (including differential leukocyte count) and hepatic function tests should be performed once every 2 weeks. If these adverse reactions are observed, administration should be discontinued and appropriate measures should be taken. Physicians should conduct periodical blood test during the treatment period with the product and be alerted to these adverse reactions.

② If thrombotic thrombocytopenic purpura (TTP), agranulocytosis, and liver disorder etc. are suspected from the conditions of the patient on medication with the product, physicians should conduct haemogram or liver function tests as necessary and take appropriate measures.

[Clinical Data]

(The Latest data from results of foreign clinical trials for this stent conducted in accordance with the conditions for approval were added.)

2

List of products subject to Early Post-marketing Phase Vigilance

(As of May 1, 2008)

Nonproprietary name Brand name	Name of the marketing authorisation holder	Date of EPPV initiation
Eplerenone Selara Tablets 25 mg, 50 mg, and 100 mg	Pfizer Japan Inc.	November 13, 2007
Estradiol Divigel 1 mg	Pola Pharma Inc.	November 20, 2007
Imiquimod Beselna Cream 5%	Mochida Pharmaceutical Co., Ltd.	December 10, 2007
Darunavir Ethanolate Prezista Tablets 300 mg	Janssen Pharmaceutical K.K.	December 10, 2007
Insulin Detemir (Genetical recombination) Levemir 300, Levemir 300 FlexPen	Novo Nordisk Pharma Ltd.	December 14, 2007
Nelarabine Arranon G Injection 250 mg	GlaxoSmithKline K.K.	December 14, 2007
Erlotinib Hydrochloride Tarceva Tablets 25 mg, 100 mg, and 150 mg	Chugai Pharmaceutical Co., Ltd.	December 18, 2007
Methylphenidate Hydrochloride Concerta Tablets 18 mg and 27 mg	Janssen Pharmaceutical K.K.	December 19, 2007
Beraprost Sodium Careload LA Tablets 60 μg	Toray Industries, Inc.	December 19, 2007
Beraprost Sodium Berasus LA Tablets 60 μg	Kaken Pharmaceutical Co., Ltd.	December 19, 2007
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*[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	AnGes 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

*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”

Reference Material 1

Manuals for Management of Individual Serious Adverse Drug Reactions

The Manuals for Management of Individual Serious Adverse Drug Reactions have been presented in "Pharmaceuticals and Medical Devices Safety Information" No. 230 and No. 237. In March/April 2008, the third series of the manuals including "peptic ulcer" and "anaphylaxis", etc. have been finalized and are available at the MHLW website and pharmaceuticals and medical devices information website.
The manual names and common initial symptoms included in the Manuals for Management of Individual Serious Adverse Drug Reactions, presented above are shown in the **Table 1**, and the list of the manuals is shown in **Table 2**.
It is hoped that these manuals will be used by healthcare providers including physicians, dentists, and pharmacists as well as patients for achieving early recognition of and prompt response to serious adverse reactions.

Table 1 Manuals for Management of Individual Serious Adverse Drug Reactions released in March/April 2008

Manual name (adverse drug reaction)	Common initial symptoms
Drug-induced liver disorder	"Malaise", "Anorexia", "Pyrexia", "Jaundice", "Rash", "Feeling queasy/Vomiting", and "Itching"
Ileus paralytic	"Feeling of fullness in stomach", "Significant constipation", "Abdominal pain", "Feeling queasy", and "Vomiting"
Peptic ulcer	"Stomach feeling heavy", "Hyporexia", "Heartburn", "Feeling queasy", "Pain in stomach", "Fasting epigastric pain", "Black stools", and "Haematemesis"
Pseudomembranous colitis	"Frequent diarrhea", "Viscous stool", "Feeling of fullness in stomach", "Abdominal pain", "Pyrexia", and "Feeling queasy"
Neuroleptic malignant syndrome	"Hyperthermia of 37.5°C and above without certain cause", "Sweat", "Absentminded", "Tremulous limbs", "Rigidity bodily", "Difficulty in speaking", "Drooling", "Swallowing difficulty", "Pulse quickens", "Breathing rate increased", and "Blood pressure increased"
Anaphylaxis	Dermatological symptoms such as "Itchy skin", "Urticaria", and "Erythema/Skin red", gastrointestinal symptoms such as "Gastralgia" and "Feeling queasy", respiratory symptoms such as "Scratchy voice", "Sneezing", "Itchy throat", and "Respiratory discomfort", and "Abnormal vision"
Angiooedema	"Sudden swelling of lips, eyelids, tongue, mouth, face, and neck", "Throat obstruction", "Respiratory discomfort", and "Difficulty in speaking"
Laryngeal oedema	"Throat obstruction", "Respiratory discomfort", and "Whistling sound when inhale"
Urticaria/Angiooedema due to nonsteroidal anti-inflammatory drug	"Sudden swelling of lips, eyelids, tongue, mouth, face, and neck", "Throat obstruction", "Respiratory discomfort", and "Difficulty in speaking"

Table 2 Full list of the Manuals for Management of Individual Serious Adverse Drug Reactions (including those at drafting stage) (As of April 2008)

