事　務　連　絡
平成27年9月29日

各都道府県衛生主管部（局）薬務主管課　御中

厚生労働省医薬食品局審査管理課

かぜ薬等の製造販売承認基準の英訳について

一般用医薬品のうち、下記のかぜ薬等の製造販売の承認基準（通知）については、別添のとおり、当該基準の英訳を作成したのでお知らせいたします。

記

別添	通知名	発出年月日等
1	かぜ薬の製造販売承認基準について	平成27年3月25日付け薬食発0325第28号
2	解熱鎮痛薬の製造販売承認基準について	平成27年3月25日付け薬食発0325第30号
3	鎮咳去痰薬の製造販売承認基準について	平成27年3月25日付け薬食発0325第26号
4	鼻炎用内服薬の製造販売承認基準について	平成27年3月25日付け薬食発0325第23号
5	胃腸薬製造（輸入）承認基準について	昭和55年4月22日付け薬発第520号
6	瀉下薬製造（輸入）承認基準について	昭和57年5月17日付け薬発第463号
7	鎮暈薬製造（輸入）承認基準について	昭和59年6月1日付け薬発第381号
8	眼科用薬製造（輸入）承認基準について	昭和61年7月29日付け薬発第623号
9	ビタミン主薬製剤製造（輸入）承認基準について	昭和63年2月1日付け薬発第90号
10	浣腸薬製造（輸入）承認基準について	昭和63年2月1日付け薬発第94号
11	駆虫薬製造（輸入）承認基準について	平成元年3月28日付け薬発第300号
12	鼻炎用点鼻薬製造（輸入）承認基準について	平成3年2月1日付け薬発第109号
13	外用痔疾用薬製造（輸入）承認基準等について	平成7年3月22日付け薬発第277号
14	みずむし・たむし用薬製造（輸入）承認基準等について	平成10年5月15日付け薬発第447号
15	鎮痒消炎薬の製造販売承認基準について	平成23年11月1日付け薬発第1号

別添 1

Provisional Translation
from Japanese Original

Mar 25, 2015
Notification PB No.28

The Standards for Marketing Approval of Cold Remedies

1. Scope of Cold Remedies

The scope of either medicines subject to these standards covers all oral medicines intended for use in treating cold symptoms (Kampo medicine* formulas are not covered).

*Kampo medicine is traditional Japanese medicine.

2. Approval Standards

The approval standards for cold remedies are as follows. For either medicines 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 combined are shown in Table 1.
b. At least 1 of the active ingredients from Group 1 or 2 in Column I of Table 1 must be included. However, in the case of formulas consisting of crude drugs only, Earthworm (Lumbricus) from Column XVI of Table 1 should be combined instead of them.
c. Active ingredients from different columns of Table 1 may be combined with each other, unless otherwise stipulated.
d. Active ingredients from Column VIII of Table 1 may be combined only in formulas that contain active ingredients from Column II of the table.
e. Up to 3 of the active ingredients from Group 1 in Column I of Table 1 can be combined.
f. When the active ingredients from Column II, III, IV, V, VI, VIII, IX, or X or the Kampo medicine formulas from Column XVII of Table 1 are combined, one ingredient can be used from each Column. However, the active ingredients from Groups 2 and 3 in Column VI of Table 1 may be combined at the same time.
g. When the active ingredients from Group 2 in Column I of Table 1 are combined, they should not be combined simultaneously with the active ingredients from Group 1 or 3 in the same column.
h. When the active ingredients from Group 2 from Column I of Table 1 are combined, they should not be combined simultaneously with the active ingredients from Group 2 in Column III, Group 3 in Column VI, from Column VII, Column XIII or Column XIV, Earthworm from Column XVII or the Kampo medicine formulas from Column XVII.
i. When the active ingredients from Group 3 in Column I of Table 1 are combined, they should be combined simultaneously with acetaminophen from Group 1 in the same column, and should not be combined simultaneously with other active ingredients from the same column.
j. When the active ingredients from Group 3 in Column I of Table 1 are combined,

they should not be combined simultaneously with the active ingredients from Group 3 in Column II, Group 2 in Column III, from Column VI, Column XIII or the active ingredients from Column XIV, Earthworm from Column XVI, or the Kampo medicine formulas from Column XVII.

