Table of contents

Regulatory actions
Anticaries products - final monograph : USA 1
Bromocriptine : update 1
Australia 1
Brazil 1
Italy 2
Malaysia 2
Sri Lanka 2
Domperidone : Japan 2
Hydroxyquinolines : India 2
Ibopamine : Netherlands 2
Interferon alfa & interferon beta : Japan 2
Iodixanol and iotrolan 3
Isopropyl unoprostone : Japan 3
Naftidrofuryl : Germany 3
Pancreatins (high-dose) : UK 3
Phenylpropanolamine (PPA) : USA 4
Salicylamide : Malaysia 4
Drug surveillance
Measles rubella vaccine : UK 4
Mefenamic acid (syrup) : Japan 5
Mefloquine : Malaysia 5
New developments
New indications 6
New formulations 6
Newly approved products 6
Medical devices
Bovine collagen plug 8
Excimer laser system 9
Liver stent approved : USA 9
Pap screening system approved : USA 9
Retinal photic injuries & operating microscopes : USA 10
Veterinary medicine
Ceftiofur 10
Sarafloxacin 10

DRS/IES/96.4

The aim of this Newsletter is to disseminate information on the safety and efficacy of pharmaceutical products, based on information received from our network of "drug information officers" and other sources such as specialized bulletins and journals. The information is produced in the form of résumés in English, with translation of the titles in French and Spanish. Full texts may be obtained on request.

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Table des matières

Decisions réglementaires

Produits contre les caries – monographie finale pour les produits vendus en pharmacie : EUA 1

Bromocriptine – indications restreintes : mise à jour : Australie, Brésil, Italie, Malaysie, Sri Lanka 1

Dompéridone – fiche technique révisée : état de choc ou symptomes anaphylactoïdes : Japon 2

Hydroxyquinolines en combinaisons à dose fixe – prohibition : Inde 2

Ibopamine – indications restreintes : Pays Bas 2

Interféron alfa et interféron bêta – fiches techniques révisées : diabète sucré : Japon 2

Iodixanol et iotrolan – demande de documentation et suspension : hypersensitivité : Allemagne 3

Isopropyl unoprostone – fiche technique révisée: trouble de la cornée : Japon 3

Naftidrofuryl en infusion – révocation de l'approbation : Allemagne 3

Extraits pancréatiques à haute dose et la colonophathie fibrosante – recommandations d'utilisation : Royaume-Uni 3

Phenylpropanolamine (PPA) – réglementation proposée : avertissement sur l'étiquette : EUA 4

Salicylamide – homologation rejetée : Malaysie 4

Pharmacovigilance

Vaccin anti-rougeole/rubéole – revue des effets indésirables : Royaume-Uni 4

Acide méfénamique (sirop) – utilisation dans la persistence du *ductus arteriosus* du nouveau-né : Japon 5

Mefloquine – effets indésirables psychiatriques : Malaysie 5

Nouveautés

Nouvelles indications 6

Nouvelles formes 6

Produits récemment approuvés 6

Dispositifs à usage médical

Bouchon de collagen bovin – approuvé pour arrêter l'hémorrhagie : EUA 8

Systèmes de laser excimer – approuvés dans les troubles de la cornée : EUA 9

Extenseur (stent) hépatique – approuvé pour l'hémorrhagie répétitive : EUA 9

Système de sélection Pap – approuvé : EUA 9

Lésions rétinales photiques dues aux microscopes chirurgicales – rappel : EUA 10

Médecine vétérinaire

Ceftiofur – approuvé dans la pododermatite chez le bovin : EUA 10

Sarafloxacine – approuvée chez la dinde et le poulet à rôtir : EUA 10

Indice

Decisiones reglamentarias

Productos contra la caries – última monografía sobre los productos de venta libre : EE.UU 1
Bromocriptina – indicaciones restringidas : actualización : Australia, Brasil, Italia, Malasia, Sri Lanka 1
Domperidona – hoja de datos revisida : choque o síntomas de anafilaxis : Japón 2
Hidroxiquinolinas en combinaciones de dosis fija – prohibición : India 2
Ibopamina – indicaciones restringidas : Países Bajos 2
Interferón alfa e interferón beta – hojas de datos revisadas : diabetes mellitus : Japón 2
Iodixanol e iotrolán – petición de datos y suspensión : reacciones de hipersensibilidad : Alemanía 3
Unoprostona isopropílica – hoja de datos revisada : trastornos corneales : Japón 3
Naftidrofurilo – formulación para infusión : aprobación revocado : Alemania 3
Pancreatinas (dosis alta) y colonopatía fibrosante – recomendaciones sobre el uso : Reino Unido 3
Fenilpropanolamino (PPA) – norma propuesta : etiqueta de advertencia : EE.UU 4
Salicilamida – registro denegado : Malasia 4

