DRUG HANDBOOK

BANNED, WITHDRAWN AND RESTRICTED DRUGS IN THE PHILIPPINES

Health Action Information Network
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INTRODUCTION

This is a revised edition of a special issue of *The Drug Monitor*, first published in October 1986 and reprinted twice because of the demand. This revised edition appeared as the October 1987 issue of *The Drug Monitor*, and now has additional changes to explain technical terms. The interest reflects public concern over hazardous drugs and the needs that were mentioned in the first edition of this compilation: information and research.

People need information on drugs, especially those of questionable safety; but there is still not enough information and, instead, too much misinformation, on the issue of "banned" drugs. This compilation is based on directives issued by the Department of Health's Bureau of Food and Drugs (BFAD) on drugs that have been *banned, withdrawn* or *restricted.* Also included are drugs that were voluntarily withdrawn by manufacturers. Much of the information, ironically, had to be taken from the United Nations which has published two editions (1983, 1987) of a *Consolidated List of Products Whose Consumption And/Or Sale Have Been Banned, Withdrawn, Severely Restricted or Not Approved by Governments.*

This document is also intended as a research paper, to identify some of the problems in the enforcement of government regulations on pharmaceuticals. Our research shows that a number of administrative orders are apparently not being followed, unless new orders have been issued to cancel previous ones. Unfortunately, the bureaucratic maze continues to limit access to vital regulatory documents. There is also the issue of ethics, where drug companies withdraw or reformulate products without necessarily informing the public or even the government regulatory authorities.

The status of drugs in different countries is mentioned for purposes of comparison. In some cases there are double standards, where drugs no longer used in the First World continue to be distributed in the Third World. The multinational drug companies argue that the discrepancy is due to different standards used by national regulatory authorities, which can be a problem for countries such as the Philippines where the Bureau of Food and Drugs seems to be too quick to approve new drugs and too slow to withdraw old drugs shown to have problems of safety or efficacy. In principle, the Philippines tends to follow the US Food and Drug Administration although there are drugs available locally that have been banned or withdrawn in other countries.

The present listing only provides "baseline" data—where we are today. We still have other problem drugs which medical and consumer groups feel should be banned or strictly regulated due to reasons of safety or efficacy. There is therefore also a section on "problem" drugs that need to be banned or strictly regulated. The list is based on the experiences of HAIN and other members of the Philippine Drug Action Network (PDAN), where we have been able to identify widely used drugs which pose too much of a risk to public safety. We will continue to provide updated information through *The Drug Monitor* and through future editions of this compilation.

With the Department of Health promising to delist dangerous and inessential drugs, we hope this compilation will help the public to take action even as the government continues its deliberations.

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USING THIS BOOKLET

This booklet is divided into four parts. The first part lists drugs which have been banned or withdrawn. These drugs are not supposed to be sold or distributed in the country, but may still be on the market, either as old stocks or as foreign donations. Note that in some cases, as with oxyphenybutazone (Tanderil, Tandalgesic), the manufacturer voluntarily stopped production but did not recall stocks already in the market. In other cases, manufacturers simply state that they have ceased production, although the information is not available unless one asks for it or checks the companies' lists of products.

The second part of the booklet lists "restricted" drugs. **These are not banned drugs.** They are still allowed on the market, but are subject to a number of restrictions imposed by the Bureau of Food and Drugs. The problem is that these restrictions, such as a limitation of indications (uses), or the matter of enclosing warning statements in the drug's package, are often poorly enforced.

The terms "restricted" and "regulated" are open to broad interpretation. Many drugs, such as antibiotics, are supposed to be available only with a doctor's prescription. For narcotic drugs and other pharmaceuticals with addictive potential, a special form (the S-2) is required from physicians with a license issued by the Dangerous Drugs Board. These drugs are not listed in this compilation since there are hundreds of such products.

The third part consists of "other problem drugs", those which have been withdrawn or strictly regulated in other countries because of safety problems, but which are still available, sometimes without prescription, in the Philippines. Some of these drugs are discussed in Parts I and II but are included again in this section to emphasize the need for stricter regulatory action. The criterion used for this section is safety. There are many other drugs which the Philippine Drug Action Network believes should be withdrawn because they are inessential or irrational. These drugs are not covered in this compilation because there are several hundred of them. These inessential drugs are not necessarily dangerous, but they are needless additions to drug expenditures.

The last part consists of indexes of generic names and brand names of the drugs cited in this compilation. "Aspirin" and "acetylsalicylic acid (ASA)" are generic names. These are usually found on the drug package in small print, sometimes under "ingredients". A drug may be sold under as many as 60 different brand names. Aspirin, for in-

stance, may be sold as Aspilet or Cortal or Supirin. It is often difficult to tell what the active ingredient or ingredients may be from the brand name alone. The indexes are intended to help you to look up both generic and brand names.

To be systematic, the booklet lists the drugs alphabetically, according to their *generic* name, but the known brand names are also given. Note that we have listed only the brand names found in the Philippine Index of Medical Specialties (PIMS). This is why it is important to check a drug's generic name when you are looking for information. We have attempted to include the many synonyms for each drug but a complete listing, especially if we were to include chemical names, would make this booklet too long and difficult to use.

We would appreciate your feedback—comments, suggestions and corrections—especially since PIMS only lists about 20 per cent of the brand names sold in the Philippines. The difficulty in tracking down problem drugs reflects the confusion caused by the proliferation of brand names and inessential products in the country. We hope that this situation will be corrected when a National Drug Policy is implemented.

