Provisional Translation (as of April 2016)*

Administrative Notice
March 28, 2016

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 Antitussives and Expectorants of the Administrative Notice Appendix 3 have been amended in accordance with the "Partial revision of the " The Standards for Marketing Approval of Antitussives and Expectorants" (March 28, 2016 PSEHB/ELD Notification No.0328-10), and we hereby inform that as in the Appendix 3. In addition, we inform you that the description updates in the Appendix 5 and the Appendix 14 of the Administrative Notice.

Description

Appendix	Notification name	Date of issue, etc.
3	The Standards for Marketing Approval of Antitussives and Expectorants	Mar 25, 2015 Notification PB No.26 （Mar 28, 2016 Partial revision）
5	The Standards for Marketing Approval of Gastrointestinal Medicines	Apr 22, 1980 Notification PFSB No.520 Final revision Mar 28, 1986
14	The Standards Marketing Approval of Athlete's Foot and Ringworm Remedies	May 15, 1998 Notification PSB No.447

Appendix 3

Provisional Translation
from Japanese Original

Mar 25, 2015
Notification PB No.26
(Mar 28, 2016, Partial Revision)

The Standards for Marketing Approval of Antitussives and Expectorants

1. Scope of Antitussives and Expectorants

The scope of remedies subject to these standards covers oral remedies (including troches and drops) intended for use as antitussives and expectorants.
However, remedies based on Kampo medicine* formulas and non-Kampo crude drug remedies consisting of crude drug only are not covered.
*Kampo medicine is traditional Japanese medicine.

2. Approval Standards

The approval standards for antitussives and expectorants are as follows.
For remedies not conforming to these standards, efficacy and safety data 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 lists the active ingredients that may be used.
The types of active ingredients that may be used in troches and drops are limited to those marked by in Table 1. The active ingredients from Column X should only be combined for troches and drops.
b. One ingredient from Columns I, II, III, XII, or XIII of Table 1 must be included. However, cases where only the active ingredients from Groups 2 and 3 in Column VI of the same table are combined simultaneously are excluded.
c. Active ingredients from different columns of Table 1 may be combined with each other, unless otherwise stipulated.
d. Active ingredients from Group IX of Table 1 may be combined only in remedies that contain active ingredients from Column I or VIII in this table.
e. In Columns I to III and Columns V to X of Table 1, only 1 ingredient from each group may be used.
However, cases where only the active ingredients from Groups 2 and 3 in Column VI of the same table are combined simultaneously are excluded.
f. Active ingredients from Column XII of Table 1 should not be combined simultaneously with the active ingredients from Column II or V of the same table.
g. Active ingredients from Group 2 in Column I of Table 1 should not be combined simultaneously with the active ingredients from Columns III, IV, V, XII, XIII, or XIV.
h. Active ingredients from Column IV of Table 1 should not be combined simultaneously with the active ingredients from Group 2 in Column I, or from Columns V, XII, or XIII.
i. Active ingredients from Group 2 in Column VI of Table 1 should not be combined simultaneously with the active ingredients from Column V, XII, or XIII of the same table.
j. Active ingredients from Group 3 in Column VI of Table 1 should not be

combined simultaneously with the active ingredients from Column V, XII, or XIII of the same table.

k. Active ingredients from Group 2 in Column VIII of Table 1 should not be combined simultaneously with the active ingredients from Column V or XIII of the same table.

(2) Quantities of Active Ingredients

a. The maximum single dose and maximum daily dose of each active ingredient in Table 1 should be the doses specified in the same table, unless otherwise specified.
b. When the active ingredients from Column IX are combined with those from Column II, V, or XII of Table 1 are combined, the maximum single and daily doses of the ingredients in Column IX should be half of the amounts specified in Table 1.
c. When 2 or more of the active ingredients from Columns II and V of Table 1 are combined or when 2 or more of the active ingredients from Column XII, XIII, or XIV are combined, the sum of the values obtained by dividing the amounts of each of the active ingredients by their respective maximum daily doses should not exceed 1.
d. The lower limit of the combined amounts of each active ingredient in Table 1 should be half of the maximum single or daily dose, unless otherwise specified. However, for the active ingredients from Column IX, the limit should be 1/5th.
e. When the active ingredients from Group 2, Column VI of Table 1 are combined simultaneously with only the active ingredients from Group 3 in the same column, the single dose should be 4 mg and the daily dose should be limited to 12 mg.
f. The single dose of the active ingredients from Group 3 in Column VI of Table 1 should be limited to 250 mg and the daily dose should be limited to 750 mg.
g. The single dose of the active ingredients from Group 2 in Column VIII of Table 1 should be 0.334 mg as clemastine and the daily dose should be limited to 1 mg as clemastine.
h. In the case of troches and drops containing Group I ingredients from Column X of Table 1 and having a dosage regimen for children, the coefficients given in Table 2 should not be used to calculate the combined amount of the ingredients from Column X.
i. In the case of troches and drops to be taken 5 to 6 times per day, the lower limits of the combined amounts of each active ingredient should be half of the maximum daily dose.
j. When the active ingredients from Column II of Table 1 are combined simultaneously with the active ingredients from Column V, the lower limits of the combined amounts should be as follows.