k. When the active ingredients from Group 2 in Column II of Table 1 are combined, they should not be combined simultaneously with the active ingredients from Column XIV or the Kampo medicine formulas from Column XVII.

l. When the active ingredients from Group 3 in Column II of Table 1 are combined, they should not be combined simultaneously with the active ingredients from Group 3 in Column I or from Column XIV or the Kampo medicine formulas from Column XVII.

m. When the active ingredients from Group 2 in Column III of Table 1 are combined, they should not be combined simultaneously with the active ingredients from Group 2 in Column I, Group 3 in Column I, from Column IV, Column VIII, Column IX, Column XIII, Column XIV or Column XV, or Kakkontokakikyo from Column XVII.

n. When the active ingredients from Group 2 in Column VI of Table 1 are combined, they should not be combined simultaneously with the active ingredients from Group 3 in Column I, from Column VIII, Column XIII, Column XIV or the Kampo medicine formulas from Column XVII.

o. When the active ingredients from Group 3 in Column VI of Table 1 are combined, they should not be combined simultaneously with the active ingredients from Group 2 in Column I, Group 3 in Column I, from Column VIII, Column XIII, Column XIV or the Kampo medicine formulas from Column XVII.

p. When the active ingredients from Column VII of Table 1 are combined, they should not be combined simultaneously with the active ingredients from Group 2 in Column I or from Column VIII or the Kampo medicine formulas from Column XVII.

q. When the active ingredients from Column VIII of Table 1 are combined, they should not be combined simultaneously with the active ingredients from Group 2 in Column III, Group 2 and Group 3 in Column VI, from Column VII, Column XIII or Column XIV or the Kampo medicine formulas from Column XVII.

r. When the active ingredients from Column IX of Table 1 are combined, they should not be combined simultaneously with the active ingredients from Group 2 in Column III, from Column XIII or Column XIV or the Kampo medicine formulas from Column XVII.

s. Combinations of glycyrrhizinic acid and its salts from Column IX of Table 1 and Glycyrrhiza from Column XV are not acceptable.

t. Combinations of Ephedra herb or Kampo medicine formulas containing Ephedra herb or their extracts and the active ingredients from Group V of Table 1 are not acceptable.

u. Combinations between the Kampo medicine formulas from Column XVII of Table 1 and the active ingredients from Column XIII, XIV, XV or XVI are not acceptable.

v. Apart from Kososan formula, Kampo medicine or non-Kampo crude drug medicines must be in the extract form when used in combinations.

w. The crude drugs used in the Kampo medicine formulas from Column XVII of Table 1 and their combination ratios must be as specified in Table 2.

(2)Quantities of Active Ingredients

a. The maximum daily dose of each of the active ingredients is that specified in Table 1, unless otherwise specified. However, when the active ingredients from Column V or XIII in Table 1 are combined with the ingredients in Column X, 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 2/3rd.

b. When 2 or more of the active ingredients from Group 1 in Column I of Table 1 are combined or when 2 or more of the active ingredients from Column XIII, XIV, or XV 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.

c. When the active ingredients from Group 1 in Column I of Table 1 are combined with Earthworm, Kakkonto formula, Maoto formula, or Kakkontokakikyo, the sum of the values obtained by dividing the amounts of the active ingredients or the formulations combined by their respective maximum daily doses should not exceed 1.

d. When used in combinations, the amounts of the Kampo medicine formulas from Column XVII of Table 1 must not be less than 1/5th and not more than half of the maximum daily dose.

e. The lower limit of the amounts of each of the active ingredients should be half of the maximum daily dose, unless otherwise specified.

f. When 2 or more of the active ingredients from Group 1 in Column I of Table 1 are combined, the lower limit of the amounts should be 1/5th of the maximum daily dose for each active ingredient, and the sum of the values obtained by dividing the amounts of each of the active ingredients by their respective maximum daily doses should be not less than half.

g. When used in combinations, the lower limit of the amounts of the active ingredients from Columns X and XII of Table 1 is 1/5th of the maximum daily dose.

h. When used in combinations, the lower limit of the amounts of glycyrrhizinic acid and its salts from columns IX of Table 1 and the active ingredients from Columns XIII, XIV, XV, and XVI is 1/10th of the respective maximum daily doses. However, in the case of combination with Earthworm as described in (1) b, the maximum daily dose from Column XVI should be combined.

