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ADMINISTRATIVE ORDER
No. 163 s. 2000

SUBJECT: RECLASSIFYING ALL PHARMACEUTICAL PRODUCTS CONTAINING MORE THAN 25mg TO 50mg OF PHENYLPROPANOLAMINE TO PRESCRIPTION DRUGS AND PROHIBITING THE REGISTRATION OF THOSE CONTAINING MORE THAN 50 mg

Phenylpropanolamine (PPA) is a pharmaceutical active ingredient used in many Over-the-Counter (OTC) and Prescription (Rx) cough and cold medications for relief of nasal stuffiness and sinus congestion in allergic and non-allergic rhinitis, common colds and sinusitis. PPA has been in the local market for at least forty years with no report of serious adverse drug reaction.

On November 6, 200, the USFDA issued a public health warning concerning the risk of hemorrhagic stroke associated with the use of PPA as an appetite suppressant. This warning was based on the report of the Hemorrhagic Stroke project (HSP) submitted by the Yale University School of Medicine.

The Bureau of Food and Drugs (BFAD) undertook its own review of USEDA warning and HSP study through its own pool of consultants. Highlights of this review as follows:

1. The HSP study has some methodological flaws which raise questions about validity of its results, the “stroke cases” in the study were not compatible to the “control” as there were more hypertensive subjects and smokers in the former than the latter. Therefore, the higher incidence of stroke in the study group could be due to factors independent of their PPA use. Moreover, there was a predominance of African-American patients in the study group, and its well-known that, even without PPA, there is a higher incidence of strokes among such patients relative to the white population.

2. The significant results of the HSP study focused mainly on PPA used for weight reduction by women in doses ranging from 75-150 mg. *No drug containing these doses is registered and legally marketed in the Philippines*. The PPA content of most cough-cold medicines in the Philippines is only 12.5 mg. To 25 mg. with only two products containing 50 mg. per tablet.

3. In the more than forty years that PPA has been in the Philippine market, there has been no report of any serious adverse drug reaction linked to the use of PPA-containing cough-cold medicines.

The BFAD findings run in the same direction as that of the United Kingdom's Committee on Safety of Medicines (UKCSM). The UKCSM observed that "the US study did not find a risk of hemorrhagic stroke associated with use of PPA in cold and flu remedies but suggested an increased risk when used in products as long-term slimming aids (appetite suppressants)"

In the light of the BFAD findings based in available scientific data and as a precautionary measure in the interest of consumer protection, the Bureau of Food and Drugs hereby issues the following directives:

1. All drug products containing PPA at doses of 25 mg. or below shall continue to be classified as over-the-counter (OTC) products.

2. All drug products containing PPA at doses more than 25 mg to 50 mg shall be classified or reclassified as prescription drugs. They shall be subject to the following rules:

    2.1 they shall be dispensed only with a doctor's prescription

    2.2 Their labels shall bear the following:

        (a) Rx symbol; and
        (b) A prominent boxed warning that is easily read and understood, informing the consumer of the risks associated with using PPA at such doses;

    2.3 In all their packaging inserts, drug literatures and other information materials, it shall be emphasized that PPA at such doses is contraindicated in patients with severe cardiovascular disorders, tachycardia, hypertension, diabetes mellitus, hyperthyroidism and concomitant intake of monoamine oxidase inhibitors (MAO-I's).

    2.4 There shall not be any advertisement of drug products containing PPA at such doses in the newspapers, radio, television or any other form of mass media. Advertisements and promotions shall be limited to medical, journals, publications and literature solely intended for medical and allied professions

3. Renewal of License to Operate

    2.1 The LTO shall have the following validities for all categories of salt manufacturer:
        2.1.1 Initial Period (Initial Application) – 2 (two) years
        2.1.2 Subsequent Period (Renewal Application) – 2 (two) years

    2.2 Renewal of license can be made at least one month prior to expiration of the LTO provided that set standards and requirements have been complied. Failure to comply with BFAD requirements and standards shall be the oasis for non-renewal of LTO

4. Administrative Sanction

    4.1 Salt manufacturers who fail to register/apply for a LTO will not be allowed to distribute, trade or sell their salt in the market/food industry.

4.2 Grounds for Revocation of LTO

4.2.1 Non-compliance to BFAD requirements and standards

4.2.2 Misrepresentation of any material fact in the application/petition form and in any documentation used as a basis for issuing the LTO

4.2.3 Any deficiency in Good manufacturing Practice that is likely to result in the contamination of raw materials and finished product such as: improperly stored litter.\, waste, refuse which may be a source of breeding place or harborage for rodents and inc\sects; excessively dusty roads/areas that may constitute a source of contamination where salt is exposed; inadequately drained areas that may contribute to salt seepage land providing a breeding place insects or pathogenic micro-organisms.

4.3 Re-application after Revocation

No salt manufacturer whose LTO was revoked may apply for a LTO within 5 years after the revocation of its license.

5. Schedule of Fees

5.1 Filing fee of PPh 50.00 upon submission of complete documents

5.2 Fee for LTO (valid for 1 year) journals, publications and literature solely intended for medical and allied professions.

6. All drugs containing PPA at doses exceeding 50 mg shall no longer registrable. The manufacturer, distribution and sale of any drug product containing PPA at doses exceeding 50 mg shall be deemed illegal and punishable under Republic Act No. 3720 (The Food, Drug, Devices and Cosmetics Act).

This order shall take effect immediately.

(Sgd) ALBERTO G. ROMUALDEZ,JR.,MD
Secretary of Health