Field	Name of cooperating society	Subject adverse drug reaction
Dermatologicals	The Japanese Dermatological Association	○ Stevens-Johnson syndrome ○ Toxic epidermal necrosis ○ Drug-induced hypersensitivity syndrome Acute generalized exanthematous pustulosis Dermatitis contact
Hepatic	The Japan Society of Hepatology	○ Drug-induced hepatic disorder
Renal	The Japanese Society of Nephrology	○ Acute renal failure ○ Nephritis interstitial Nephrotic syndrome Pyelonephritis Nephrogenic diabetes insipidus Tumour lysis syndrome
Blood	The Japanese Society of Hematology	○ Aplastic anaemia ○ Bleeding tendency ○ Drug-induced anaemia ○ Agranulocytosis ○ Thrombocytopenia ○ Thrombosis ○ Disseminated intravascular coagulation Thrombotic thrombocytopenic purpura Heparin-induced thrombocytopenia
Respiratory system	The Japanese Respiratory Society	○ Interstitial pneumonia ○ Asthmatic attack due to nonsteroidal anti-inflammatory drug ○ Acute lung injury/Acute respiratory distress syndrome Pulmonary oedema Acute eosinophilic pneumonia Pulmonary alveolar haemorrhage Pleural effusion
Alimentary tract	The Japanese Society of Gastroenterology	○ Ileus paralytic ○ Peptic ulcer ○ Pseudomembranous colitis Pancreatitis (acute pancreatitis) Severe diarrhoea
Cardiovascular system	The Japanese Circulation Society	Ventricular tachycardia Cardiac failure congestive
Nervous and musculo-skeletal system	The Japanese Society of Neurology	○ Drug-induced parkinsonism ○ Rhabdomyolysis ○ Leukoencephalopathy Peripheral neuropathy Meningitis aseptic Acute disseminated encephalomyelitis Guillain-Barre syndrome Dyskinesia Convulsion/Epilepsy Ataxia Headache
Psychiatric	The Japanese Society of Clinical Neuropsychopharmacology	○ Neuroleptic malignant syndrome Drug-induced depression Akathisia Serotonin syndrome/Tremor
	The Japan Pediatric Society	Drug withdrawal syndrome neonatal

Field	Name of cooperating society	Subject adverse drug reaction
Metabolism and endocrine	The Japan Endocrine Society	○ Pseudoaldosteronism Hyperthyroidism Hypothyroidism
	The Japan Diabetes Society	Hypoglycaemia Hyperglycaemia
Hypersensitivity	The Japanese Society of Allergology	○ Anaphylaxis ○ Angioedema ○ Laryngeal oedema ○ Urticaria/Angiooedema due to nonsteroidal anti-inflammatory drug
Sensory organs (visual)	The Japanese Ophthalmological Society	Retinal disorder/Visual field defects Glaucomas
Oral cavity	The Japanese Society of Oral and Maxillofacial Surgeons	Drug-induced stomatitis Taste disturbance
Bones	The Japanese Society of Oral and Maxillofacial Surgeons	Osteonecrosis of the jaw
	The Japanese Orthopaedic Association	Osteoporosis
Urinary organs	The Japanese Urological Association	Urinary retention (dysuria) Cystitis haemorrhagic
Ovary	The Japan Society of Obstetrics and Gynecology	Ovarian hyperstimulation syndrome
Sensory organs (auditory)	The Oto-Rhino-Laryngological Society of Japan, Inc.	Deafness
Carcinoma	The Japan Society of Clinical Oncology	Palmar-plantar erythrodysaesthesia syndrome (hand and foot syndrome)

Note) Manuals marked with "○" are published.

Reference Material 2

Increasing the number of cooperating hospitals in the project for "Japan Drug Information Institute in Pregnancy"

The Japan drug information institute in pregnancy provides and coordinates teratology information service as described in "Pharmaceuticals and Medical Devices Safety Information" No. 235. From April 1, 2008, the institute has gained collaboration from six newly added cooperating hospitals (providing consultation using the documents prepared by the Japan drug information institute in pregnancy) to strengthen the system for consultation and collecting information regarding pregnancy and drugs for user's further convenience. Names of the cooperating hospitals are presented below.

[Information on "Japan Drug Information Institute in Pregnancy" and cooperating hospitals]

"Japan Drug Information Institute in Pregnancy" − Setagaya-ku, Tokyo
in National Center for Child Medical Health and Development (NCCHD)
URL: http://www.ncchd.go.jp/kusuri/index.html

(Cooperating hospitals) ○Joined since 2007 ◉Joined since 2008

◉ Hokkaido University Hospital − Sapporo-shi, Hokkaido

○ National Hospital Organization Sendai Medical Center − Sendai-shi, Miyagi
URL: http://www.snh.go.jp/Medicine/index.html

○ Tsukuba University Hospital − Tuskuba-shi, Ibaraki

○ Federation of National Public Service Personnel Mutual Aid Associations Toranomon Hospital − Minato-ku, Tokyo

○ St. Luke's International Hospital − Chuo-ku, Tokyo

◉ Japanese Red Cross Nagoya First Hospital − Nagoya-shi, Aichi

◉ National Hospital Organization Kanazawa Medical Center − Kanazawa-shi, Ishikawa

◉ Nara Medical University Hospital − Kashihara-shi, Nara

○ Osaka Medical Center and Research Institute for Maternal and Child Health − Izumi-shi, Osaka
URL: http://www.mch.pref.osaka.jp/osirase/ninshin/index.html

◉ Hiroshima University Hospital − Hiroshima-shi, Hiroshima

◉ Kyushu University Hospital − Fukuoka-shi, Fukuoka