Farmacovigilancia

Vacuna contra el sampión y la rubéola – análisis de las reacciones adversas : Reino Unido 4
Acido mefenámico (jarabe) – uso en casos de conducto arterioso permeable del recién nacido : Japón 5
Mefloquina – efectos adversos psiquiátricos : Malasia 5

Novedades

Nuevas indicaciones 6
Nuevas formulaciones 6
Productos recientemente aprobados 6

Dispositivos médicos

Tapón de colágeno bovino – aprobado para detener hemorragias : EE.UU 8
Systemas de laser excimer – aprobado para afecciones de la córnea : EE.UU 9
Stent hepático – aprobado para evitar recidivas hemorrágicos : EE.UU 9
Prueba de Papanicolau – sistema de cribado : aprobado : EE.UU 9
Lesiones fóticas retinianas causadas por microscopios operatorios – recordatorio : EE.UU 10

Médicina veterinaria

Ceftiofur – aprobado para el flemón interdigital del ganado : EE.UU 10
Sarafloxacin – aprobado para pavos y pollos parrilleros : EE.UU 10

Regulatory actions

Anticaries products – final monograph for over-the-counter products

United States of America. In the context of its ongoing review of over-the-counter drug products, the Food and Drug Administration has issued a final rule establishing the active ingredients that are considered safe for use in anticaries drug products.

The following products are acceptable:

- sodium fluoride

dentifrice (850 to 1,150 ppm total fluorine)

paste : 0.188% to 0.254% with ≥ 650 ppm available fluoride ion concentration;

powder : 0.188% to 0.254% with ≥ 850 ppm available fluoride ion concentration and poured bulk density of 1.0 to 1.2 g/ml;

rinse : 0.05%

rinse : 0.02%

rinse : acidulated phosphate fluoride with 0.02% fluoride ion

rinse : acidulated phosphate fluoride with 0.01% fluoride ion.

- sodium monofluorophosphate (850 to 1,150 ppm total fluorine) :

dentifrice : 0.654% to 0.884% with ≥ 800 ppm available fluoride ion as $PO_3F=$ and F- combined.

sodium monofluorophosphate (1,500 ppm total fluorine) :

dentifrice : 1.153% with ≥ 1,275 ppm available fluoride ion as $PO_3F=$ and F- combined.

-stannous fluoride :

dentifrice : (850 to 1,150 ppm total fluorine)

0.351% to 0.474% with an available fluoride ion concentration of:

. ≥700 ppm for products containing abrasive other than calcium pyrophosphate;

or

. ≥290 ppm for products containing the abrasive calcium pyrophosphate;

rinse : 0.1%

gel : 0.4% in an anhydrous glycerin gel.

The products listed below are not acceptable (those marked with an asterisk are, however, acceptable when used to prepare acidulated phosphate fluoride treatment rinses):

calcium sucrose phosphate
dicalcium phosphate dihydrate
disodium hydrogen phosphate*
phosphoric acid*
sodium dihydrogen phosphate
sodium dihydrogen phosphate monohydrate
sodium phosphate
sodium phosphate, dibasic anhydrous reagent*
sodium bicarbonate.

The directions for use have been revised to include the following : *"Instruct children under 12 years of age in the use of this product (to minimize swallowing). Supervise children as necessary until capable of using without supervision."*

The full text of this final rule is available on request.

Reference: Federal Register 60(194): 51474-52510 (1995).

Bromocriptine - restricted indications; update

Following reports of serious adverse reactions (including stroke, myocardial infarction and seizures) associated with the use of bromocriptine (Parlodel : Sandoz) in the inhibition of physiological lactation, several countries have taken restrictive measures. Résumés of these measures are given below:

Australia. The Australian Drug Evaluation Committee has recommended that the indications for bromocriptine should be tightened to exclude the suppression of established postpartum lactation and that bromocriptine should only be used to prevent the onset of lactation in the puerperium for clearly defined medical reasons (therapy should be continued for 14 days to prevent rebound lactation).

Reference: Gazettal Notice - Recommendations of the Australian Drug Evaluation Committee, 17 February 1995.

Brazil. The indication of bromocriptine as a suppressant of lactation has been abolished. *Reference:* Portaria SVS/MS No. 15 of 14 February 1996, Boletín SOBRAVIME 20, January-March 1996.

Italy. The Ministry of health has withdrawn the indication "inhibition of lactation" from products containing bromocriptine.

Reference: Gazzetta Ufficiale della Repubblica Italiana, 13 April 1995.

Malaysia. The Drug Control Authority has withdrawn the approval for the use of bromocriptine in the suppression of postpartum lactation since adverse reactions associated with the use of bromocriptine are considered to outweigh its marginal benefit.

Reference: Berita Ubat-Ubatan (Drug Information). Vol. 9, No. 3, p. 4, September 1995.

Sri Lanka. Bromocriptine is no longer indicated in the suppression of lactation.