i. In cases where indications for treatment of coughing and sputum are based only on the active ingredients from Columns XIII, XIV, or XV of Table 1, when used in combinations, the lower limits of the active ingredients from Columns XIII, XIV, or XV should be half of the respective maximum daily doses.
However, in cases where 2 or more of the crude drugs from Column XV are combined, the lower limit should be 1/5th of the respective maximum daily doses, and the sum of the values obtained by dividing the amounts of each of the active ingredients by their respective maximum daily dose should be not less than half.

j. The daily dose of the active ingredients from Group 2 in Column I of Table 1 should be limited to 450 mg.

k. The daily dose of the active ingredients from Group 3 in Column I of Table 1 should be limited to 300 mg, and the amount of acetaminophen from Column 1 in the same column, which is combined simultaneously, should be limited to 450 mg.

l. The daily dose of the active ingredients from Group 2 in Column II of Table 1 should be limited to 1 mg as clemastine.

m. The daily dose of the active ingredients from Group 3 in Column II of Table 1 should be limited to 4 mg.

n. The daily dose of the active ingredients from Group 2 in Column III of Table 1 should be limited to 30 mg.

o. The daily dose of the active ingredients from Group 3 in Column VI of Table 1 should be limited to 750 mg.

(3)Dosage Forms

The dosage forms are tablets, capsules, pills, granules, powders, and syrups.

(4)Dosage and Administration

a. Except for syrups, cold remedies are to be taken by oral administration 3 times a day within 30 minute after a meal. Syrups are to be taken, in principle, after every meal, However, if required, they can also be taken before going to bed. If it is absolutely necessary, they can be taken approximately every 4 hours up to a maximum of 6 times a day.
b. For hard capsules, 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.
c. For tablets 6 mm in diameter or less, dosage for children under 3 years of age is not approved.
d. For other dosage forms, dosage for infants under 3 months of age is not approved.
e. For children under the age of 15 years, the maximum daily doses acceptable are the values obtained by multiplying the amount of the active ingredient given in 2 (2) by the coefficients for each age group in Table 3, unless otherwise specified. The maximum single dose of syrups is calculated by using the range of coefficients, and dissolving or suspending 1/6th of the calculated value in water to make less than 10 mL in each case.
f. For formulas containing aspirin, aspirin aluminum, and sasapyrine from Group 1 in Column I, the active ingredients from Group 2 in Column 1, promethazine methylenedisalicylate from Group 1 in Column II, or the active ingredients from Group 3 in Column II, dosage for children under 15 years of age is not approved.
g. For formulas containing the active ingredients from Group 3 in Column VI, dosage for children under 8 years of age is not approved.
h. For formulas containing the active ingredients from Group 3 in Column I or Group 2 in Column II or tranexamic acid from Column IX, dosage for children under 5 years of age is not approved.
i. For formulas containing the active ingredients from Group 2 in Column III, dosage for children under 3 years of age is not approved.
j. For formulas containing tranexamic acid from Column IX of Table 1 with dosage for children under 15 years of age, 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) in Table 1 by the coefficient corresponding to the respective age group in Table 3.

(5)Indications

Relief of various symptoms of a common cold: running nose, stuffy nose, sneezing, sore throat, cough, phlegm (sputum), chills (feeling cold due to fever), fever, headache, joint pain, and muscle pain.

However, when any single type of the active ingredients listed in the right column of the following table is not included, the indications in the left column of the table cannot be claimed.

Left column	Right column
Runny nose, stuffy nose, sneezing	Ingredients from Column II of Table 1
Cough	Ingredients from Columns III, IV, V, XIII, or XIV of Table 1
Phlegm (sputum)	Tipepidine citrate or tipepidine hibenzate from Column III of Table 1 or the ingredients from Columns V, VI, VII, XIII, or XV

(6)Packaging Units

For syrups, the maximum volume of the containers is a 2-day supply at the maximum daily dosage for children aged 6 years.