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1

BANNED AND WITHDRAWN DRUGS

The following drugs have been banned or withdrawn from the market

SINGLE INGREDIENTS

Aminophenazone

Synonyms: Aminopyrine, amidopyrine, dimethylaminoantipyrine, dimethylaminophenazone

Administrative Order issued October 1983 disapproves its use in treatment of pain from spastic conditions because of the risk of agranulocytosis (a blood disorder). Used to be sold under the brand names Ergotam, Gardan, Irgapyrine, Locidin, Optalidon, Prydon, Spasmo-Cibalgin and Spasmo-Dimanyl.

Gardan has since been reformulated and the aminophenazone replaced by metamizole or dipyrone, while in Spasmo-Cibalgin, aminophenazone has been replaced by propyphenazone. The new formulations simply substitute other drugs from the same family of pyrazolone drugs (see page 33).

Amrinone

Oral preparations of this cardiac drug (Inocor) have supposedly been withdrawn by its manufacturer, Winthrop, although no official announcement was ever made. The oral preparations are no longer listed in PIMS.

Anabolic steroids

Some manufacturers have withdrawn their anabolic steroid products from the Philippines and other countries in response to pressure from health and consumer groups. These products are synthetic derivatives of the male hormone testosterone and were promoted as "growth stimulants" and as aids for convalescence. These claims have been disputed. Products which are no longer listed in the latest edition of PIMS are:

Ethylestrenol - Fertabolin
Methandienone (methandrostenolone) - Dianavit
Methenolone acetate (metendone acetate) - Fortabol
Stanozolol - Winstrol, Cetabon

Note that there are still other anabolic steroids listed in PIMS. These are discussed, together with the controversial claims about anabolic steroids, on page 31.

Arsenic-based Ingredients

Banned in any form for use in pharmaceuticals. Arsenic is a strong poison.

Azanidazole

Synonym: Triclofos sodium

Administrative order issued May 1981 withdrew the drug for treatment of trichomoniasis. No reason given for the withdrawal. May have been sold as Triclos.

Bromelains

[See discussion under Proteolytic Enzymes, page 14.]

Chloroform

Administrative order issued April 1978 prohibits its use as an ingredient in human drugs and cosmetics because of possible carcinogenic (cancer-causing) effects.

Chlortetracycline

Pediatric preparations banned. (See discussion under Tetracyclines, page 16.)

Brand name of adult preparation of chlortetracycline: Aureomycin

Chymotrypsin

[See discussion under Proteolytic Enzymes, page 14.]

Clioquinol

Synonyms: Chinoform, chloroiodoquin, chlorojodochin, cliquinol, iodochlorhydroxyquin, iodochlorhydroxyquinol, iodochlorhydroxyquinoline, iodochloroquine, iodochloroxine, 5-chloro-7-iodo-8-quinolinol, 7-iodo-5-chloroxine

Withdrawn from domestic market, but exported upon request of importing country. It used to be sold as Entero-Vioform, Mexaform and Intestopan Forte.

It is still found in drug preparations for external use (Betnovate, Diproform, Dreniform, Locorten-Vioform, Quadriderm, Synlar-C, Vioform-HC).

The drug is associated with sub-acute myelo-optic neuropathy (SMON), a crippling, sometimes fatal disease of the nervous system.

Cyclamates

Administrative order issued January 1971 prohibits the use of this sweetening agent in drugs because of reports of carcinogenicity (cancer-causing potential).

Danthron

In January 1987, Riker announced that it had decided voluntarily to cease manufacture of their laxative danthron (Dorbanex) after animal studies suggested that long-term administration of high doses of the drug was associated with the development of intestinal and liver tumors.

Diclofenac sodium

Administrative order issued September 1983 supposedly withdrew this drug because of fears of exposure of children to agranulocytosis, leucopenia and thrombocytopenia (all blood disorders). The administrative order has apparently been rescinded since the products, Arthrifen and Voltaren/SR, are still available without adequate warnings on possible adverse effects in children.

In January 1987, Ciba-Geigy announced that it would revise its warnings on package inserts about possible acute renal (kidney) failure to be "more precise and explicit". Ciba-Geigy clarifies that they feel the risk of renal failure is not confined to diclofenac alone but is common to all other non-steroidal anti-inflammatory drugs (NSAIDs). The World Health Organization says it has no information to suggest that diclofenac is less safe that the other NSAIDs or that children are particularly liable to adverse reactions.

Diethylstibestrol (DES)

Administrative order issued in 1973 bans its use in livestock and poultry preparations due to its carcinogenicity (cancer-causing potential). The hormone was widely used among pregnant women in the 1950s and 1960s, with the result that the daughters born to these women have higher rates of vaginal cancer. Its use in human

medicine has declined but some veterinarians and livestock raisers use the hormone to fatten animals.

Dihydrostreptomycin

Administrative order issued in 1972 withdrew the drug, singly or in combination with other drugs, because of possible damage to the vestibular area in the ear. It also has potential toxic effects on the kidneys. Streptomycin sulphate has the same potential side effects as dihydrostreptomycin, but with lower risk. This drug should be reserved mainly for the treatment of tuberculosis. The injectable form is sold under the brand names Strepcin, Streptomycin Sulfate and Streptorex.

There are potential problems because streptomycin is found in combination with other antibiotics such as penicillin (eg, Combiotic, Dicrysticin, Penstrep).

Streptomycin is also often combined with chloramphenicol, another antibiotic with possible serious side effects (blood disorders). These streptomycin-chloramphenicol combinations are often abused as antidiarrheals. Popular brand names include Chlorostrep, Dostrol, Kemistrep and Marcomycin Strep. Streptomycin is also found in the antidiarrheals Guanamycin, Polymagma and Streptomagma.