- When the active ingredients from Column II of Table 1 are indicated for “cough,” “cough associated with wheezing (wheezy, whistling),” or “sputum,” the lower limit of the amounts of the ingredients in Column V should be 1/5th of the maximum single and daily doses.
- When other ingredients with an indication of “coughing” are combined, the lower limits of the amounts of ingredients from both Column II and V should be 1/5th of the respective maximum single and daily doses.
  However, in the case of proportional combinations, lower limits should be such that the sum of the values obtained by dividing the amount of each active ingredient by its maximum daily dose equals half.
- When the active ingredients from Column V of Table 1 are indicated for “cough associated with wheezing (wheezy, whistling)” or “sputum,” the lower limit of the amounts of the ingredients in Column II should be 1/5th of the maximum single and daily doses.

k. When used in combinations, the lower limit of the daily amounts of the active ingredients from Column XI of Table 1 is 1/5 of the maximum daily dose.
l. The lower limits of the amounts of crude drugs should be 1/10th of the maximum daily dose. However, when the indications approved for a particular crude drug are claimed, the lower limit should be half of the maximum daily dose.

(3) Dosage Forms

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

(4) Dosage and Administration

a. The dosage is "3 to 4 times a day," and the timing of doses or intervals between doses must also be indicated.
However, as for troches, drops, and oral solutions, and syrups, the dosage may be up to 6 doses per day. For dosages of 5 to 6 doses a day, troches and drops should be taken at intervals of at least 2 hours and oral solutions and syrups at intervals of about 4 hours, in principle.
b. The dosage for troches and drops should be allowed to dissolve slowly in the mouth without chewing.
c. For hard capsules, troches, syrups, and soft capsules larger than 6 mm in diameter, pills, and tablets, dosage for children under 5 years of age is not approved. Even for capsules smaller than 6 mm in diameter, dosage for children under 3 years of age is not approved.
d. Dosages for infants under 3 months of age are not approved.
e. For remedies containing promethazine hydrochloride or promethazine methylene disalycilate from Group 1 in Column VIII of Table 1, dosage for children under 15 years of age is not approved.
f. For remedies containing the active ingredients from Group 3 in Column VI of Table 1, dosage for children under 8 years of age is not approved.
g. For remedies containing the active ingredients from Column IV of Table 1 or the active ingredients from Group 2 in Column VIII, dosage for children under 5 years of age is not approved.
h. For remedies containing the active ingredients from Group 2 in Column I of Table 1, dosage for children under 3 years of age is not approved.
i. The maximum daily dose for children under 15 years of age is the amount obtained by multiplying the maximum daily dose in Table 1 by the coefficient corresponding to the respective age group in Table 2, unless otherwise specified.
j. The maximum single dose of the active ingredients in oral solutions and syrups is 1/6th of the maximum daily dose (for children under 15 years of age, the maximum daily dose according to i. above), and the maximum single dose is 10 mL, unless otherwise specified.
k. For remedies containing the active ingredients from Group 2, Column I of Table 1 with dosage for children under 15 years of age, the maximum single dose is 10 mg and the maximum daily dose is 30 mg. The maximum daily dose for children under 15 years of age is the amount obtained by multiplying the maximum daily dose (30 mg) by the coefficient corresponding to the respective age group in Table 2.
l. For remedies containing the active ingredients from Column IV of Table 1 with dosage for children under 15 years of age, the maximum single dose is 140 mg and the maximum daily dose is 420 mg. The maximum daily dose for

children under 15 years of age is the amount obtained by multiplying the maximum daily dose (420 mg) by the coefficient corresponding to the respective age group in Table 2.

(5) Indications

a. The indications include “cough, cough associated with wheezing (wheezy, whistling), and sputum.”
However, for indications in the left column of the following table to be claimed, at least 1 of the ingredients from the corresponding right column must be included.
b. When the active ingredients from Column IV of Table 1 are combined, the indications are “cough or sputum associated with sore throat.” However, they should be combined concomitantly with any ingredient with indications of “cough” and “sputum” from the left column of the next table.
c. When only the active ingredients from Group 2 and Group 3 in Column VI of Table 1 are combined concomitantly, the indications are “sputum and cough with sputum”.
d. For troches and drops, in addition to the above indications, the following may also be given: hoarse voice due to throat inflammation, rough throat, throat discomfort, sore throat, and swollen throat.

Left column	Right column
Cough	Ingredients from Columns I, II, III, XII, or XIII of Table 1
Cough associated with wheezing (wheezy, whistling)	Ingredients from Column II, V, or XII in Table 1, except for cases in which an ingredient from Column I of Table 1 is also combined.
Phlegm (sputum)	Tipepidine citrate or tipepidine hibenzate from Group 1 in Column I of Table 1 or the ingredients from Columns II, V, VI, VII, XII, or XIV
Cough associated with sore throat and sputum	Ingredients from Column IV of Table 1, only when combined concomitantly with any ingredient with indications of “cough” and “sputum.”
Sputum and cough with sputum	Only when combined concomitantly with only the ingredients from Group 2 and Group 3 in Column VI of Table 1.

(6) Packaging Units

The maximum volume of containers for oral solutions and syrups is a 4-day supply at the maximum daily dose for adults (15 years of age and older).