Table 1

Active ingredients and Maximum Daily Doses

Category		Name of active ingredient	Maximum daily dose (mg)
Column I	Group 1	Aspirin	1500
		Aspirin aluminum	2000
		Acetaminophen	900
		Ethenzamide	1500
		Sasapyrine	1500
		Salicylamide	3000
		Lactylphenetidine	600
	Group 2	Ibuprofen	450
	Group 3	Isopropylantipyrine	300
Column II	Group 1	Isothipendyl hydrochloride	7
		Difeterol hydrochloride	90
		Tripelenamine hydrochloride	100
		Thonzylamine hydrochloride	50
		Fenethazine hydrochloride	50
		Methodilazine hydrochloride	8
		Chlorpheniramine maleate	7.5
		d-Chlorpheniramine maleate	3.5
		Carbinoxamine diphenyldisulfonate	7.5
		Diphenylpyraline hydrochloride	4
		Diphenylpyraline teoclate	4.5
		Diphenhydramine hydrochloride	75
		Diphenhydramine salicylate	75
		Alimemazine tartrate	5
		Diphenhydramine tannate	75
		Triprolidine hydrochloride	4
		Mebhydrolin napadisilate	150
		Promethazine methylenedisalicylate	40
		Carbinoxamine maleate	7.5
		Difeterol phosphate	90
	Group 2	Clemastine fumarate	1 [as clemastine]
	Group 3	Mequitazine	4
Column III	Group 1	Alloclamide hydrochloride	75
		Tipepidine citrate	60
		Cloperastine hydrochloride	48
		Chloperastine phendizoate	84
		Codeine phosphate	48
		Dihydrocodeine phosphate	24
		Dibunate sodium	90
		Tipepidine hibenzate	75
		Dextromethorphan hydrobromide	48
		Dextromethorphan phenolphthalinate	72
		Carbetapentane citrate	48
	Group 2	Dimemorfan phosphate	30
Column IV		Noscapine	48
		Noscapine hydrochloride	48

Column V		dl-Methylephedrine hydrochloride dl-Methylephedrine saccharinate	60 60
Column VI	Group 1	Guaifenesin Potassium guaiacolsulfonate Potassium cresolsulphonate	250 250 250 (135)
	Group 2	Bromhexine hydrochloride	12 (8)
	Group 3	L-carbocysteine	750
Column VII		Ethyl L-cysteine hydrochloride	300
Column VIII		Belladonna total alkaloid Isopropamide iodide extract	0.3 (0.12) 6 (1.5)
Column IX		Glycyrrhizinic acid and its salts Tranexamic acid	39 [as glycyrrhizinic acid] 750 (280)
Column X		Caffeine and sodium benzoate Caffeine hydrate Anhydrous caffeine	300 150 150
Column XI		Vitamin B_1, its derivatives, and their salts Vitamin B_2, its derivatives, and their salts Vitamin C, its derivatives, and their salts Hesperidin, its derivatives, and their salts	25 (1) 12 (2) 500 (50) 90 (18)

Column XII	Glycine	900
	Magnesium silicate	3000
	Synthetic aluminum silicate	3000
	Synthetic hydrotalcite	4000
	Magnesium oxide	500
	Dihyrdoxyaluminum and aminoacetate (aluminum glycinate)	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

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

Crude drugs and Kampo medicine formulas

Classification	Name of crude drug or Kampo medicine formula	Maximum daily dose (g)	
		Extract (converted to the amount of crude drug or preparation)	Powder
Column XIII	Ephedra Herb	4	–
Column XIV	Nandina Fruit	10	–
Column XV	Cherry Bark	4	–
	Polygala Root	5	–
	Glycyrrhiza	5	1.5
	Platycodon Root	4	2
	Plantago Seed	5	–
	Plantago Herb	10	–
	Lycoris Radiata Bulb	0.8	–
	Senega	4	1.5
	Fritillaria Bulb	2.5	1.5

Classification	Name of crude drug or Kampo medicine formula	Maximum daily dose (g)	
		Extract (converted to the amount of crude drug or preparation)	Powder
Column XVI	Fennel	3	–
	Phellodendron Bark	3	3
	Coptis Rhizome	3	1.5
	Zedoary	3	3
	German Chamomile Flower	10	–
	Cinnamon Bark	5	1
	Gentian	0.5	0.5
	Oriental Bezoar	–	0.02
	Animal gall (including Bear Bile)	0.5	0.5
	Adenophora Root	5	2.5
	Ginger	3	1
	Atractylodes Lancea Rhizome	5	2
	Clove	2	0.5
	Citrus Unshiu Peel	5	3
	Atractylodes Rhizome	5	2
	Earthworm (Lumbricus)	3	2
	Panax Japonicus Rhizome	6	3
	Ginseng	6	3
Column XVII	Kakkonto	25	–
	Kakkontokakikyo	29	–
	Keishito	15	–
	Kososan	11	6
	Saikokeishito	24	–
	Shosaikoto	24	–
	Shoseiryuto	24	–
	Bakumondoto	30	–
	Hangekovokuto	16	–
	Maoto	13	–

(Note) Powder combinations will not be accepted where no maximum daily dose is given in the powder column.