[See discussion on chloramphenicol, page 25.]

Domperidone

Injectable forms of this anti-emetic (anti-vomiting agent) (Motilium) were withdrawn worldwide by Janssen, its manufacturer, in January 1985 following reports of cardiotoxicity during intravenous administration. The injectable form is no longer listed in PIMS.

Doxycycline

Pediatric preparations banned. [See discussion under tetracyclines, page 16.]

Brand names of doxycycline include: Doxin-100, Dyna Doxycycline, Hyclate, Lexcycline, Odicycline, Vibramycin.

Elemental phosphorus

Banned for use or sale. No reason given.

Ethylestrenol

[See discussion under anabolic steroids, page 7.]

Feprazone

This is an anti-inflammatory that is structurally related to phenacetin (page 14). It used to be sold locally as Methrazone but this drug has not been listed in PIMS since 1985. It was voluntarily withdrawn in several countries following reports of skin reactions and other questions on its safety.

Indoprofen

"Ordered" withdrawn in October 1985 following reports that prolonged use induces irritation and ulceration of the gastrointestinal tract. Actually withdrawn voluntarily by the manufacturer as early as 1984 after animal studies showed it had carcinogenic (cancer-causing) effects. Brand name: Flosint.

Isoxicam

Voluntary worldwide withdrawal in October 1985 by its manufacturer following reports of severe skin reactions, some of which were fatal. An announcement was never made in the Philippines although the product, Maxicam, was withdrawn from PIMS starting in 1986.

Lysozyme chloride

[See discussion under Proteolytic Enzymes, page 14.]

Mercuric derivatives

Administrative order issued November 1983 ordered the phase-out of such compounds in topical preparations due to dubious safety and efficacy. It has an irritant effect on the skin and its disinfectant qualities are weak. Absorption into the body can result in chronic mercury poisoning and acrodynia (pink disease) in infants.

Examples of products with mercuric derivatives are Mercurochrome and Merthiolate (Tincture of Thiomersal). Some cosmetic preparations may still be using mercuric derivatives. Mercury is also reported to be present in a Chinese drug available locally: Watermelon Frost, used for sore throat and burns.

Methandienone (methandrostenolone)

[See discussion under Anabolic Steroids, page 7.]

Methapyrilene

Banned in 1980. Used to be part of antihistamine preparations Allerest, Antamin and Phenedrine. Carcinogenic (cancer-causing) in animal tests.

Methenolone Acetate (Metendone Acetate)

[See discussion under Anabolic Steroids, page 7.]

Minocycline

Pediatric preparations banned. [See discussion under Tetracyclines, page 16.]

Brand name: Minocin.

Neomycin

Banned in antidiarrheal preparations by administrative order in 1982 due to risks of pseudomembranous colitis, renal damage, neuro-muscular damage and ototoxicity (ear damage). Used to be found in many antidiarrheals such as Belkamycin, Diacin, Donnagel with Neomycin, Electromycin, Furamide, Gepsomycin, Kaltin with Neomycin, Kaopecona, Kaopectate with Neomycin, Kaopecyn, Lomotil with Neomycin, Merbental-S and Poldemycin.

The World Health Organization states that neomycin's value in diarrhea is widely questioned.

Neomycin is still used in Neozep and Neozep-H (nasal sprays, but not in the cold tablets).

It is also found in several skin preparations, often in combination with corticosteroids. PIMS lists a warning that preparations with neomycin "used repeatedly or in the presence of excessive skin damage may cause deafness". Such products include: Betnovate with Neomycin, Cortiderm-N, Decilone, Fluocidan-N, Halcicomb, Kenacomb, Lidex NGN, Neo-Synalar, Pimafucort, Predex, Supracortin 3, Trimycin-H and Trofodermin.

It is also found in eye drops: Decadron with Neomycin, Dexa-Polyspectran, Opthaldrop, Polyspectran OS, Predmycin-P.

PIMS has the following warning for ear drops containing neomycin: "Owing to the potential risk of ototoxicity, antibiotic-containing preparations should be used with caution in the presence of perforations of the tympanic membrane [ear drum]." The following ear drops have neomycin: Neozep Otic, Aplosyn Otic, Cortisporin, Decadron with Neomycin, Kenacomb, Polyspectran OS, Synalar Otic.

Neomycin is also found in many veterinary antibiotic preparations.

Nomifensine

Hoechst, its manufacturer, voluntarily withdrew the drug Merital in February 1986 after consumer groups exposed cases of liver damage, blood reactions, influenza-like reactions and fatal reactions. The drug was being promoted as an anti-depressant.

Norpseudoephedrine

Synonym: Cathin

Administrative order issued in October 1983 bans the use of this drug to control appetite. There is a risk of drug dependency and other adverse effects such as apathy, depression, chronic gastroduodenitis, dyspeptic disorders and dreamy euphoria with talkativeness. Brand name: Mirapront N.

Oxyphenbutazone

Ciba-Geigy voluntarily withdrew its brand names of oxyphenbutazone (Tanderil, Tandalgesic, Realin), an analgesic, in 1985 after pressure from international consumer groups over its many possible side effects, including aplastic anemia (bone marrow disorders) and agranulocytosis (depression of white blood cell production). The drug is still sold by other companies under the brand names Mindaril and Reozon. Arthrazone, another brand name, is no longer listed in PIMS.

Oxytetracycline

Pediatric preparations banned. [See discussion under Tetracyclines, page 16.]

