Provisional Translation (as of January 2016)*

Administrative Notice
December 14, 2015

To: Pharmaceutical Affairs Section, Prefectural Health Department (Bureau)

Evaluation and Licensing Division,
Pharmaceutical Safety and Environmental Health Bureau,
Ministry of Health, Labour and Welfare

Partial revision of "English version of the Standards for Marketing Approval of Cold Remedies, etc."

Of the OTC drugs, the marketing approval standards (notifications) for cold remedies have been translated into English in the "English version of the Standards for Marketing Approval of Cold Remedies, etc." (September 29, 2015 Administrative Notice, hereinafter referred to as "Administrative Notice"). The Standards for Marketing Approval of Oral Remedies for Rhinitis of the Administrative Notice Appendix 4 have been amended in accordance with the "Partial revision of "The Standards for Marketing Approval of Oral Remedies for Rhinitis"" (December 14, 2015 PSEHB/ELD Notification No. 1214-2), and we hereby inform that as in the Appendix 4.

Description

Appendix	Notification name	Date of issue, etc.
4	The Standards for Marketing Approval of Oral Remedies for Rhinitis	Mar 25, 2015 Notification PB No.23 （Dec 14, 2015 Partial revision）

Appendix 4

Provisional Translation
from Japanese Original

Mar 25, 2015
Notification PB No.23
(Dec 14, 2015, Partial Revision)

The Standards for Marketing Approval of Oral Remedies for Rhinitis

1. Scope of Oral Remedies for Rhinitis

The scope of remedies subject to these standards covers oral medicines (with the exception of cold remedies, anti-allergic agents, remedies based on Kampo medicine* formulas) formulated with the intent of relieving symptoms of rhinitis.

*Kampo medicine is traditional Japanese medicine.

2. Approval Standards

The approval standards for oral remedies for rhinitis are as follows.

For remedies not conforming to these standards, data concerning the efficacy and safety and reasons justifying the combination should be submitted; the preparation in question will be reviewed based on these data.

(1) Types of Active Ingredients

a. Table 1 shows the types of active ingredients that may be used.
b. The active ingredients that must be used are those listed in Column I of Table 1.
c. Active ingredients from different columns of Table 1 may be combined with each other, unless otherwise stipulated.
d. When active ingredients from Column I, Column III, or Column IV are to be combined, only 1 ingredient from each column may be used.
e. When active ingredients from Column II of Table 1 are combined, up to 2 active ingredients from Group 1 may be used, but only 1 from Group 2 may be used.
However, the combination of dl-methylephedrine hydrochloride and l-methylephedrine hydrochloride or that of pseudoephedrine hydrochloride and pseudoephedrine sulfate is not permitted.
f. When the active ingredients from Group 2 in Column I of Table 1 are combined, only formulas other than oral solutions and syrups can be used. They should not be combined concomitantly with the active ingredients from Column V.

(2) Quantities of Active Ingredients

a. The maximum daily doses of individual active ingredients should be those given in Table 1, unless otherwise indicated. The maximum single dose is 1/3rd of the maximum daily dose. However, the maximum single dose of oral solutions and syrups is 1/6th of the maximum daily dose.
b. When active ingredients from Column IV of Table 1 are combined with those of Group 1 in Column II, the maximum daily dose of ingredients from Column IV should be half of those specified in Table 1.
c. When 2 or more active ingredients from Column II of Table 1 are combined, the sum of the

values obtained by dividing the amount of each active ingredient by the respective maximum daily dose should not exceed 2.

d. The lower limit of the daily dose for each active ingredient from Column I of Table 1 is half of its maximum daily dose.
e. The lower limit of the daily dose for each active ingredient from Columns II and IV of Table 1 is 1/5th of its maximum daily dose.
f. The lower limit of the daily dose for each active ingredient from Columns III and V of Table 1 is 1/10th of its maximum daily dose.
g. The daily dose of the active ingredients from Group 2 in Column I of Table 1 should be limited to 4 mg.

(3) Dosage Forms

The dosage forms are capsules, granules, pills, powders, tablets, oral solutions (with the exception of elixirs; hereinafter the same should apply), and syrups.