Table 2

Name of Kampo medicine formula		Kakkonto	Kakkontokakikyo	Keishito	Kososan	Saikokeishito	Shosaikoto	Shoseiryuto	Bakumondoto	Hangekovokuto	Maoto
Component crude drugs and combination ratios	Scutellaria Root					2	3				
	Pueraria Root	8	8								
	Glycyrrhiza	2	2	2	1	2	2	2	2		2
	Platycodon root		4								
	Apricot Kernel										4
	Cinnamon Bark	3	3	4		3		3			3
	Cyperus Rhizome				4						
	Brown Rice								10		
	Magnolia Bark									3	
	Schisandra Fruit							3			
	Bupleurum Root					5	7				
	Asiasarum Root							3			
	Peony Root	3	3	4		3		3			
	Ginger	1	1	1	1	1	1	2		1	
	Perilla Herb				2					2	
	Jujube	4	4	4		2	3		3		
	Citrus Unshiu Peel				3						
	Ginseng					2	3		2		
	Ophiopogon Tuber								8		
	Pinellia Tuber					4	5	5	5	5	
	Poria Sclerotium									5	
	Ephedra Herb	4	4					3			4

Table 3

Age coefficients

Age group	Coefficient
15 years of age and over	1
11 to under 15 years of age	2/3
7 to under 11 years of age	1/2
3 to 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

別添２

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The Standards for Marketing Approval of Antipyretic Analgesics

1. Scope of Antipyretic Analgesics

The scope of formulas subject to these standards covers oral medicines intended for the relief of pain or fever (cold remedies, formulations based on Kampo medicine* formulas and those consisting of crude drugs only are not covered).

*Kampo medicine is traditional Japanese medicine.

2. Approval Standards

The approval standards for antipyretic analgesics are as follows. For remedies 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 shown in Table 1.
b. Either one of the active ingredients from Group 1, Group2, and Group3 in Column I of Table 1 must be included.
c. Active ingredients from different columns of Table 1 may be combined with each other, unless otherwise stipulated.
d. Up to 3 of the active ingredients from Group 1 or 2 in Column I of Table 1 can be combined.
e. When the active ingredients from Group 3 in Column I of Table 1 are combined, they should not be combined simultaneously with the active ingredients from the same column. However, this rule does not apply when they are combined simultaneously with either one of acetaminophen from Group 1 of the same column, ethenzamide in Group 2, and the active ingredients from Group 4.
f. When the active ingredients from Group 3 in Column 1 of Table 1 are combined or when they are combined simultaneously with either one of acetaminophen in Group 1 and ethenzamide in Group 2 in the same column, the active ingredients from Columns II, III, IV, V, VI, VIII, and IX can be combined. However, when the active ingredients from Group 3 in Column I of Table 1 are combined at the maximum single dose, none of the other ingredients should be combined.
g. When the active ingredients from Group 4 in Column I of Table 1 are combined, they should be combined simultaneously with either one of acetaminophen from Group 1, ethenzamide from Group 2 and the active ingredients from Group 3 in the same column, and should not be combined simultaneously with other active ingredients from Groups 1 and 2 in the same column.
h. When the active ingredients from Group 4 in Column I of the Table 1 are combined simultaneously with acetaminophen from Group 1, ethenzamide from Group 2 and the active ingredients from Group 3 in the same column, the active ingredients from Columns II, IV, V, VI, VIII, and IX can be combined.
i. When the active ingredients from Column II or IV of Table 1 are combined, only one ingredient can be used from the same column.