Reference: The Sri Lanka Prescriber, Vol. 3, No. 3, September 1995.

[See also Pharmaceuticals Newsletter Nos. 5/6, May/June 1995: Canada]

Domperidone - revised data sheet : shock or anaphylactoid symptoms

Japan. The Pharmaceutical Affairs Bureau has revised the product information for the gastrointestinal motility agent, domperidone (Nauzelin : Kyowa Hakko, tablets, fine granules, dry syrup, suppositories) to include the precautionary statement that shock or anaphylactoid symptoms (rash, redness, dyspnoea, edema, labial edema, etc.) may occur. The patient should be kept under careful observation and the medication discontinued and appropriate measures instituted should any such symptoms appear.[1]

The injectable formulation of domperidone was already associated with such symptoms in the 1980s and was withdrawn in several countries. [See Monthly Mailing to Information Officers: Nos. 86/9 (Austria, Egypt), 85/11 (Japan), 85/9 (Belgium)]

Reference: 1) Information on Adverse Reactions to Drugs No. 134, November 1995, Pharmaceutical Affairs Bureau, Ministry of Health & Welfare, Tokyo.

Hydroxyquinolines in fixed-dose combinations - banned

India. The Drugs Controller has banned the manufacture, sale and distribution of fixed- dose combinations of hydroxyquinolines with other drugs, except for preparations intended for external use.

This action has been taken because the fixed-dose combination products are considered either as not having the therapeutic value claimed or purported to be claimed for them, or they contain ingredients and in quantities for which there is no therapeutic justification, thus posing a potential public health risk.

Reference: The Eastern Pharmacist, February 1996.

Ibopamine – restricted indications

Netherlands. The Committee for the Evaluation of Medicines has restricted the indications for the dopaminergic agent, ibopamine, after a recent international study was discontinued having shown results of higher mortality in the treated group than in the placebo group. Ibopamine was formerly indicated for mild cardiac insufficiency or moderate to severe cardiac insufficiency in combination with diuretics, ACE inhibitors or digoxin.

The approved indications are now: mild cardiac insufficiency in combination with diuretics. Treatment must be withdrawn gradually if the symptoms worsen.

Reference: Pharmaceutisch Weekblad 130(37/38): 999 (1995).

Interferon alfa and interferon beta – revised data sheets : diabetes mellitus

Japan. The Pharmaceutical Affairs Bureau has received 36 reports of cases of exacerbation of diabetes mellitus including 3 patients with diabetic coma and 25 cases of development of diabetes mellitus following treatment with interferon alfa or interferon beta.

The package insert already includes a caution against the potential risk of diabetes mellitus associated with interferons. The Bureau urges greater caution in the use of these products, and the product information has consequently been reinforced to state that patients receiving interferon alfa or interferon beta should be monitored periodically and blood and urine sugar tests carried out. If any abnormality is observed, appropriate measures should be taken.

Reference: Information on Adverse Reactions to Drugs No. 133, September 1995, Pharmaceutical Affairs Bureau, Ministry of Health & Welfare, Tokyo.

Iodixanol and iotrolan – call for data and suspension : hypersensitivity reactions

Germany. The Federal Institute for Drugs and Medical Devices has requested the manufacturer of the non-ionic contrast media, iodixanol (Visipaque, Schering) and iotrolan (Isovist 280, Schering), to provide additional data on adverse reactions to these products.

The Institute notes that an increased number of hypersensitivity reactions have been observed after the administration of iodixanol or iotrolan, some occurring several hours later. The main reactions were erythemas, itching, edematous swelling and urticaria. Occasionally swellings in the respiratory area and bronchospasms occurred and, in rare cases, hypotension. The delayed hypersensitivity reactions are usually not as severe as an anaphylactic reaction of the immediate type; however, they hold a serious risk for patients who may experience life-threatening situations at a time when they are no longer under medical supervision.

Pending the re-evaluation of these products, the manufacturer has temporarily suspended marketing of iotrolan (Isovist 280).

References:

1) Communication from the Federal Institute for Drugs and Medical Devices, Berlin, 28 November 1995.
2) Rapid Alert – Pharmacovigilance, Federal Institute for Drugs and Medical Devices, 13 October 1995.

Isopropyl unoprostone – revised data sheet : corneal disorder

Japan. The Pharmaceutical Affairs Bureau has received 5 reports of cases of corneal lesion associated with the use of the prostaglandin, isopropyl unoprostone, in ocular hypertension and glaucoma. The Bureau urges physicians to exercise caution in the use of isopropyl unoprostone, especially when co-administered with multiple eyedrop preparations, although the mechanism of this reaction remains unclear.

Reference: Information on Adverse Reactions to Drugs No. 133, September 1995, Pharmaceutical Affairs Bureau, Ministry of Health & Welfare, Tokyo.