Table 1

Active Ingredients and Maximum Single and Daily Doses

Category		Name of active ingredient	Maximum single dose (mg)	Maximum daily dose (mg)
Column I	Group1	Alloclamide hydrochloride	25	75
		Tipepidine citrate Cloperastine	20	60
		hydrochloride Chloperastine	20	60
		phendizoate Codeine phosphate	35	105
		Dihydrocodeine phosphate	20	60
		Dibunate sodium Tipepidine	10	30
		hibenzate	30	90
		Dextromethorphan hydrobromide	25	75
		△Dextromethorphan	20	60
		phenolphthalinate	30	90
		Carbetapentane citrate	20	60
	Group2	Dimemorfan phosphate	15 (10)	60 (30)
Column II		Trimethoquinol hydrochloride	2	6
		△ *dl*-Methylephedrine hydrochloride *l*-Methylephedrine hydrochloride	25	75
			25	75
		Methoxyphenamine hydrochloride	50	150
Column III		△Noscapine	20	60
		Noscapine hydrochloride	20	60
Column IV		Tranexamic acid	250 (70)	750 (280)
Column V		Aminophylline	100	300
		Diprophylline	100	300
		Theophylline	200	600
		Proxyphylline	70	210
Column VI	Group 1	Foeniculated ammonia spirit (as 1 ingredient) Ammonium chloride	2mL	-
			300	900
		△Guaifenesin	100	300
		△Potassium guaiacolsulfonate	90	270
		△Potassium cresolsulphonate	90	270
		l-Menthol	-	90
	Group 2	Bromhexine hydrochloride	4 (2)	12 (8)
	Group 3	L-carbocysteine	250	750
Column VII		Ethyl L-cysteine hydrochloride	100	300
		Methyl L-cysteine hydrochloride	100	300

Column VIII	Group1	Alimemazine tartrate	2.5	7.5
		Isothipendyl hydrochloride	4	12
		Iproheptine hydrochloride	50	150
		Difeterol hydrochloride	30	90
		Tripelenamine hydrochloride	25	75
		Thonzylamine hydrochloride	20	60
		Fenethazine hydrochloride	30	90
		Chlorpheniramine maleate	4	12
		d-Chlorpheniramine maleate	2	6
		Carbinoxamine diphenyldisulfonate	4	12
		Diphenylpyraline hydrochloride	2	6
		Diphenylpyraline teoclate	3	9
		Diphenhydramine hydrochloride	30	90
		Diphenhydramine salicylate	40	120
		Diphenhydramine tannate	50	150
		Fenethazine tannate Triprolidine	45	135
		hydrochloride Promethazine	2	6
		hydrochloride Promethazine	5	15
		methylene disalycilate	6	18
		Carbinoxamine maleate	4	12
		Difeterol phosphate	30	90
	Group2	Clemastine fumarate	0.334 [as clemastine]	1 [as clemastine]
Column IX		Caffeine and sodium benzoate	100	300
		Caffeine hydrate	100	300
		Anhydrous caffeine	100	300
Column X		△Chlorhexidine hydrochloride	5	-
		△Cetylpyridinium chloride	1	-
		△Dequalinium chloride	0.25	-
Column XI		Glycine		900
		Magnesium silicate		3000
		Synthetic aluminum silicate		3000
		Synthetic hydrotalcite		4000
		Magnesium oxide		500
		Dihyrdoxyaluminum and aminoacetate		1500
		Aluminum hydroxide gel (as dried aluminum hydroxide gel)		1000
		Dried aluminum hydroxide gel		1000
		Aluminum hydroxide-Sodium hydrogen carbonate coprecipitate		900
		Aluminum hydroxide-Magnesium carbonate mixed dried gel		3000
		Aluminum hydroxide-Magnesium carbonate-Calcium carbonate coprecipitate		1500
		Magnesium hydroxide-Aluminum potassium sulfate coprecipitation product		1800
		Magnesium carbonate		2000
		Magnesium aluminometasilicate		1500

(Crude drugs)

Category	Name of crude drug or Kampo medicine formula	Maximum daily dose (g)	
		Extract (converted to the crude drug amount)	Powder
Column XII	Ephedra Herb	4	-
Column XIII	Nandina Fruit	10	-
Column XIV	Cherry Bark Polygala	4	-
	Root Glycyrrhiza	5	-
	Platycodon Root	5	1.5
	Apricot Kernel	4	2
	Plantago Seed Plantago	4	-
	Herb Lycoris Radiata	5	-
	Bulb Senega	10	-
	Ipecac Fritillaria	0.8	-
	Bulb	4	1.5
		0.05	0.05
		2.5	1.5
Column XV	Gambir	-	2
	Fennel	3	-
	Scutellaria Root	6	3
	Trichosanthes Seed	2	-
	Cinnamon Bark	5	1
	Oriental Bezoar	-	0.02
	Schisandra Fruit	5	-
	Asiasarum Root Aster	3	-
	Root	5	-
	Musk Adenophora	-	0.01
	Root Ginger	5	2.5
	Mulberry Bark Perilla	3	1
	Herb	5	-
	Panax Japonicus Rhizome	2	-
	Citrus Unshiu Peel Ginseng	6	3
	Ophiopogon Tuber	5	3
	Pinellia Tuber	6	3
		10	-
		5	-

(Note) A numerical value within parentheses is the lower limit of amounts for combination.