(2)Quantities of Active Ingredients

a. The maximum daily dose of each active ingredient should be the dose specified in Table 1, unless otherwise specified.
b. The lower limit of the single dose for the individual active ingredients in Groups 1 or 2 in Column 1 of Table 1 is half of the maximum single dose. When 2 or more of the active ingredients from Groups 1 and 2 in Column 1 are combined, the lower limit of the daily dose should be 1/5th of the maximum daily dose or half of the maximum single dose, whichever is lower.
c. The lower limit of the daily dose for the active ingredients from Column II or IV of Table 1 is 1/5th of the maximum daily dose or half of the maximum single dose, whichever is lower.
d. When used in combinations, the lower limit of the daily amounts of the active ingredients from Column VI of Table 1 is 1/5 of the maximum daily dose. However, if the medicine is taken up to twice a day, the lower limit for the single dose is 1/15th of the maximum daily dose.
e. When 2 or more of the active ingredients from Groups 1 and 2 in Column I of Table 1 are combined, the sum of the values obtained by dividing the combined amounts of each of the active ingredients by their respective maximum daily doses (the dose within parenthesis for acetaminophen) should not exceed the combination coefficients shown in Table 2, and it must be more than half of the respective coefficient.
f. In the case where 2 or more active ingredients from Group 1 or 2 in Column I of Table 1 are combined, the sum of the values obtained by dividing the amounts of each of the active ingredients in the combination by their respective maximum daily doses should not exceed 1.
g. When the active ingredients from Group 1 or 2 in Column I of Table 1 are combined with the active ingredients from column VII, the stipulation in 2 (2) e will apply.
h. The lower limit of the daily dose for the active ingredients from Columns VII, VIII, or IX of Table 1 should be 1/10th of the maximum daily dose.
i. When only the active ingredients from Group 3 among the active ingredients from Column I of Table 1 are combined, the maximum single dose is either 200 mg or 150 mg. In the case where a single dose of 200 mg is combined, the maximum daily dose is 400 mg.
j. When the active ingredients from Group 3 in Column I of Table 1 are combined simultaneously with acetaminophen from Group 1 in the same column or ethenzamide from Group 2 in the same column, combinations of doses should be limited to those shown in Table 3.
k. When the active ingredients from Group 4 in Column I of Table 1 are combined simultaneously with acetaminophen from Group 1 in the same column, ethenzamide from Group 2 in the same column, or the active ingredients from Group 3 in the same column, combinations of doses should be limited to those shown in Table 4.

(3)Dosage Forms

The dosage forms should be tablets, capsules, pills, granules, and powders.

(4)Dosage and Administration

A. The following stipulations have been made.
   a. Once a day administration
      Take the medicine not more than once a day. If possible, avoid taking the medicine on an empty stomach.

b. Twice a day administration

Take the medicine not more than twice a day with an interval of at least 6 hours between doses. If possible, avoid taking the medicine on an empty stomach.

c. Three times a day administration

Take the medicine not more than 3 times a day with an interval of at least 4 hours between doses. If possible, avoid taking the medicine on an empty stomach.

B. Dosages for infants under 3 months of age are not approved.

C. For formulas containing aspirin, aspirin aluminum, sasapyrine, and sodium salicylate from Group 2 in Column I of the Table 1, the active ingredients from Group 3 in Column 1, or the active ingredients from Group 4 in Column I, dosage for children under 15 years of age is not approved.

D. For formulas containing the active ingredients from Column III of Table 1, dosage for children under 5 years of age is not approved.

E. For hard capsules, soft capsules larger than 6 mm in diameter, pills, and tablets, dosage for children under 5 years of age is not approved.

F. For soft capsules smaller than 6 mm in diameter, pills, and tablets, dosage for children under 3 years of age is not approved.

G. For children under the age of 15 years, the maximum daily doses acceptable are the values obtained by multiplying the amount of the active ingredient given in 2 (2) by the coefficients for each age group in Table 5.

H. For formulas containing the active ingredients from Column III 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) in Table 1 by the coefficient corresponding to the respective age group in Table 5.

(5) Indications

The indications should be within the following scope.