Naftidrofuryl - infusion formulation : approval revoked

Germany. The Federal Institute for Drugs and Medical Devices has revoked the marketing approval for the injectable formulation of the vasodilator, naftidrofuryl (Praxilene : Lipha, 40 mg). This formulation was suspended in February 1995 after reports of two fatal cases of hypersensitivity reactions associated with its use. Subsequently cases of other serious adverse reactions were reported in other countries (including severe hepatic and cardiac reactions). [See also Pharmaceuticals Newsletters No. 4, April 1995, and No. 10, October 1995).

Reference: Pharmazeutische Zeitung 141(6): 432 (1996).

Pancreatins (high dose) and fibrosing colonopathy – recommendations on use

United Kingdom. Following reports of fibrosing colonopathy (bowel strictures) in 13 children between 2 and 13 years of age with cystic fibrosis who were receiving high-strength pancreatic enzyme supplements, the Committee on Safety of Medicines established a Working Party to review all the available information. Based on their findings, the Committee has made the following recommendations:

- Three formulations of high-strength pancreatic enzymes should not be used in children aged 15 years or less with cystic fibrosis (Pancreas HL, Nutrizym 22 and Panzytrat 25,000).
- The total dose of pancreatic enzyme supplements used in patients with cystic fibrosis should not usually exceed 10,000 units of lipase per kg body weight per day.
- If a patient receiving any pancreatin preparation develops abdominal symptoms that are new to the patient or any change in existing abdominal symptoms, they should be reviewed to exclude the possibility of colonic damage. [See also Pharmaceuticals Newsletters No. 2, February 1995, No. 10, October 1994, No.4, April 1994]

Reference: Current Problems in Pharmacovigilance Vol. 21, November 1995.

Phenylpropanolamine (PPA) - proposed rule : warning label

United States of America. The Food and Drug Administration has proposed new warning labelling for all

over-the-counter (OTC) drugs that contain phenylpropanolamine (PPA). The warnings will advise consumers not to take a PPA-containing drug with any other product that contains PPA, phenylephrine, pseudoephedrine or ephedrine. The proposed labelling will also require that PPA-containing weight control products be used by adults only (i.e. over 18 years of age).

Since PPA is an ingredient not only in OTC weight control products, but also cough-cold, allergy and nasal decongestant remedies, the FDA is concerned that taking more than the recommended dose may pose a risk to health. Some data indicate that PPA in OTC drugs may increase the risk of haemorrhagic stroke.

Haemorrhagic stroke differs from ischaemic stroke in that it results from bleeding into the brain, whereas ischaemic stroke results from a blood vessel blockage that impairs the blood flow to the brain. Although, to date, there is no evidence of a definite link between using OTC products containing PPA and haemorrhagic stroke, the agency is awaiting further data from an industry-sponsored safety study on PPA.

In the interim, the agency believes that warnings on the safe use of these products are required.

In reviewing all available information, it appears that the possible risk posed by PPA may be enhanced when consumers inadvertently exceed normal doses either by consuming more than the recommended dose or by simultaneously taking the drug in other products labelled for different uses. PPA affects the central nervous system and should not be taken with other products that have similar effects on the body. PPA also interacts with monoamine oxidase inhibitor antidepressants, inducing potentially life-threatening adverse effects. In addition, persons with high blood pressure, diabetes, heart or thyroid disease should not use PPA without consulting a doctor.

References:
1) FDA Talk Paper, dated 14 February 1996.
2) Federal Register 61(31) : 5912-5916 (1996).

Salicylamide – psychiatric adverse effects

Malaysia. The Drug Control Authority has rejected an application for registration of products containing salicylamide because of limited proof of the effectiveness of salicylamide when used as a sole ingredient or as an adjuvant in analgesic or antipyretic preparations.

Manufacturers were given six months in which to remove the products concerned from the market.

Reference: Berita Ubat-Ubatan (Drug Information) Vol. 9, No.3, p.4, September 1995.

Drug surveillance

Measles rubella vaccine – review of adverse reactions

United Kingdom. The Committee on Safety of Medicines has reviewed reports of adverse reactions to measles rubella vaccine after the 1994-95 vaccination campaign (8 million children were vaccinated).

The estimated reporting frequency was 1 per 6,700 children immunized and the most frequent adverse reactions reported are summarized below:

Cardiovascular	5%
Immunological	4%
Gastrointestinal	11%
Musculoskeletal	4%
Neurological (including syncope)	17%
Respiratory	6%
Skin (including allergic rash)	24%
General symptoms and signs	21%
Miscellaneous	8%

There were 91 reports of serious neurological reactions which are detailed in the table below:

Serious reactions	No. of reports	Reporting rate
Encephalitis	11	1 in 730,000
Subacute sclerosing panencephalitis (SSPE)	1	1 in 8,000,000
Convulsions (within first hour of immunization)	29	1 in 280,000
Convulsions (1-24 hours)	8	)1 in
(>24 hours)	24	)250,000
Optic neuritis	5	1 in 1,600,000
Guillain-Barré syndrome	3	1 in 2,500,000
Facial palsy	7	1 in 1,000,000
Miscellaneous neuropathies	3	–

Most reactions were minor and self- limiting. 530 children had a serious reaction (0.007%) and none had a fatal outcome. Most children recovered completely.