Brand names (oral and injectable preparations) of oxytetracycline include: Chemotrex 500, Clinmycin, Ditropan, Elicyclin, Intermycin, Leydoxycline, Oxy-Tetra, Oxytrin, PMS-Oxytetracycline, Ter-

ramycin. It is also found in Bisolvomycin, a cough preparation, and in combination with proteolytic enzymes (See below.)

Papain

[See discussion under Proteolytic Enzymes, below.]

Penicillins (topical)

All ointments and topical preparations with penicillins have been banned since 1976 due to possible hypersensitivity reactions when absorbed through the skin.

Phenacetin

Administrative order issued in June 1980 stopped registration of new pharmaceutical preparations containing the drug due to risk of methenoglobelemia, a blood disorder. Used to be found in Apracur, Denta-Sal-Fyne, Doloxene, Saridon and Sinutab. Of these five brand name products, Doloxene, Saridon and Sinutab are still on the market but have been reformulated.

[See also discussion on APC combinations, page 18.]

Pirprofen

Disapproved for use in May 1983 because of potential risk to the liver and lack of advantage over existing anti-rheumatic drugs.

Brand name: Rengasil.

Propyphenazone

Synonym: Isopropylantipyrine

This is a pyrazolone derivative (see page 33) that may cause blood disorders. Roche used to include this drug in its brand name product Saridon but has since reformulated it. There are two other products on the market that still use propyphenazone: Avamigran and Spasmo-Cibalgin.

Proteolytic enzymes

Generic Names: Bromelains, chymotrypsin, lysozyme chloride, papain, seaprose-S, streptodornase, streptokinase, trypsin.

In March 1987, the Bureau of Food and Drugs (BFAD) ordered the withdrawal of all pharmaceutical products containing proteolytic enzymes because they were found to be ineffective. These enzymes are found in many drugs promoted as anti-inflammatories, supposedly useful in hastening healing after surgical, obstetrical or dental procedures, accidental trauma or infectious and allergic reactions. The BFAD, using findings from the US Food and Drug Administration (FDA), rejects these claims. The BFAD withdrawal took effect on October 30, 1987. Many of the products with protelytic enzymes are combined with tetracyclines (see page 16).

Brand names of drugs with proteolytic enzymes include:

Ampilase, Ananase, AP-Tetracycline HCl with Papain, Betanase, Betanase-T, Biopase Combi, Brotase, Carispas, Carispas plus Tetracycline HCl, Chemolase, Chymoral, Chymoral Forte, Combiopaze, Cypase, Danzen, Dentake, Dentozyme, Dofracycline with Papain, Enzodrase, Evanase, Evase-T, Flemizyme, Grotryp Dragees, Inokyme, Interpace, Kimose, Kizezyme, Larypront, Leftose, Leyden Tetracycline HCl with Papain, Lysapaze, Lysozyme, Lysomoxil, Lysoxyme, Lyzozima, Martipase, Medicepase, Mentazyme, Milase, MW-Tetra with Papain, MX-Tetra with Papain, Neusym, Oxypase, Oxytetra plus with Lysozyme, Papain, Papase, Papain with Tetra, Papase with Tetra, Phlogilase, Pic-Tetra with Papain, Tetranase, Texyn with Papain, Teynotrase with Papain, Traumalase, Tromase, Unimycinase with Debrinase, Varidase and Venimase.

Seaprose-S

[See discussion above on Proteolytic Enzymes.]

Sodium dibunate

This cough suppressant was ordered withdrawn in April 1982 because of the risk of reduction in granular leucocytes (white blood cells) with prolonged use in humans. Tests with experimental mice resulted in sudden death due to central nerve lesions. Still found in the cough preparation Irax.

Stanozolol

[See discussion under Anabolic steroids, page 7.]

Streptodornase

[See discussion above on Proteolytic enzymes.]

Streptokinase

[See discussion on Proteolytic enzymes on page 14.]

Sulfathiozole sodium and derivatives

Ordered withdrawn as an antidiarrheal in May 1971 due to risk of crystaluria (formation of crystals in the urine) with constant use. Still sold under the brand name Sultrin, in combination with other sulfonamides, for vaginal infections (intravaginal use).

Suloctidil

"Ordered" withdrawn in October 1985 following reports of adverse effects on the liver. Actually withdrawn voluntarily by the manufacturer. Sold under the brand name Sulocton.

Suprofen

In May 1987, McNeil (Johnson & Johnson) voluntarily withdrew suprofen worldwide following health and consumers groups' complaints that the drug caused renal (kidney) impairment. No announcement has been made in the Philippines. Brand name: Suprocil. Also sold in other countries as Suprol.

Tetracyclines, pediatric

Pediatric preparations banned in 1978 because of various risks including discoloration of the teeth and nails. It is deposited in bones and may cause rarefaction (thinning of the bones) and retarded bone growth. Contra-indicated in women during the last stage of pregnancy because tetracycline is deposited in the fetal skeleton. These drugs are not banned, but they should not be used for children and women during the latter half of pregnancy.

Brand names of tetracycline include: Achromycin, Alphacycline, Ambracyn, Cyclabid, Diocycline, Guayacycline, Hostacycline, Metrocycline, Monocycline, Mysteclin-C, Mysteclin V, Sigmamycin, Sumycin, Tetrabid, Tetracycline Upjohn, Tetracyn, Tetrex, Theracine, Triocycline, Tropicycline, Unimycin, Unilab/Tetracycline, Winitrex.