1) Relief of headache, toothache, pain after tooth extraction, sore throat (throat pain), earache, joint pain, neuralgia, lumbago, muscular pain, pain due to stiff shoulders, contusion pain, bone fracture pain, pain associated with sprain (sprain pain), painful menses (menstrual pain), and traumatic pain

2) Relief of fever at the time of chills (feeling cold due to fever) and fever

Table 1

Active Ingredients and Maximum Single and Daily Doses

Category		Active ingredient	Maximum single dose (mg)	Maximum daily dose (mg)
Column I	Group 1	Acetaminophen	300	900 (1500)*
		Lactylphenetidine	200	600
	Group 2	Aspirin	750	1500
		Aspirin aluminum	1000	2000
		Ethenzamide	500	1500
		Sasapyrine	500	1500
		Salicylamide	1000	3000
		Sodium salicylate	1000	3000
	Group 3	Ibuprofen	200	450
	Group 4	Isopropylantipyrine	150	450
Column II		Allylisopropylacetylurea	60	180
		Bromvalerylurea	200	600
Column III		Tranexamic acid	250 (93.4)**	750 (280)**
Column IV		Caffeine and sodium benzoate	150	300
		Caffeine hydrate	120	250
		Anhydrous caffeine	120	250
Column V		Vitamin B_1, its derivatives, and their salts		25 (1)**
		Vitamin B_2, its derivatives, and their salts		12 (2)**
		Vitamin C, its derivatives, and their salts		500 (50)**
		Hesperidin, its derivatives, and their salts		90 (18)**

Column VI	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

* The figure in parentheses is used when the maximum daily dose of each active ingredient is calculated as specified in 2 (2) e.

** The figures in parentheses are the lower limits of the amounts in a combination.

(Crude drugs)

Category	Active ingredient	Maximum daily dose (g)	
		Extract (converted to the crude drug amount)	Powder
Column VII	Earthworm(Lumbricus)	3	2
Column VIII	Japanese Valerian	6	2
	Glycyrrhiza	5	1.5
	Cinnamon Bark	5	1
	Peony Root	5	2
	Mountan Bark	6	2
Column IX	Japanese Zanthoxylum Peel	2	1
	Ginger	3	1
	Citrus Unshiu Peel	5	3

Table 2

Combination Coefficient for Combining 2 or More of Active Ingredients from Group 1 or 2 in Column I

Administration / Number of active ingredients combined	Three times daily	Twice daily	Once daily
Two active ingredients	34/30	32/30	18/30
Three active ingredients	38/30	36/30	19/30

Table 3

Combination Patterns for Combining Active Ingredients from Group 3 in Column I and Active Ingredients from Group 1 or 2 in Column I

(daily dose, -: combination not acceptable)

Group 3 in Column I		450mg	432mg	390mg
Group 1 in Column I	Acetaminophen	195mg	-	390mg
Group 2 in Column I	Ethenzamide	-	252mg	-

Table 4

Combination Patterns for Combining Active Ingredients from Group 4 in Column I and Active Ingredients from Group 1, 2 or 3 in Column I

(daily dose, -: combination not acceptable)

Group 4 in Column I		450mg	450mg	300mg
Group 1 in Column I	Acetaminophen	750mg	-	-
Group 2 in Column I	Ethenzamide	-	750mg	-
Group 3 in Column I	Ibuprofen	-	-	100mg

Table 5

Range of Age Coefficients

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

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Provisional Translation
from Japanese Original

Mar 25, 2015
Notification PB No.26

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	20	60
		Cloperastine hydrochloride	20	60
		Chloperastine phendizoate	35	105
		Codeine phosphate	20	60
		Dihydrocodeine phosphate	10	30
		Dibunate sodium	30	90
		Tipepidine hibenzate	25	75
		Dextromethorphan hydrobromide	20	60
		ΔDextromethorphan phenolphthalinate	30	90
		Carbetapentane citrate	20	60
	Group2	Dimemorfan phosphate	15 (10)	60 (30)
Column II		Trimethoquinol hydrochloride	2	6
		Δ*dl*-Methylephedrine hydrochloride	25	75
		l-Methylephedrine hydrochloride	25	75
		Methoxyphenamine hydrochloride	50	150
Column III		ΔNoscapine	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)	2mL	-
		Ammonium chloride	300	900
		ΔGuaifenesin	100	300
		ΔPotassium guaiacolsulfonate	90	270
		ΔPotassium 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
		Lysozyme chloride	20	60