The immunization campaign successfully prevented an expected epidemic of measles during which it was predicted there would be approximately 150,000 cases of measles, with an estimated 50 fatalities.

Reference: Current Problems in Pharmacovigilance Vol. 21, November 1995, Committee on Safety of Medicine, London.

Mefenamic acid (syrup) - use in neonatal patent ductus arteriosus

Japan. Mefenamic acid (syrup) is indicated for the relief of fever and pain in acute upper respiratory tract inflammation (including acute bronchitis). The drug is also prescribed for patent ductus arteriosus in extremely premature infants, although this is not an approved indication in Japan. Intravenous administration of indometacin is the approved treatment for this anomaly, or surgical correction by ligation of the ductus arteriosus in refractory cases.

Seven cases involving infants have been reported in which serious clinical manifestations occurred (acute renal failure in one case and necrotizing enterocolitis in 6 cases) following administration of mefenamic acid for this purpose, four of which resulted in death. Duration of treatment was 1-2 days and signs of adverse events emerged 2-13 days after the start of medication. It remains uncertain whether necrotizing enterocolitis was due to extreme prematurity of the infants or to intestinal ischaemia arising from patent ductus arteriosus.

Reference: Information on Adverse Reactions to Drugs No. 134, November 1995, Pharmaceutical Affairs Bureau, Ministry of Health & Welfare, Tokyo.

Mefloquine – psychiatric adverse effects

Malaysia. The Adverse Drug Reactions Advisory Committee reports a case of a 21-year old white male patient who was admitted to hospital in a stuporous state. He was conscious, staring blankly ahead with no eye contact, no motor or verbal response. There was no focal neurological deficit. The patient had no evidence of external injury or trauma, except for a few abrasions over both feet. CT scan of the brain and EEG were normal, as were other systems.

At the time of admission, no information on the patient's background or past history was available. His condition was initially thought to be due to drug overdose. However, naloxone 4 mg (intravenous) did not produce any response. The patient's serum was negative for salicylates, opiates and cannabis.

After 9 days, he started to come out of his stuporous state and from then on continued to show improvement. It was later revealed that he had been taking oral mefloquine for malaria prophylaxis for the previous six months. He had no history of psychiatric illness. [See also Pharmaceuticals Newsletter Nos. 11/12, November 1994 and Alert No. 2, 8 August 1989]

Reference: Berita Ubat-Ubatan (Drug Information) Vol. 9, No.3, p.9, September 1995.

New developments

New indications

diltiazem

Tildiem LA, Lorex Synthélabo, : UK
capsules 200 mg (new strength), 300 mg
calcium channel blocker
New indications: Angina pectoris.

ofloxacin

Oflocin, Janssen-Cilag : Australia
tablets 100, 200 mg
quinolone antibacterial agent
New indications: Acute exacerbation of chronic bronchitis due to *Haemophilus influenzae* and pneumonia due to *Streptococcus pneumoniae*.

paclitaxel

Taxol, Bristol-Myers Squibb : UK
concentrate for infusion 30 mg/5 ml vial
(6 mg/ml)
antineoplastic
Extended indications: Treatment of metastasized breast carcinoma unresponsive to standard anthracycline therapy or in patients for whom anthracycline therapy is not indicated.

New formulations

clarithromycin

Klacid, Abbott : Australia
New formulation: paediatric granules for reconstitution 125 mg/5 ml, 250 mg/5 ml
macrolide antibiotic
New indications: Acute streptococcal pharyngitis and tonsillitis caused by *Streptococcus pyogenes*; skin and skin structure infections (including impetigo); acute otitis media (penicillins remain the drugs of first choice); disseminated or localized infections due to *Mycobacterium avium* or *M.intracellulare* in immunocompromised children, including those with HIV infection; community- acquired pneumonia including infections due to *Chlamydia pneumoniae*, *Mycoplasma pneumoniae* and *Legionella pneumophila*.

granisetron

Kytril, Smithkline Beecham : UK
New formulation: solution for injection 1 mg/vial
antiemetic serotonin antagonist
New indications: Postoperative nausea and vomiting; and cytostatic-induced nausea and vomiting in children.

felodipine

Munobal, Astra : Germany
New formulation: slow release tablet 5 mg
calcium-channel antagonist
Indications: Hypertension.

nedocromil

Tilarin, Fisons : UK
New formulation: nasal spray 1%
antiallergic
Indications: Prophylactic treatment of seasonal allergic rhinitis and treatment of symptoms, including rhinorrhoea and sneezing.