Table 2

Range of Age Coefficients

Age	Coefficient
15 years of age and older	1
11 to under 15 years of age	2/3
8 to under 11 years of age	1/2
5 to under 8 years of age	1/3
3 to under 5 years of age	1/4
1 to under 3 years of age	1/5
3 months to under 1 year of age	1/10

Appendix 5

Provisional Translation
from Japanese Original

Apr 22, 1980
Notification PFSB No.520
Final revision Mar 28, 1986

The Standards for Marketing Approval of Gastrointestinal Medicines

1. Scope of Gastrointestinal Medicines

The scope of preparations subject to these standards covers all medicines for oral use formulated with the intent of relieving symptoms of gastrointestinal diseases (evacuants and Kampo medicine* formulas are not covered).

*Kampo medicine is traditional Japanese medicine.

2. Approval Standards

The approval standards for gastrointestinal medicines are as follows.

For preparations not conforming to these standards, efficacy and safety data 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) The types of active ingredients that may be used are shown in Table 1.

(b) Preparations mainly containing active ingredients from Column I, II, III, or IV can be mutually combined with other active ingredients from Columns I, II, III, and IV as well as the active ingredients from Columns V (limited to those with a "□" mark in Groups 3, 4, and 5), VII, and VIII.

However, notwithstanding the above rules, preparations having their main active ingredients only from Column I cannot include the following active ingredients: those in Group 2 of Column IV or those with a "□" mark in Group 5 of Column V. Preparations mainly containing active ingredients only from Column IV cannot include the active ingredients from Column VII.

(c) Preparations mainly containing active ingredients from Column V of Table 1 can include the active ingredients from Column I, II, III, IV, or VI (limited to Scopolia Extract in Group 1 and ingredients in Group 4).

(d) Preparations mainly containing active ingredients from Column VI of Table 1 can include the active ingredients from Column I (except Group 3), II, III, or V (limited to Groups 3 and 4).

However, preparations mainly containing active ingredients from Group 1 of Column VI cannot include the active ingredients from Column II (limited to Nux Vomica Extract in Group 1 or ingredients in Group 3). When the active ingredients from Column VI (except for Group 4) are used in combination, they should be limited to 1 type from each group.

(e) When the active ingredients from Column VII (except for Group 9) of Table 1 are used in combination, they should be limited to 1 type from each group.

(f) The active ingredients from Column I (excluding Group 3) and Group 2 of Column II cannot be combined in the same preparation.

(g) When the same active ingredient appears in at least 2 columns of Table 1, it

should not be duplicated in the formula.

(h) Berberine chloride and berberine tannate in Group 1 of Column V must not be combined with Coptis Rhizome or Phellodendron Bark in Group 1 of Column II or Group 5 of Column V of Table 1. Glycyrrhizinic acid, its salts, and glycyrrhiza extracts in Group 3 of Column VII cannot be combined with Glycyrrhiza in Group 9 of Column VII.

(i) The vitamins given in the Appendix may be combined with the active ingredients listed in Table 1 as long as there is good reason for their combination and the effect is mild.

(2) Quantities of Active Ingredients

(a) The maximum daily doses of the active ingredients listed in Table 1 (except for those in Group 1 of Column III and Group 1 of Column IV) should correspond to data in Table 1. The maximum single dose should be 1/3rd of the maximum daily dose.

(b) When not less than 2 active ingredients in Group 1 or Group 2 of Column I listed in Table 1 are combined, the sum of the values obtained by dividing the amount of each active ingredient by its respective maximum daily dose should not exceed 2.

(c) When at least 2 active ingredients in Group 2 or Group 3 of Column II are combined, or when at least 2 active ingredients in Group 2 of Column III or at least 2 active ingredients in Group 1, 2, 3, or 4 of Column V of Table 1 are included, the sum of the values obtained by dividing the amount of each active ingredient by its respective maximum daily dose should not exceed 1 for any group.

(d) When the crude drugs marked with "*" in Group 1 of Column II in Table 1 are combined in preparations for which the main active ingredient comes from Column I, the daily dose of the crude drug concerned should not be more than 1/10th of the maximum daily dose shown in Table 1.

(e) When preparations whose main active ingredients are from Groups 1 and 2 of Column I and which are tested for acid-neutralizing capacity or pH by the methods specified elsewhere, the acid-neutralizing capacity of the daily dose of the preparation should not be less than 150 mL when expressed as the amount of 0.1N hydrochloric acid consumed, and the pH of the preparation should not be less than 3.5.
The acid-neutralizing capacity of a single dose of the preparation should be not less than 50 mL.

(f) In preparations mainly containing active ingredients from Group 1 of Column III of Table 1, the digestive activity of the digestive enzymes included in a single dose of the preparation should not be less than the minimum daily unit for at least 1 of the following: starch saccharifying activity, starch dextrinizing activity, starch liquefying activity, protein digesting activity, fat digesting activity, fibrin saccharifying activity, or fibrin disintegrating activity specified in Group 1 of Column III.
The minimum unit for a single dose shall be 1/3rd of the minimum daily unit.

(g) For preparations mainly containing active ingredients from Group 1 of Column IV in Table 1, the minimum daily dose of the active ingredient concerned should be the amount shown in Table 1, and the minimum single dose should be 1/3rd of the minimum daily dose.