[Also see chlortetracycline (page 8), doxycycline (page 10), minocycline (page 12), oxytetracycline (page 13) and proteolytic enzymes (page 14).]

Tienilic acid

Synonym: Ticrynafen

In 1980, Smith-Kline withdrew this diuretic (agent which increases flow of urine), sold under the brand name Selacryn, following reports that prolonged use in some patients resulted in death due to liver dysfunction.

Triazolam

Supposedly withdrawn in June 1983 following reports of adverse effects such as severe anxiety, depersonalization, paranoia, parasthesis (partial loss of sensation) and "feeling of unreality". The administrative order has apparently been rescinded and the drug is available under the brand name Halcion. Only low-dose tablets are available, a policy enforced in other countries as well.

Trypsin

[See discussion under Proteolytic enzymes, page 14.]

Yohimbic acid

Ordered to be phased out in 1981 due to lack of evidence of efficacy. It continues to be sold under the brand name Mysgen, which combines yohimbic acid with methyltestosterone, ginseng, vitamin E and nicotinate "to improve physical and mental work capacity... intensify male image or profile, and enhance sexual fulfillment".

Another drug, Tonovan, which has been removed from PIMS starting in late 1986, combined yohimbic acid with mesterolone, tocopherol acetate, strychnine nitrate and nicotinate for "male climacteric, impotence and sterility secondary to androgen deficiency".

Yohimbic acid is not only unproven as an aphrodisiac but has been found risky when used by patients with kidney or liver disorders.

Ziperol

Ordered withdrawn in June 1982 as an antitussive (cough suppressant) following studies showing respiratory arrest in rhesus monkeys with administration of the drug. Brand name: Respilene.

Zomapirac sodium

Voluntary withdrawal by Johnson and Johnson in March 1983 following fatal allergic reactions in the US. The drug was promoted as an analgesic. Brand name: Zomax.

COMBINATION PRODUCTS

Acetylsalicylic acid, Phenacetin and Caffeine (APC)

This combination of analgesics was disapproved in June 1980 due to risks associated with phenacetin (page 14).

Ampicillin and Oxyphenbutazone

Combination drug disapproved for use in October 1983 due to inflexibility of dosage. Ampicillin is an antibiotic while oxyphenbutazone (page 13) is an analgesic.

Antibiotics in Cold Preparations

Such combination products were ordered withdrawn in May 1971 as there is no occasion when a fixed combination is preferable over individual components given separately.

A number of cough preparations, however, still incorporate antibiotics and may be misused as cold remedies. Among the cough preparations which include antibiotics are: Bisolcillin, Bisolvomox, Bisolvomycin, Bisolvonat, Erybron and Lovicin. Some physicians still prescribe antibiotics separately for colds but this is irrational.

Antibiotics with Vitamins

Administrative order in May 1971 ordered withdrawal of antibiotics combined with vitamins because they were considered irrational and not necessary for antibacterial activity. Isoniazid, an anti-tuberculosis drug, is allowed to be sold in combination with vitamin B6.

Mysteclin-C is listed in the latest edition of PIMS as a combination of tetracycline, amphotericin B and vitamin C.

Atropine in Combination with Other Drugs

Atropine is a drug that can cause dysuria (difficult urination), tachycardia (rapid heartbeat), palpitation and blurring of vision. The Bureau of Food and Drugs has banned combinations of atropine with furazolidone and dimethylpolysiolxane (simethicone).

It also gave a warning over atropine combined with diphenoxylate hydrochloride because of the possible side-effects of atropine and because the combination drug masks signs of dehydration. These warnings were issued in September 1976. Diphenoxylate with atropine is still sold under the brand name Lomotil. In 1983, Lomotil's manufacturer featured paid advertisements in local newspapers clarifying that they were promoting Lomotil only as treatment for the symptoms of diarrhea and not as therapy for dehydration. It has warnings that the drug is not recommended for children below the age of two. Another company also produces diphenoxylate with atropine, under the brand name Diarsed. It warns against using the drug for children under 30 months.

Carbocysteine and Promethazine

This combination has been disapproved for use in respiratory diseases since December 1982 because it is an irrational combination. Carbocysteine is a mucolytic (mucus softening agent) found in many cough preparations, while promethazine is an antihistamine.

Cycloserine and Isoniazid

This combination of two anti-tuberculosis drugs was ordered withdrawn in September 1978 for lack of proof of efficacy.

Dicyclomine hydrochloride, Doxylamine succinate and Pyridoxine hydrochloride

In June 1983, Merrell Dow voluntarily stopped production of this anti-emetic (anti-vomiting) combination, sold under the brand names Bendectin, Debendox, Lenotan and Mobental. The action was taken following reports that the drug, used by women suffering from nausea in pregnancy, may have adverse effects on the fetus.

Dicyclomine HCl (also known as dicycloverine) was the ingredient that was supposed to have harmful effects on the fetus. Medical experts still disagree on the effects of the drug and Merrell Dow has won, as well as lost, in several lawsuits brought against them by women who had used the drug. Dicyclomine HCl is an anti-emetic (anti-vomiting agent) and is still found in Acolin, Algelan-Plus,

Bentyl, Bentylgesic, Diatabs, Dicyclo, Emetal, Kolanticon, Kolantyl, Kremil-S, Relestal, Ropectin and Veragel-DMS. The World Health Organization notes that its use in infants has been associated with irritability, restlessness, convulsions and apnoea (temporary lapses in breathing).