Newly approved products

acamprosate calcium

Campral, Lipha : Germany, UK
coated tablet 333 mg
psychotherapeutic agent

Indications: Alcohol withdrawal.

**alendronic acid*
Fosamax. Merck Sharp & Dohme : Finland, Iceland, Switzerland, UK; Fosamax. Merck & Co. : USA
tablet 10 mg
biphosphonate
Indications: Treatment of osteoporosis in postmenopausal women.

**cilnidipine*
Cinalong, Fujirebio; Atelec, Ajinomoto; Siscard, Nippon Boehringer Ingelheim : Japan
tablet 5, 10 mg
calcium channel blocker
Indications: Hypertension.
Contraindications & Precautions: As for other drugs of this class.

**cisatracurium besilate*
Nimbex, Glaxo Wellcome : Netherlands;
Nimbex, Wellcome : UK
solution for injection 2 mg/ml,
5 mg/ml
non-depolarising muscle relaxant
Indications: Skeletal muscle paralysis; to facilitate intubation.

citalopram
Cipramil, Lundbeck : UK
tablet 10, 20, 40 mg
antidepressant
Indications: Depression.

docetaxel
Taxotere, Rhone-Poulenc Rorer : UK, USA
concentrate for infusion 20, 80 mg
antineoplastic agent
Indications: Monotherapy for locally advanced or metastatic breast cancer in patients who are resistant or have recurrent disease after a cytotoxic therapy or who have relapsed during adjuvant cytotoxic therapy (including an anthracycline).

famciclovir
Famvir, Smithkline Beecham : Netherlands
tablet 250 mg
antiviral agent
Indications: Dermal herpes infections due to varicella zoster in immunocompetent patients when severe complications are anticipated; genital herpes in immunocompetent patients.

ferristene
Abdoscan, Nycomed : Germany, Netherlands
dynosphere granules corresponding to 23.4 mg
Fe/dose (sachets 100 mg/6 g)
contrast medium
Indications: Magnetic resonance imaging of the abdomen.

ferumoxside
Endorem, Guerbet : UK
suspension for injection 86.9 mg
diagnostic aid (iron oxide nanoparticles consisting of colloidal particles of nonstoichiometric magnetite)
Indications: Detection of focal liver lesions by magnetic resonance imaging.

follitropin alfa
Gonal-F, Serono : EU, UK
powder for injection 75, 150 IU

follicle stimulating hormone
Indications: Superovulation for assisted reproduction technologies.

formoterol
Foradil, Ciba-Geigy : UK
capsule 12 µg
β-adrenoreceptor agonist
Indications: Prevention of airways obstruction (including nocturnal asthma) and prevention of exercise-induced bronchospasm in patients requiring long-term regular bronchodilator therapy. Such patients should normally also be receiving regular and adequate doses of inhaled anti-inflammatory agents or oral corticosteroids.

galactose
Echovist, Schering : UK
granules for reconstitution (microparticles) 200,1,000 mg/ml
contrast medium
Indications: Contrast medium for ultrasound imaging of the female genital tract.

galactose + palmitic acid
Levovist, Schering : Germany
granules for reconstitution (microparticles) 999 mg galactose + 1 mg palmitic acid
contrast medium
Indications: Sonography of blood flow in patients with heart disease, peripheral artery and vein disease; and in patients with tumours to determine the extent of vascularization.
Contraindications: Galactosaemia.

gemcitabine
Gemzar, Lilly : Germany, UK
powder for injection 200 mg, 1 g
antineoplastic agent
Indications: Germany: Advanced adenocarcinoma or cystadenocarcinoma of the exocrine pancreas. *UK:* Non-small cell lung carcinoma.

interferon beta-1b
Betaferon, Schering : Australia
solution for injection 9.6 million IU (0.3 mg) in 3 ml glass vials
human fibroblast interferon
Indications: Relapsing-remitting multiple sclerosis.

**ioxilan*
Imagenil, Chugai : Japan
solution for intra-arterial or intravenous injection 623.4 mg/ml (300 mg I/ml), 727.3 mg/ml (350 mg I/ml),
contrast agent
Indications: 300: cerebral angiography, aortography, selective angiography, acroangiography, digital subtraction arteriography, digital subtraction venography, contrast-enhanced computed tomography and intravenous urography.; 350: angiocardiography, aortography, selective angiography, acroangiography, digital subtraction arteriography, digital subtraction venography, contrast-enhanced computed tomography, and intravenous urography
Contraindications: As for other drugs of this class.

meropenem
Meronem, Zeneca : UK
powder for injection 250, 500 mg, 1 g
antibacterial agent
Indications: Severe infections due to susceptible microorganisms.

mirtazapine
Remergil, Organon : Germany
coated tablets 15, 30 mg

tetracyclic antidepressant
Indications: Treatment of depression.

moexipril
Perdix, Schwarz : UK
film-coated tablets 7.5, 15 mg
angiotensin-converting enzyme (ACE) inhibitor
Indications: Treatment of hypertension as monotherapy. Second line therapy for the treatment of hypertension in combination with diuretics or calcium antagonists.