(4) Dosage and Administration

a. Dosage and administration are to be 3 times a day, in principle. The times of administration and intervals between them should be clearly indicated, but intervals between doses should be 4 or more hours. For oral solutions and syrups, taking them up to 6 times a day is acceptable, but when dosing is 6 times a day, each dose is to be taken at approximately 4-hour intervals, in principle.
b. Dosage for infants less than 3 months of age is not approved.
c. For formulas containing promethazine hydrochloride or promethazine methylenedisalicylate from Group 1 in Column I of Table 1 and the active ingredients from Group 2 in Column I, dosage for children under 15 years of age is not approved.
d. For formulas containing pseudoephedrine hydrochloride or pseudoephedrine sulfate from Group 1 in Column II of Table 1, dosage for children under 3 years of age is not approved.
e. For hard capsules, and soft capsules, pills, and tablets larger than 6 mm in diameter, dosage for children under 5 years of age is not approved.
f. For soft capsules, pills, and tablets of a diameter of 6 mm or less, dosage for children under 3 years of age is not approved.
g. The maximum daily dose for children under 15 years of age is that obtained by multiplying the maximum daily doses listed in Table 1 by the coefficient for the respective age groups in Table 2.
h. The maximum single dose for oral solutions and syrups is 10 mL.

(5) Indications

The indications are to be within the following scope:

Relief of the following symptoms due to acute rhinitis, allergic rhinitis or sinusitis; sneezing, runny nose (excessive nasal discharge), stuffy nose, watery eyes, sore throat, dull headache (heaviness in the head).

(6) Packaging Units

The maximum volume of containers for oral solutions and syrups is a 4-day supply at the maximum daily dose.

Table 1 Active Ingredients and Maximum Daily Doses

Category		Active ingredient	Maximum daily dose
Column I	Group1	Alimemazine tartrate Isothipendyl	5mg
		hydrochloride Iproheptine	12mg
		hydrochloride Difeterol	150mg
		hydrochloride Tripelenamine	90mg
		hydrochloride Thonzylamine	100mg
		hydrochloride Methodilazine	50mg
		hydrochloride Chlorpheniramine	8mg
		maleate	12mg
		d-Chlorpheniramine maleate	6mg
		Carbinoxamine diphenyldisulfonate	7.5mg
		Diphenylpyraline hydrochloride	12mg
		Diphenylpyraline teoclate	4.5mg
		Diphenhydramine hydrochloride	75mg
		Diphenhydramine salicylate	75mg
		Diphenhydramine tannate Triprolidine	75mg
		hydrochloride Promethazine	6mg
		hydrochloride Promethazine	15mg
		methylenedisalicylate Carbinoxamine	40mg
		maleate	16mg
	Group2	Mequitazine	4mg
Column II	Group 1	Phenylephrine hydrochloride Pseudoephedrine	30mg
		hydrochloride Pseudoephedrine sulfate	180mg
		dl-Methylephedrine hydrochloride l-	180mg
		Methylephedrine hydrochloride	110mg
		Methoxyphenamine hydrochloride	110mg
			150mg
	Group 2		as total alkaloids
		Datura Extract	0.6mg
		Belladonna (Total) Alkaloids	0.6mg
		Belladonna Extract Isopropamide	60mg
		iodide extract Scopolia Extract	7.5mg
			60mg
	Group 1	Glycyrrhizinic acid and its salts	as glycyrrhizinic acid 200mg

Column III	Group 2	Glycyrrhiza	Extract (converted to the crude drug amount)	Powder
			5g	1.5g
Column IV		Caffeine and sodium benzoate		300mg
		Caffeine hydrate		300mg
		Anhydrous caffeine		300mg
Column V			Extract (converted to the crude drug amount)	Powder
		Schizonepeta Spike	3g	-
		Asiasarum Root Ginger	3g	-
		Magnolia Flower	3g	1g
		Peucedanum Root	3g	-
		Angelica Dahurica Root	3g	-
			3g	1g

Table 2

Range of ages and coefficients

Age	Coefficient
15 years of age and over 11 to	1
under 15 years of age 7 to	2/3
under 11 years of age 3 to	1/2
under 7 years of age	1/3
1 to under 3 years of age	1/4
6 months to under 1 year of age	1/5
3 months to under 6 months of age	1/6