Doxylamine succinate is an antihistamine with sedative effects. It is used as a sleeping aid in the US but with warnings that it should not be used by patients with asthma, glaucoma or enlargement of the prostate gland. It is also contra-indicated among pregnant and nursing women. This antihistamine is found in Bentylgesic (an antispasmodic), Nethaprin, Nethaprin Plus and Nethaprin Dospan (anti-asthmatics, despite its contra-indication for asthma in the US) and in Meracold-DM and Mercodol (cough and cold preparations).

Pyridoxine hydrochloride is vitamin B6.

Dipotassium clorazepate, Acepromazine and Acepromethazine

This combination was disapproved for use in March 1983 due to liver toxicity and parkinsonism. Acepromazine is approved for veterinary use only. All three drugs are tranquillizers.

Etidocaine hydrochloride and Adrenaline tartrate

This combination was disapproved in March 1977 due to risk of hypertensive (high blood pressure) crisis. Brand name: Duranest.

Guiacol, Camphor and Ether

Combinations of these ingredients mixed with an alcohol (eg, phenol, cresol, eucalyptol, chlorobutanol) were ordered phased out in November 1983 since they are ineffective in cough relief and may cause lipoid pneumonia and lipodystrophy.

Metoclopramide and Polidocanol

This combination was disapproved for use in March 1983 because of liver toxicity. Earlier editions of PIMS do not list such a combination. Metoclopramide is an anti-emetic (anti-vomiting agent) while polidocanol is used as a local anesthetic and spermicide.

Neomycin sulfate, Polymyxin B sulfate, Nystatin and Acetarsol

This combination for use in trichomonial vaginitis was disapproved in September 1977 as irrational and possibly harmful.

Nitrimidazine, Nystatin and Tetracycline HCl

Disapproved since November 1983 for use in mixed vaginal infections because it is an irrational combination.

Norethindrone acetate and Ethinyl estradiol

This is a hormonal combination that has been misused as a pregnancy test and for abortion. Schering AG has withdrawn its formulation, Cumorit, from the Philippines and other countries. There are, however, similar products still on the market. (See discussion on High Estrogen-Progesterone Preparations, page 33.)

Phenylbutazone and Clofexamide

Disapproved in November 1983 for use in rheumatoid arthritis because of risks of toxicity of phenylbutazone (page 27).

Pyrazolones in Combination

An administrative order in May 1979 disapproved combinations of:

antipyrine with brompheniramine maleate, salicylamide, quinine, ascorbic acid, caffeine;

dipyrone with diphenhydramine and diazepam;

phenyldimethylpyrazolone with brompheniramine maleate, methyl ephedrine hydrochloride, sodium salicylate and ascorbic acid;

dipyrone with primaverin HCl.

[See discussion on aminophenazone (page 7) and metamizole or dipyrone (page 27)]

Pyrilamine maleate (Mepyramine), Pamabrom and Acetaminophen

This combination was disapproved as a mild diuretic through lack of pharmacological basis but it is sold as Midol PMS for "pre-men-

strual syndrome". Its package says the drug "gives you the comforting effectiveness of a strong pain reliever; *a diuretic to ease the distress of bloating and water retention that causes those abdominal pains,* and a non-narcotic ingredient that helps calm tension, irritability and anxiety." (emphasis added)

The pain reliever is paracetamol (acetaminophen). The diuretic is pamabron and the "non-narcotic ingredient" for tension is pyrilamine maleate, an antihistamine.

Strychnine in Combination

This is banned for use or sale but it was an ingredient in the product Tonovan, which is no longer listed in PIMS. Strychnine is a powerful drug which stimulates the central nervous system but it is so dangerous that its main use is as a rat poison.

Tetracycline, Guiacol sulfate and Lidocaine HCl

Withdrawn in November 1983 as an irrational combination.

2

DRUGS WITH IMPORTANT RESTRICTIONS

The following drugs have important restrictions related to their use

Aspirin

Synonym: Acetylsalicylic acid (ASA)

Administrative order issued in August 1986 requires that aspirin packaging should contain the following warning: "Children and teenagers should not use this medicine for chicken pox or flu symptoms before a doctor is consulted about Reye's syndrome, a rare but serious illness." The warnings are still absent in most aspirin products.

Brand names of products containing aspirin include Anacin, Asaped, Ascriptin, Aspilet, Cordex Forte, Cortal, Doloxene, Ecotrin, Medicol, Midol, Neo-Novaldin, Persantin Plus, Robaxisal, Saridon, Supirin, Thomapiril, Zacitrin.

Boric acid and Boric salts

Administrative order issued in 1973 prohibits the use of boric acid and boric salts in all products for oral use and in products for use in infants and children below the age of three. Products for external use must carry a special warning. These products have been reported to cause disturbances in circulation, profound shock, convulsion and death, if absorbed into the body.

Boric acid is still sold as an eyewash. It is also found in the product Collyrium with Ephedrine (eye drops).

Chloramphenicol

An administrative order issued in July 1982 restricts the use of chloramphenicol for typhoid fever, meningitis and brain abscess. The severe restriction was imposed because of the antibiotic's possible side effect of agranulocytosis (a blood disorder).

The drug is frequently abused as an antidiarrheal, either as a single preparation (Arnocetin, Bactichlor, Biomycetin, Biophenicol, Catilan, Chemicol, Chlomitate, Chlorabicine, Chlorambid, Chloramphen, Chloromycetin, Compacol, Danmycetin, Hospicol, Intermycetin, Jerramphenicol, Kemicetine, Marcomycin, Metacol, Neophenicol, Oliphenicol, PMS-Chloramphenicol, Pediachlor, Scanicol, Unilab/Chloramphenicol, Venimicetin, Verachlor) or in combination with streptomycin (Chlorostrep, Dostrol, Kemistrep, Marcomycin Strep).