**mycophenolic acid (mycophenolate mofetil)*
CellCept, Roche : UK
capsules 250 mg
inhibitor of inosine monophosphate dehydrogenase; cytostatic
Indications: In combination with ciclosporin and corticosteroids for the prophylaxis of acute transplant rejection in patients receiving allogeneic renal transplants.
Contraindications: Hypersensitivity. Safety and effectiveness in children has not been established. *Precautions:* Patients receiving mycophenolic acid as part of an immunosuppressive regime are at increased risk of developing lymphomas and other malignancies particularly of the skin. Over- suppression of the immune system can also increase susceptibility to infection. Effective contraception must be used and pregnancy excluded before starting therapy. Contraception must be maintained during therapy and for six weeks after discontinuation.
Adverse reactions: Diarrhoea, leukopenia, sepsis, vomiting and higher frequency of certain types of infection.

proguanil
Paludrine, ICI Pharmaceuticals : Australia
tablet 100 mg
antimalarial agent
Indications: Malaria prophylaxis.

**raltitrexed*
Tomudex, Zeneca : UK
powder for injection 2 mg
antineoplastic agent
Indications: Rectal cancer, colon cancer.

ranitidine bismuth citrate
Pylorid, Glaxo : Netherlands; UK
coated tablet 400 mg
histamine H_2-receptor antagonist + bismuth salt
Indications: Duodenal ulcer, peptic ulcer disease, benign gastric ulcer; eradication of *Helicobacter pylori* and prevention of recurrent duodenal ulcer in combination with antibiotic therapy (clarithromycin or amoxicillin).

rimexolone
Rimexel, Organon; Rimexolone Ophthalmic Suspension 1%, Alcon : UK
Rimexel: powder for reconstitution 40 mg/vial; *Rimexolone Ophthalmic Suspension*: eyedrops 1%
corticosteroid
Indications: Rimexel: Rheumatoid arthritis. *Rimexolone Ophthalmic Suspension 1%*: eye inflammation, corneal inflammation, allergic conjunctivitis, uveitis, postoperative eye inflammation.

**seratrodast*
Bronica, Takeda : Japan
tablets 40, 80 mg; granules 10%
antihistamine
Indications: Bronchial asthma.

**troglitazone*
Noscal, Sankyo : Japan
tablets 100 mg, 200 mg
antidiabetic agent
Indications: Non-insulin dependent diabetes mellitus in patients who do not respond to conventional therapies.

Precautions: Since troglitazone has a potential to cause hypoglycaemia when used concomitantly with another antidiabetic drug, hypoglycaemic symptoms and countermeasures should be thoroughly explained to the patient. If any hypoglycaemic symptom appears, one of the drugs should be withdrawn temporarily or the dose reduced.
Note: Only to be administered to patients with a definite diagnosis of diabetes mellitus.

vinorelbine
Navelbine, Pierre Fabre : Germany
fluid for intravenous injection 10 mg/ml
antineoplastic agent
Indications: Advanced non-small cell lung cancer, as monotherapy or in combination with cisplatin; advanced anthracycline-resistant breast cancer; in patients with a good general condition.

Medical devices

Bovine collagen plug – approved to stop bleeding

United States of America. The Food and Drug Administration has approved a medical device – the Vasoseal Vascular Hemostasis Device: Datascope Corporation – to be used to help stop wounds from bleeding after balloon angioplasty and related surgery. The device is a one-inch long soft cylindrical plug made of bovine collagen. It is intended to reduce the time required by doctors to stop bleeding in the leg artery after balloon angioplasty, which unblocks clogged heart arteries, and angiography, in which pictures of the arteries are taken.

After each of these procedures, which are performed with a catheter inserted into a leg artery at the groin and threaded to the heart, the doctor must remove the catheter and apply manual pressure to the groin for up to 30 minutes to stop the leg artery from bleeding at the site of the incision.

The new plug reduces the time of this manual pressure. It is inserted into the groin through a sheath and plugs the wound in the artery to stop it from bleeding. It is absorbed into the body in about six weeks.

The FDA's approval was based on a clinical study which showed that the plug stopped bleeding about 75% faster overall than did manual pressure and was shown to be equally as safe. In angiography, the plug stopped bleeding in 5 minutes compared to 18 minutes manually; in angioplasty, it stopped bleeding in 8 minutes compared to 30 minutes manually. There was no significant difference in complications in the leg from use of the plug.
Reference: Reference: FDA Talk Paper T95-54, 2 October 1995.