(3) Dosage Form

The dosage forms should be capsules, granules, pills, fine granules, powders, electuaries, tablets, infusions, decoctions, or liquids for oral use (limited to mildly

acting preparations mainly containing ingredients from Column I or II).

(4) Dosage and Administration

(a) In principle, dosage and administration should be 3 times a day.
Oral liquids mainly containing ingredients from Column I or II, or preparations mainly containing ingredients from Column V or VI listed in Table 1 can be taken 1 to 3 times a day, and if they are taken not less than 2 times a day, the interval between doses must not be less than 4 hours.

(b) For infusions and decoctions, the method of preparation at the time of use should be indicated.

(c) The time of administration (such as before or after meals, between meals) and the administration interval should be indicated.

(d) Dosage in infants less than 3 months of age is not approved.

(e) For capsules, pills, or tablets larger than 6 mm in diameter, dosage in children less than 5 years of age is not approved.

(f) For pills or tablets smaller than 6 mm in diameter, dosage in children less than 3 years of age is not approved.

(g) The maximum daily dose for children less than 15 years of age should be obtained by multiplying the maximum daily doses listed in Table 1 by the values given in the coefficient column for the corresponding age ranges stated in Table 2.

(h) The minimum daily doses specified in (2) (e) and (2) (f) should be multiplied by the values given in the coefficient column for the corresponding age ranges in Table 2 to obtain the minimum daily dose for children less than 15 years of age. However, the minimum daily doses specified in (2) (g) should be applied irrespective of age.

(5) Indications

(a) The range of indications for preparations mainly containing active ingredients from the columns of Table 1 (except Columns VII and VIII) is shown in Table 3. When active ingredients from at least 2 of Columns I, II, III, and IV are used as the main ingredients, the indications should cover all of those in the columns concerned.
The indications in Column III of Table 3 can be claimed for preparations whose main active ingredients are from Group 1 in Column III, only if the minimum daily units of at least 1 of the following are achieved: starch saccharifying activity, starch dextrinizing activity, starch liquefying activity, protein digestive activity, and fat digestive activity.

(b) For preparations claiming the indications mentioned in Column V or VI of Table 3, the indications listed in the other columns of the same table should not be claimed.

(c) Notwithstanding the above standards, the indications in Column I of Table 3 cannot be claimed in cases where Nux Vomica Extract in Group 1 of Column II is included in preparations containing active ingredients from Column I in Table 1.
In addition, the indications in Column I of Table 3 cannot be claimed for preparations containing active ingredients only from Group 3 of Column I in Table 1.

(Table 1)

Classification		Active ingredient	Maximum daily dose
Column I	Group 1	Dried aluminum hydroxide gel	3 g
		Magnesium aluminosilicate	4 g
		Magnesium silicate	6 g
		Synthetic aluminum silicate	10 g
		Synthetic hydrotalcite	4 g
		Magnesium oxide	1 g
		Magnesium hydroxide-aluminum hydroxide co-precipitate	4 g
		Aluminum hydroxide gel	30 mL (1.2 g as aluminum oxide)
		Aluminum hydroxide-sodium bicarbonate co-precipitate	2 g
		Dried mixed aluminum hydroxide and magnesium carbonate gel	3 g
		Aluminum hydroxide-magnesium carbonate-calcium carbonate co-precipitate	4 g
		Magnesium hydroxide	2.4 g
		Sodium bicarbonate	5 g
		Magnesium carbonate	2 g
		Precipitated calcium carbonate	3 g
		Magnesium aluminometasilicate	4 g
		Anhydrous dibasic calcium phosphate	2.4 g
		Dibasic calcium phosphate	3 g
		Cuttlefish Bone	3 g
		Abalone Shell	3 g
		Oyster Shell	3 g
	Group 2	Aminoacetic acid	0.9 g
		Dihydroxyaluminum aminoacetate	3 g
	Group 3	Scopolia Extract	30 mg

Classification		Active ingredient	Maximum daily dose (g)		Classification		Active ingredient	Maximum daily dose (g)	
			Extract (converted to crude drug amount)	Powder				Extract (converted to crude drug amount)	Powder
Column II	Group 1	Aniseed	3	1	Column II	Group 1	Citrus Unshiu Peel	5	3
		Aloe	–	0.15			*Capsicum	–	0.1
		Fennel	3	1			Bitter Orange Peel	5	3
		Turmeric	6	2			Animal bile (including Bear Bile)	–	0.5
		Lindera Root	5	1			Picrasma Wood	5	0.5
		Isodon Herb	10	3			Nutmeg	3	1
		Scutellaria Root	6	3			Ginseng	6	3
		Phellodendron Bark	3	3			Mentha Herb (including peppermint)	3	1
		Coptis Rhizome	3	1.5			Long pepper	2	0.5
		Processed Garlic Bulb	–	0.2			Atractylodes Rhizome	5	2
		Zedoary	3	3			Hop Strobile	3	1
		Pogostemon Herb	8	3			Nux Vomica Extract	–	0.03
		Calamus Root	6	2			Menyanthes trifolia herb	4	1.3
		Processed Ginger	3	1					
		Orange Fruit	5	2			Saussurea Root	3	1
		Immature Orange	5	2			Bitter Cardamon	3	1
		Cinnamon Bark	5	1			Japanese Gentian	1.5	0.5
		Gentian	1.5	0.5			Alpinia Officinarum Rhizome	3	1
		Red Ginseng	6	3					
		Magnolia Bark	5	1.5			Fennel Oil	0.08	
		Euodia Fruit	3	1			Cinnamon Oil	0.03	
		*Pepper	5	1.5			Ginger Oil	0.03	
		Calumba	5	1.5			Cardamon Oil	0.03	
		Condurango	9	3			Clove Oil	0.02	
		*Japanese Zanthoxylum Peel	3	1			Bitter Orange Peel Oil	0.03	
		Resurrection Lily Rhizome	6	2			Mentha Oil	0.03	
		Perilla Fruit	6	3			Lemon Oil	0.03	
		Amomum Seed	3	1			*l*-Menthol	0.18	
		Ginger	3	1			*dl*-Menthol	0.18	