Clofibrate

An administrative order issued in 1980 restricts use of this drug for "certain patients only" because it causes hepatic tumors in rodents and there is an increased risk of malignancy and cholelithiasis (gallstones) with use in humans. It is sold under the brand names Atromid-S and Lipaten, mainly to prevent hyperlipidemia (high lipids or fats in the blood). Lipaten is indicated, in PIMS, for "prophylaxis of degenerative processes".

In the US and other countries, the use of clofibrate is advised only for patients with high plasma lipid concentrations which do not respond to dietary measures. The World Health Organization observes that there have been increased reports of mortality among patients receiving clofibrate.

Ephedrine

All drugs containing ephedrine were classified as prescription drugs in 1982. These drugs should be given with caution to patients with organic heart disease because ephedrine raises blood pressure and quickens heart rate. It stimulates the central nervous system. Its presence in many cough syrups makes it attractive to drug dependents. Drugs containing ephedrine include: Antamin, Asbral, Asmasolon, Asthma-Bisolvon, Bisolvon Compositum, Bromo-Ephedrine, Bronchicum, Coderex, Fentrin, Franol TF, Maledrine, Marax, Meracold, Mucobron, Mucobron Forte, Mucobron CM, Phenedrine, Pulmo Dexacillin, Protussa, Socortuss, Tedral. Also found in the eye drops Collyrium with Ephedrine.

Furazolidone

Synonym: Nitrofuran compound

Approved for restricted use only because animal tests have shown the drug to have cancer-causing potential. It is found in several antidiarrheal preparations: Diafuran, Diapectolin, Diatreat, Diazept, Furendia, Furoxone, F-zolidone and Pseudo-Ambin. There are no warnings in PIMS on furazolidone's carcinogenic (cancer-causing) potential. Since 1977, the US Food and Drug Administration has withdrawn furazolidone/kaolin/pectin preparations and has prohibited their export.

Hexachlorophene

Administrative order issued in 1972 restricts the use of hexachlorophene in skin preparations because it can be absorbed and cause

side effects, including brain damage, in infants. Used to be found in Phisohex.

Loperamide

Administrative order in November 1982 restricts the use of this antidiarrheal drug. The order states that it is contra-indicated in children below two years of age due to the risk of central nervous system damage. Sold under the brand names Alomide, Imodium, Lormide, Rodderhea and VCP Loperamide. PIMS warns against using loperamide for children below the age of two.

The World Health Organization recommends that the drug should not be used in children below the age of five.

Metamizole

Synonyms: Dipyrone, noramidopyrine, noramidazophen, novaminsulphone, methampyrone, sulpyrine, sodium-N-methylaminomethanesulphonate

Severely restricted since 1977 because of risks of blood disorders. It is to be used only as a "last resort in serious and life-threatening situations where less toxic antipyretics (fever-reducing agents) have failed or are not tolerated." Warnings are required in package inserts. The drug is found in Avafortan, Baralgin, Bipyrine, Buscopan, Dolo-Neurobion, Gardan, Gifaril, Lagalgin, Melubrin, Novaldin, Spastrin Forte, Unagen, Unigesic, Visceralgine Forte.

[See page 33 for further discussion on pyrazolone derivatives.]

Phenylbutazone

Recommended for use only when other agents fail because of the number of possible side effects on the blood, liver, and kidneys. Ciba-Geigy voluntarily decided in 1985 to revise its package inserts limiting the use of phenylbutazone to four types of arthritis: active ankylosing spondylitis, acute gouty arthritis, acute rheumatoid arthritis and acute attacks of osteoarthritis. Moreover, the use of phenylbutazone is recommended only when other therapeutic measures have been tried and found unsatisfactory. Ciba-Geigy's brand names of phenylbutazone—Butazolidin, Delta-Butazolidin and Irgapyrine—are no longer listed in PIMS.

Other companies are still producing phenylbutazone under the following brand names: Alaxan, Nortaludin, Nordex, Pyrazon and

Skelan Forte. United, the manufacturer of Alaxan, has supposedly replaced phenylbutazone with ibuprofen.

Rifampicin

Administrative order issued in December 1982 disapproved the use of this antibiotic for urinary and respiratory tract infections. It should be reserved as the last resort treatment for mycobacterial infections (ie, tuberculosis and leprosy) where there is bacterial resistance. Products containing rifampicin include: Abrifam, Dipicin, Iso-Ramp, Medifam, Pyrina, Rambutol, Ramicin, Ramicin Iso, Ramp, Resfamer with INH, Resimin, Rifadin, Rifater, Rifatrexin, Rifatrexin-INH, Rifanah, Rimactane, Rimactazid and Syntaxil.

Some manufacturers now include gonorrhea as an indication for rifampicin.

3

OTHER PROBLEM DRUGS

The following drugs should be reviewed by the Department of Health for possible withdrawal or stricter regulations because of safety problems

Anabolic steroids

Anabolic steroids are sometimes misprescribed to "promote growth" among children. The World Health Organization notes that these drugs should be limited to selected patients with chronic debilitating and emaciating diseases, particularly associated with cancer or anaplastic anemia (a blood disorder). These drugs are synthetic derivatives of the male hormone testosterone and are therefore sometimes called androgens. Gilman and Goodman's textbook on pharmacology states that "androgens are ineffective in promoting anabolism in acute illness, severe trauma, and protein depletion associated with severe illness." Other medical experts express fears that these drugs may actually stunt growth and cause liver damage. As hormones, they may have a masculinizing effect on women. Paradoxically, these substances have a feminizing effect on men because they also have progestational (female hormone) qualities.