Excimer laser systems – approved in corneal conditions

United States of America. The Food and Drug Administration has announced its approval of the excimer laser device (Excimed UV200LA and SVS Apex Excimer Laser Systems: Summit Technology) for phototherapeutic keratectomy procedures to treat:

- superficial corneal dystrophies (granular, lattice and Reis-Buckler's);
- epithelial basement membrane dystrophy;
- irregular corneal surfaces (secondary to Salzmann's degeneration, keratoconus nodules and other irregular surfaces);
- corneal scars and opacities (after trauma, surgery, infection and secondary to pathology).

Reference: Reference: Federal Register 60(129): 35214 (1995).

Liver stent - approved to stop recurrence of bleeding

United States of America. The Food and Drug Administration has approved a new implantable medical device – the Wallstent TIPS Endoprosthesis: Schneider USA Inc. – to be used to prevent the recurrence of bleeding from veins of the oesophagus in patients with cirrhosis.

The device is a flexible metal stent which is threaded into the liver via a catheter through a vein in the neck. It then expands and remains permanently in place allowing blood to bypass normal circulation through the scarred liver. It thus relieves the blood pressure in the liver. If untreated, this pressure can cause bleeding from veins of the oesophagus which may be fatal.

Although similar stents have been approved for other parts of the body, this is the first stent to be approved for use in the liver. It provides an alternative to current methods of treating bleeding from

oesophageal veins. The non-surgical treatments are often temporary and must be repeated. Abdominal surgery to divert blood away from the liver is a major operation compared to the relatively less invasive insertion of a stent.

The FDA's approval is based on a study in which the stent successfully diverted blood from the liver in 96 of 97 patients. Patients in the study had a significant improvement in survival compared with abdominal surgery and less bleeding after treatment compared with alternative medical treatment.
Reference: FDA Talk Paper T95-52, 29 September 1995.

Pap screening system – approved

United States of America. The Food and Drug Administration has approved a new device to select Pap smears for re-reading (the Autopap 300 QC Automatic Pap Screener System: Neopath Inc.). Pap smears are tests that detect cancer or precancerous cell changes in the cervix.

The product, which employs image processing and pattern recognition techniques, re-screens all Pap smears initially found to be normal by the cytotechnologist and picks out the most suspicious for a second review by the cytotechnologist. Use of the device increases the number of abnormal slides identified in the Pap smear reading process.

Currently, 10% of all negative smears are routinely re-screened. However, even with this quality control feature, abnormal Pap smears may go undetected. The error rate is estimated to be between 5% and 25%. In a study using the new system, 2.5% (297 out of 11,751) abnormal smears were identified that had been previously found to be normal.
Reference: FDA Talk Paper T95-55, 3 October 1995.

Retinal photic injuries from operating microscopes – reminder

United States of America. The Food and Drug Administration has reminded ophthalmologists about the potential retinal hazards from operating microscopes during cataract surgery, and has reviewed steps that can be taken to minimize the risks.

The following measures may reduce the risks of retinal photic injury during cataract surgery:

- Ensure correct angle of light incidence, light intensity, exposure time, and intensity of the blue light component.
- When using a new microscope, visually evaluate and set light levels to the lowest levels successfully used in the past.
- Replace lamps only with manufacturer- approved products.
- Because blue light has been shown to be more toxic than longer-wavelength light, the addition of a filter to exclude light below about 515 nm has been recommended, especially in cases requiring prolonged light exposure. However, a 515 nm short wavelength cut-off filter will result in a yellow light. Cut-off filters at wavelengths shorter than 515 nm to about the range of 420-435 nm will affect the colour rendition of the light less and may still provide useful reduction in the risk of injury.
- Use oblique lighting if available, or otherwise shield the pupil when the red reflex is not required or the operating field permits. Oblique lighting may be used during phases of an operation that do not require coaxial light.
- Minimize the direct exposure to the fovea.
- Educate residents about the above actions in order to help reduce the risks during training programmes and afterwards.

Prompt and accurate reporting by practitioners will help make it possible to obtain a better estimate of the incidence of retinal photic injury from operating microscopes during cataract surgery and other intraocular procedures.
Reference: Communication from the Department of Health & Human Services, FDA, 16 October 1995.

Veterinary Medicine

Ceftiofur - approved in footrot in cattle

United States of America. The Food and Drug Administration has approved a reconstituted sterile powder for intramuscular injection containing ceftiofur (Naxel: Upjohn) for the treatment of acute bovine interdigital necrobacillosis (foot rot, pododermatitis) in cattle (50 mg/ml used at 0.5 to 1.0 mg/pound body weight once daily for up to 5 days).
Reference: Federal Register 60 (191): 51718-51719 (1995).

Sarafloxacin - approved in turkeys and broiler chickens

United States of America. **The Food and Drug Administration has approved the fluoroquinolone antibacterial agent, sarafloxacin (SaraFlox: Abbott, 10%), for use in turkeys and broiler chickens in drinking water for control of mortality associated with susceptible *Escherichia coli* organisms.**

Reference: Federal Register 60 (188): 50097-50098 (1995).