		Cardamon	3	1		Group 2	Betaine hydrochloride	0.6
		Immature Citrus Unshiu Peel	5	3			L-Glutamic acid hydrochloride	1.8
		Acorus Gramineus Rhizome	6	2				
		Centaury Herb	2	0.7				
		Swertia Herb	1.5	0.05		Group 3	Carnitine chloride	0.6
		Atractylodes Lancea Rhizome	5	2				
		Perilla Herb	2	1			Bethanechol chloride	0.045
		Star Anise	3	1				
		Rhubarb	0.2	0.1		Group 4	Dried yeast	10
		Panax Japonicus Rhizome	6	3				
		Clove	2	0.5				

Classification		Active ingredient	Minimum daily unit[Note 1)]	
Column III	Group 1	Starch digestive enzymes	Starch saccharifying activity:	250 units
			Starch dextrinizing activity:	210 units
			Starch liquefying activity:	360 units
		Protein digestive enzymes	Proteolytic activity:	1,500 units
		Fat digestive enzymes	Fat digestive activity:	100 units
		Fibrin digestive enzymes	Fibrin saccharifying activity:	13 units
			Fibrin disintegrating activity:	25 units
	Group 2	Active ingredient	Maximum daily dose (g)	
		Ursodesoxycholic acid	0.06	
		Oxycholanates	0.15	
		Cholic acid	0.9	
		Bile powder	1.5	
		Bile extract (powder)	0.5	
		Dehydrocholic acid	0.5	
		Animal bile (including Bear Bile)	0.5	

Note 1) Methods for measuring the digestive activity of each digestive enzyme are specified separately.

		Active ingredient	Minimum daily dose	
Column IV	Group 1	Live bacteria for intestinal regulation	1×10^6	
	Group 2		Maximum daily dose (g)	
			Extract (converted to crude drug amount)	Powder
		Mallotus Bark	5	1.5
		Gambir	–	2
		Processed Mume	10	3
		Cassia Seed	10	3
		Geranium Herb	10	3

Classification		Active ingredient	Maximum daily dose (g)	
Column V	Group 1	Acrinol	0.3	
		Berberine chloride	0.3	
		Guaiacol	0.6	
		Creosote	0.5	
		Phenyl salicylate	1	
		Guaiacol carbonate	1.2	
		Berberine tannate	0.3	
	Group 2	Bismuth subsalicylate	3	
		Bismuth subnitrate	2	
		Bismuth subcarbonate	3	
		Bismuth subgallate	2	
		Tannic acid	1.2	
		Albumin tannate	4	
		Methylene thymol tannin	2	
	Group 3	Kaolin	10	
		Natural aluminum silicate	10	
		Aluminum hydroxynaphthoate	0.9	
		Pectin	0.6	
		Medicinal carbon	5	
	Group 4	Precipitated calcium carbonate	3	
		Calcium lactate	5	
		Dibasic calcium phosphate	3	
			Extract (g) (converted to crude drug amount)	Powder (g)
	Group 5	□ Gambir	-	2
		□ Processed Mume	10	3
		Phellodendron Bark	9	3
		Coptis Rhizome	3	1.5
		Sophora Root	3	1.5
		□ Geranium Herb	10	3
		Rhus Javanica Nutgall	-	3
		□ Crataegus Fruit Swertia	8	3
		Herb Myrica Rubra	-	0.9
		Bark	5	2

Classification		Active ingredient	Maximum daily dose	
Column VI	Group 1	Oxyphencyclimine hydrochloride	7 mg	
		Dicyclomine hydrochloride	30 mg	
		Methixene hydrochloride	8.75 mg	
		Scopolamine hydrobromide	0.3 mg	
		Atropine methylbromide	6 mg	
		Anisotropine methylbromide	30 mg	
		Scopolamine methylbromide	4.8 mg	
		l-Hyoscyamine methylbromide	2.25 mg	
		Methylbenactyzium bromide	30 mg	
		Belladonna extract	60 mg	
		Isopropamide iodide	7.5 mg	
		Diphenylpiperidinomethyldioxolane iodide	60 mg	
		Scopolia Extract	60 mg	
		Scopolia Rhizome (Total) Alkaloid citrates	1 mg	
	Group 2	Papaverine hydrochloride	90 mg	
	Group 3	Ethyl aminobenzoate	0.6 g	
			Extract (g) (converted to crude drug amount)	Powder (g)
	Group 4	Corydalis Tuber	5	1.5
		Glycyrrhiza	5	1.5
		Magnolia Bark	5	1.5
		Peony Root	5	2