Health Action International suggests that the drugs be withdrawn or placed under strict restriction for use only in hospitals and for very specific conditions.

The following drugs are anabolic steroids:

Ethylestrenol: brand names Fertabolin (withdrawn by manufacturer) and Orgaboral;
Methenolone Acetate (Metendone Acetate): brand name Fortabol (withdrawn by manufacturer);
Methandienone (Methandrostenolone): brand name Dianavit (withdrawn by manufacturer);
Nandrolone: brand names Decabolin, Orgabolin;
Stanozolol: brand names Winstrol (withdrawn by manufacturer) and Cetabon/Cetabon with Iron (withdrawn by manufacturer)

Antibiotics in Antidiarrheals

Because of growing problems of antibiotic resistance, antidiarrheal preparations should not be allowed to incorporate antibiotics. Some of these antibiotics, such as chloramphenicol and streptomycin, are dangerous in themselves, with high risks of adverse effects. There are at least 117 antidiarrheal preparations containing antibiotics, based on a study by Quanico (*The Drug Monitor*, June 1987). Among the most used are those containing furazolidone (page 26), chloramphenicol (page 25) and streptomycin (see under Dihydrostreptomycin on page 10). In addition, there is growing abuse of antidiarrheals containing polymyxin B sulfate (Polymagma, Kaores-P with polymyxin), paromycin sulfate (Humagel, Nifulidone Liquid).

The chloramphenicol-streptomycin combination drugs should be banned. Parke-Davis, in a letter to MaLAM, an Australian medical lobbying group, says that their product, Chlorostrep, will "cease to exist" in 1987. This has not been announced in the Philippines.

Antispasmodics in Antidiarrheals

These drugs should either be banned or more strictly regulated because of their potent action. These include loperamide (page 27), diphenoxylate HCl (see under Atropine on page 19) and dicyclomine HCl (page 19).

Atropine sulfate, found in Diarsed, Lomotil, Lyspafen, Rheatrol, also has potential problems because it can cause tachycardia (rapid heartbeat), decreased salivary secretion, urinary retention and adverse effects on the nervous system.

Opium tincture, which should be strictly regulated because of its addictive potential, is found in Kaobismot and Unilab Antidiarrheal.

Several drugs containing metamizole (dipyrone), such as Baralgin and Buscopan, also incorporate antispasmodics which can increase dipyrone's risk of precipitating hypotension (low blood pressure) leading to shock.

Bismuth salts

The World Health Organization observes that there is an association between prolonged intake of high doses of bismuth salts, particularly the subgallate and subnitrate, and encephalopathy (cerebral dysfunction). Because of these risks, many countries have placed these substances under strict prescription control or have banned them completely.

In the Philippines, these are found in a number of antidiarrheals: Carbo-Guanacil, Caved-S, Diatabs, Diatromyl, Euracid, Interea, Kaobismot, Neodiarel and Ropectin.

Butazones

These drugs are used as pain-killers and anti-inflammatory drugs. They are also known as pyrazolidine derivatives. Given the fact that Ciba-Geigy has voluntarily withdrawn its oxyphenbutazone (page 13) and phenylbutazone (page 21) products, the Philippine government should take action on other companies' butazone products. The American Medical Association's 1983 *Drug Evaluations* states that the usefulness of butazones "is limited by their potential serious adverse reactions", mainly blood disorders.

Camphor

Topical application and inhalation of preparations containing camphor have been reported to cause convulsions in infants. Several governments now require such preparations to carry appropriate warnings.

In the Philippines, camphor is found in Analint, Bronkinol, Eucalyptine Le Brun, Guacol, Liberol, Pacilyptol, Pulmin and Sarna.

Cyroheptadine

This is promoted as an appetite stimulant and sold under the brand names Cyproheptavit, Periactin, Periactin B-C, Periactin-Vita and Periactin Vita-M. The drug is actually an antihistamine and its efficacy as an appetite stimulant has been questioned. The World Health Organization states that the drug manufacturers' policy is that the drugs are used only under the supervision of a physician who should make sure that adequate nutritious food is available.

Depot medroxyprogesterone acetate (DMPA)

This injectable contraceptive (Depo-Provera) has been the subject of controversy because it is restricted in several countries and because some animal studies suggest that the drug is carcinogenic (cancer causing). The World Health Organization considers the drug as one whose "risk-benefit judgement differs significantly from country to country".

High Dose Estrogen-Progesterone Preparations

High-dosage combinations of estrogen and progesterone are abused as abortifacients and as pregnancy tests. It should be used only for secondary amenorrhea (although there are also questions on its usefulness for this condition) and only after pregnancy has been ruled out. Brand name preparations of this type include: Cumorit (supposedly withdrawn by its manufacturer), Gestex, Proseckon.

Pyrazolones

There are several drugs in this category and they are all associated with risk of blood disorders, particularly agranulocytosis (reduction in granulocytes or white blood cells). These drugs are considered obsolete by many pharmacologists and are no longer discussed in

many standard pharmacology textbooks. The Philippine government has banned only aminophenazone (page 7) and imposes restrictions on metamizole or dipyrone (page 27). Propyphenazone (page 14) is still allowed without restrictions except that it is a prescription drug. The metamizole-containing drugs, particularly Baralgin, Gardan, Gifaril and Novaldin are the most frequently abused, based on HAIN's community studies of drug use.

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