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	45	135
		Triprolidine hydrochloride	2	6
		Promethazine hydrochloride	5	15
		Promethazine 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		ΔChlorhexidine hydrochloride	5	-
		ΔCetylpyridinium chloride	1	-
		ΔDequalinium 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	4	-
	Polygala Root	5	-
	Glycyrrhiza	5	1.5
	Platycodon Root	4	2
	Apricot Kernel	4	-
	Plantago Seed	5	-
	Plantago Herb	10	-
	Lycoris Radiata Bulb	0.8	-
	Senega	4	1.5
	Ipecac	0.05	0.05
	Fritillaria Bulb	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	3	-
	Aster Root	5	-
	Musk	-	0.01
	Adenophora Root	5	2.5
	Ginger	3	1
	Mulberry Bark	5	-
	Perilla Herb	2	-
	Panax Japonicus Rhizome	6	3
	Citrus Unshiu Peel	5	3
	Ginseng	6	3
	Ophiopogon Tuber	10	-
	Pinellia Tuber	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

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Provisional Translation
from Japanese Original

Mar 25, 2015
Notification PB No.23

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, Column IV, or Column V 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 VI.

(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 V of Table 1 are combined with those of Group 1 in Column II, the maximum daily dose of ingredients from Column V 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, III, and V 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 IV and VI 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		5mg
		Isothipendyl hydrochloride		12mg
		Iproheptine hydrochloride		150mg
		Difeterol hydrochloride		90mg
		Tripelenamine hydrochloride		100mg
		Thonzylamine hydrochloride		50mg
		Methodilazine hydrochloride		8mg
		Chlorpheniramine 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		75mg
		Triprolidine hydrochloride		6mg
		Promethazine hydrochloride		15mg
		Promethazine methylenedisalicylate		40mg
		Carbinoxamine maleate		16mg
	Group2	Mequitazine		4mg
Column II	Group 1	Phenylephrine hydrochloride		30mg
		Pseudoephedrine hydrochloride		180mg
		Pseudoephedrine sulfate		180mg
		dl-Methylephedrine hydrochloride		110mg
		l-Methylephedrine hydrochloride		110mg
		Methoxyphenamine hydrochloride		150mg
	Group 2			as total alkaloids
		Datura Extract		0.6mg
		Belladonna (Total) Alkaloids		0.6mg
		Belladonna Extract		60mg
		Isopropamide iodide extract		7.5mg
		Scopolia Extract		60mg
Column III		Bromelain		120,000 Units
		Lysozyme chloride		90 mg (potency)
Column IV	Group 1	Glycyrrhizinic acid and its salts		as glycyrrhizinic acid 200mg
	Group 2	Glycyrrhiza	Extract (converted to the crude drug amount)	Powder
			5g	1.5g
Column V		Caffeine and sodium benzoate		300mg
		Caffeine hydrate		300mg
		Anhydrous caffeine		300mg

		Extract (converted to the crude drug amount)	Powder
Column VI	Schizonepeta Spike	3g	-
	Asiasarum Root	3g	-
	Ginger	3g	1g
	Magnolia Flower	3g	-
	Peucedanum Root	3g	-
	Angelica Dahurica Root	3g	1g

Table 2

Range of ages and coefficients

Age	Coefficient
15 years of age and over	1
11 to under 15 years of age	2/3
7 to under 11 years of age	1/2
3 to 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

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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	15	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			
		Immature Citrus Unshiu Peel	5	3			
		Acorus Gramineus Rhizome	6	2			
		Centaury Herb	2	0.7			
		Swertia Herb	1.5	0.05			
		Atractylodes Lancea Rhizome	5	2			
		Perilla Herb	2	1			
		Star Anise	3	1			
		Rhubarb	0.2	0.1			
		Panax Japonicus Rhizome	6	3			
		Clove	2	0.5			
					Group 2	Betaine hydrochloride	0.6
						L-Glutamic acid hydrochloride	1.8
					Group 3	Carnitine chloride	0.6
						Bethanechol chloride	0.045
					Group 4	Dried yeast	10

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
	Gall powder	1.5
	Gall 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	8	3
		Swertia Herb	-	0.9
		Myrica Rubra 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 mg	
			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 panthothenate	30 mg
Biotin	25 μg
Vitamin B_1, its derivatives, and their salts	25 mg
Vitamin B_2, its derivatives, and their salts	12 mg
Vitamin B_6, its derivatives, and their salts	50 mg
Vitamin C, its derivatives, and their salts	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	25 mg
Vitamin B_2, its derivatives, and their salts	12 mg