Classification		Active ingredient	Maximum daily dose (g)	
Column VII	Group 1	Sodium azulene sulfonate	0.006	
	Group 2	Aldioxa	0.3	
	Group 3	Glycyrrhizinic acid, its salts, and glycyrrhiza extracts	(as glycyrrhizinic acid) 0.2	
	Group 4	L-Glutamine	2	
	Group 5	Potassium copper chlorophyllin Sodium copper chlorophyllin	0.2 0.2	
	Group 6	Histidine monohydrochloride	0.18	
	Group 7	Pepsin decomposition products of pig stomach wall Acid hydrolysis products of pig stomach wall	0.3 0.3	
	Group 8	Methylmethioninesulfonium chloride	0.15	
	Group 9		Extract (g) (converted to crude drug amount)	Powder (g)
		Mallotus Bark	5	1.5
		Corydalis Tuber	5	1.5
		Glycyrrhiza	5	1.5

Column VIII	Dimethylpolysiloxane	0.18 g

(Table 2) Age coefficients

Age	Coefficients
15 years of age or over	1
11 to under 15 years of age	2/3
8 to under 11 years of age	1/2
5 to under 8 years of age	1/3
3 to under 5 years of age	1/4
1 to under 3 years of age	1/5
3 months to under 1 year of age	1/10

(Table 3)

Main ingredient	Indications
Column I	Hyperacidity, heartburn, feeling of discomfort in the stomach, feeling of fullness in the stomach, constricted feeling in the stomach (stomach heaviness), heaviness in the stomach, heaviness in the chest, belching (burping), nausea (retching, stomach retching, retching due to hangovers and overdrinking, sick feeling, and feeling of sickness), vomiting, excessive drinking (overdrinking), and stomachache
Column II	Loss of appetite (anorexia), feeling of fullness in the stomach and abdomen, indigestion, weak stomach, excessive eating (overeating), excessive drinking (overdrinking), heartburn, constricted feeling in the stomach (stomach heaviness), heaviness in the chest, nausea (retching, stomach retching, retching due to hangovers and overdrinking, sick feeling, and feeling of sickness), and vomiting
Column III	For promoting digestion, indigestion, loss of appetite (anorexia), excessive eating (overeating), constricted feeling in the stomach (stomach heaviness), heaviness in the chest, and feeling of fullness in the stomach and abdomen due to indigestion
Column IV	Intestinal regulation (regulation of stool), feeling of fullness in the abdomen, soft stool, and constipation
Column V	Diarrhea, diarrhea due to indigestion, food poisoning, vomiting and purging, water poisoning, loose bowels, soft stool, and diarrhea accompanied by abdominal pain[Note 1)]
Column VI	Stomachache, abdominal pain, gripping pain (colic, spasms), hyperacidity, and heartburn

Note 1) Only when scopolia extract in Group 1 of Column VI is included.

(Appendix)

1. Vitamins that can be included in preparations mainly containing active ingredients from Column II or III are indicated below, together with their maximum daily doses.

Ingredient	Maximum daily dose
Vitamin B_1, its derivatives, and their salts	25 mg

2. Vitamins that can be included in preparations mainly containing active ingredients from Column IV are listed below, together with their maximum daily doses.

Ingredient	Maximum daily dose
Nicotinamide	5 mg
Calcium pantothenate Biotin	30 mg
Vitamin B_1, its derivatives, and their salts	25 μg
Vitamin B_2, its derivatives, and their salts	25 mg
Vitamin B_6, its derivatives, and their salts	12 mg
Vitamin C, its derivatives, and their salts	50 mg
	500 mg

However, the combination of biotin and nicotinamide is permitted only when including live lactic acid bacteria or lactic acid producing bacteria for intestinal regulation.

3. Vitamins that can be included in preparations mainly containing active ingredients from Column V are listed below, together with their maximum daily doses.

Ingredient	Maximum daily dose
Vitamin B_1, its derivatives, and their salts Vitamin B_2, its derivatives, and their salts	25 mg 12 mg

Appendix 14

Provisional Translation
from Japanese Original

May 15, 1998
Notification PSB No.447

The Standards Marketing Approval of Athlete's Foot and Ringworm Remedies

1 Scope of Athlete's Foot and Ringworm Remedies

The scope of preparations subject to these standards covers external medicines intended for the relief of symptoms associated with athlete's foot and ringworm Kampo medicine* formulas and non-Kampo crude drug remedies consisting of crude drug only are not covered).

*Kampo medicine is traditional Japanese medicine.

2 Approval Standards

The approval standards for athlete's foot and ringworm remedies are as follows. For preparations deviating from these standards, efficacy and safety data 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. The types of active ingredients that may be combined are listed in Table 1.
b. At least 1 of the active ingredients from either Column I (apart from the ingredients in Groups 12 and 13) or Column II of Table 1 must be combined.
c. Active ingredients in different columns listed in Table 1 may be mutually combined.
d. When active ingredients from Column V of Table 1 are to be combined with other ingredients in the same Column, the use of only 1 ingredient is allowed.
e. Up to 3 active ingredients from Column I of Table 1 may be used. However, with the exception of undecylenic acid and zinc undecylenate in Group 1, the use of only 1 ingredient from each group is allowed. Active ingredients marked with "□" must not be combined with the other ingredients in this column.
f. When active ingredients from Group 1 of Column III or Group 1 of Column IV listed in Table 1 are to be combined, the use of only 1 ingredient from the same group is allowed.
g. Up to 3 active ingredients from Group 2 of Column III listed in Table 1 may be used. However, acetic acid should not be combined with the other ingredients in this group.
h. In Column VI, the combination of allantoin with aldioxa and the combination of glycyrrhizinic acid or its salts with glycyrrhetinic acid are not permitted. In Column VII, the combination of *d*-camphor with *dl*-camphor and the combination of mentha oil with *dl*-menthol and *l*-menthol are not permitted.

(2) Quantities of Active Ingredients

a. The maximum concentration of each of the active ingredients is shown in Table 1.
b. The minimum concentration of individual active ingredients listed in Column I (except for Groups 12 and 13) and Column II of Table 1 is 1/5th of the maximum

concentration (for ingredients with a concentration in parentheses, the minimum concentration is 1/5th of the one in the parentheses). In this case, the concentration of 1 or more ingredients must be at least half of the specified maximum concentration (for ingredients with concentrations in parentheses, the minimum concentration must be the one provided in parentheses).

c. The minimum concentration of individual active ingredients listed in Groups 12 and 13 of Column I and those listed in Columns III, IV, V, VI, VII, VIII, and IX of Table 1 is 1/10th of the maximum concentration. However, in the case of benzalkonium chloride in Group 1 of Column III, the concentration must be as listed in the maximum concentration column.

(3) Dosage Form

The dosage forms are aerosols, ointments, external liquids, and external powders.

(4) Dosage and Administration

Preparations should be applied to the skin surface several times a day. The method of application should be clearly indicated.

(5) Indications

The indications are to be within the scope of "athlete's foot, jock itch, and ringworm."

Table 1

Classification		Active ingredient	Maximum concentration (%)
Column I	Group 1	Undecylenic acid	10
		Zinc undecylenate	20
		□ Phenyl-11-iode-10-undecynoate	0 5
	Group 2	□ Exalamide	5
	Group 3	□ Clotrimazole	1
		□ Econazole nitrate	1
		□ Miconazole nitrate	1
		□ Tioconazole	1
	Group 4	□ Zinc diethyldithiocarbamate	25
	Group 5	□ Ciclopirox olamine	1
	Group 6	□ Siccanin	1 (potency)
		□ Trichomycin	15,000,000 units/100 g
		□ Pyrrolnitrin	0.5 (potency)
	Group 7	Thianthol	30
	Group 8	2,4,6-Tribromphenol caproate	2
	Group 9	Trimethylcetylammonium pentachlorophenate	2
	Group 10	□ Tolciclate	1
		Tolnaftate	2
	Group 11	□ Haloprogin	1
	Group 12	Sulfur	10
	Group 13	Hibiscus syriacus bark (converted to the crude drug amount)	10
Column II	Group 1	Salicylic acid	10 (2)
	Group 2	Zinc oxide	60 (2)
Column III	Group 1	Acrinol	0 2
		Alkylpolyaminoethyl glycine	1
		Berberine benzoate	0 5
		Isopropylmethylphenol	3
		Dequalinium chloride	0 5
		Benzalkonium chloride	0.05
		Benzethonium chloride	0 5
		Chlorhexidine hydrochloride	1
		Chlorhexidine gluconate solution	2 5
		Dequalinium acetate	1
		Hinokitiol	0 1
		Resorcin	5
	Group 2	Benzoic acid	12
		Chlorobutanol	1
		Acetic acid	2
		Phenol	2
		Iodine tincture	20

Column IV	Group 1	Diphenylpyraline hydrochloride	0 2
		Diphenhydramine hydrochloride	2
		Chlorpheniramine	0 5
		Diphenhydramine salicylate	2
		Diphenylimidazole	0 2
		Diphenhydramine	1
		Chlorpheniramine maleate	0 5
	Group 2	Crotamiton	10
Column V		Ethyl aminobenzoate	6
		Dibucaine hydrochloride	0 5
		Procaine hydrochloride	2
		Lidocaine hydrochloride	2 5
		Oxypolyethoxydodecane	3
		Dibucaine	0 5
		Lidocaine	2 5
Column VII	Group 1	Allantoin	1
		Aldioxa	0 2
		Ichthammol	6
		Glycyrrhizinic acid and its salts	1
		Glycyrrhetinic acid	1
		Methyl salicylate	2 5
		Dimethyl isopropylazulene	0.04
	Group 2	Lithospermum root (converted to the crude drug amount)	6
		Japanese angelica root (converted to the crude drug amount)	6
Column VII		*d*-Camphor	4
		dl-Camphor	4
		Thymol	2 5
		Mentha oil	0 5
		dl-Menthol	3
		l-Menthol	3
		d-Borneol	5
Column VIII		Urea	10
		Diethyl phthalate	25
Column IX		Aluminum hydroxychloride	10