Azelastine embonate, a process for its preparation and pharmaceutical preparations which contain azelastine embonate as active substance

Azelastine is an active substance with an anti-allergic and asthma-prophylactic effect. The chemical name is: 4-(p-chloro-benzyl)-2-hexahydro-1-methyl-azepin-4-yl-1-(2H)- phthalazinone (cf. DE-A-21 64 058).

One important application of azelastine as an anti-allergic agent is for oral application, particularly in the form of tablets, capsules, solutions or suspensions, and also application in the form of aerosols.

The application of azelastine in the form of solutions or suspensions, however, is not yet possible because azelastine has such an acrid bitter taste that patients refuse to accept any oral application of such azelastine solutions or azelastine suspensions. This bitter taste cannot be eliminated even on conversion into a very great variety of salts.

It has now been found that azelastine can be converted into a product, using embonic acid, which does not have the acrid bitter taste and therefore is suitable for use in, for example, orally taken preparations. Azelastine embonate is a salt of azelastine and embonic acid, wherein this salt consists of 2 moles of azelastine and 1 mole of embonic acid (see example 1).

Azelastine embonate according to the invention is especially suitable for preparing orally taken galenic preparations of azelastine in the form of stable suspensions, for example in the form of a juice. Azelastine embonate according to the invention may naturally also be

used for the preparation of other galenic preparations of azelastine such as for example tablets, capsules or sprays.

In the event that azelastine embonate according to the invention is used to prepare aqueous suspensions, these are suspensions which contain 3 to 3000 mg, preferably 15 to 240 mg, in particular 60 to 120 mg parts by weight of azelastine embonate as active substance per 100 ml of suspension. In this case an azelastine embonate with a particle size of less than 100 μm is preferably used. The pH of such a suspension is in the range 3 to 9, preferably 5 to 8, in particular 6 to 7.

An azelastine embonate suspension which consists of a thixotropic system which has a high viscosity in the rest state, but whose structure breaks up under slight mechanical stress (for example on pouring) so that the suspension (for example the juice) becomes free-flowing, is particularly favourable.

A swelling agent is used to prepare this type of thixotropic suspension in water. Suitable swelling agents are, for example, natural macromolecules (for example alginates, pectins, tragacanth gum, hydrocolloidal polysaccharides such as xanthan gum), semi-synthetic macromolecules (for example cellulose ethers), synthetic macromolecules (for example polyacrylates, polyvinyl-pyrrolidone) and inorganic hydrogel producers (for example colloidal silicic acid, bentonite). These swelling agents may be used separately or in a mixture. Due to its pronounced thixotropic properties, preparations using xanthan gum have proven especially suitable for the preparation of stable, pourable suspensions.

These swelling agents may be used separately or in a mixture. The total amount of swelling agent, per 100 ml of

suspension, is for example 0.1 to 10, preferably 0.5 to 5 g.

When using xanthan gum, the amount of xanthan gum is for example 0.1 to 3, preferably 0.3 to 1.5, in particular 0.5 to 1 g, with polyacrylates 0.1 to 1 g, with alginates and tragacanth gum 0.1 to 0.2 g, with pectins and cellulose ethers 0.5 to 5 g, with polyvinylpyrrolidone and inorganic hydrogel producers 1 to 10 g (each being per 100 ml of suspension).

Furthermore, the azelastine embonate suspensions according to the invention optionally contain preservatives, sweeteners, flavourings and colorants conventionally used in pharmaceutical or vegetable-based preparations.

Suitable preserving agents are, for example, organic acids (for example sorbic acid, benzoic acid), phenols (for example lower alkyl p-hydroxybenzoates), organic mercury compounds (for example thiomer sal), quaternary ammonium compounds (for example benzethonium chloride), aromatic and aliphatic alcohols (for example 1,2-propylene glycol, benzyl alcohol), chlorohexidine. The preservatives may also be used in the form of their salts (for example alkali metal salts such as sodium benzoate) and naturally also as mixtures.

The amount of preservative in 100 ml of suspension may be, for example, 0.05 g to 1.0 g for sorbic acid, 0.1 g to 0.2 g for benzoic acid, 0.001 g to 0.01 g for thiomer sal, 0.005 g to 0.02 g for benzethonium chloride, 10 g to 30 g for 1,2-propylene glycol, 1.0 g to 2.0 g for benzyl alcohol, 0.001 g to 0.01 g for chlorohexidine.

A mixture of lower alkyl p-hydroxybenzoates is preferably used. The sum of the lower alkyl p-hydroxybenzoates, per

100 ml of suspension, is for example between 0.1 and 0.3 g, preferably between 0.15 g and 0.25 g, in particular between 0.15 g and 0.20 g.

Suitable sweeteners are, for example, saccharin, cyclamate, aspartam, fructose, saccharose, sorbitol, mannitol and preferably xylitol. The amount of sweetener naturally depends on the sweetening value. In general, the amount, per 100 ml of suspension, is 0.005 to 0.1 for saccharin, 0.5 to 2.0 for cyclamate, 0.005 to 0.3 for aspartam, 1.0 to 60 g for fructose, saccharose, sorbitol and mannitol. For xylitol, this amount is for example 1 to 60, preferably 15 to 60, in particular 30 to 40 g.

Suitable flavourings are for example, ethereal oils (for example peppermint oil, lemon balm oil, citrus oil), fruit extracts (for example lemon, grapefruit, pineapple), aromatic drug extracts (liquorice root, aniseed, fennel), nature-identical and synthetic flavourings. Raspberry flavouring, for example, has proven to be particularly suitable.

The amount of flavouring, per 100 ml of suspension, is for example between 0.001 and 5 or even 10, preferably 0.01 to 1, in particular 0.01 to 0.1 g. In the case of raspberry flavouring a suitable amount is, for example, 0.01 to 0.1, preferably 0.01 to 0.05, in particular 0.02 to 0.04 g per 100 ml of suspension.

Suitable colorants are, for example, conventionally permitted foodstuff colorants, dyes from natural foodstuffs (for example curcumin, riboflavin, chlorophyll, xanthophylls), synthetic organic dyes (azo dyes, azo lakes), inorganic synthetic dyes (for example titanium dioxide, iron oxide). Synthetic azo dyes such as for example amaranth have proven to be particularly suitable.

The amount of colorant may be, for example, between 0.001 and 1.0, preferably 0.001 to 0.1, in particular 0.001 to 0.01 g, per 100 ml of suspension. In the case of amaranth, for example, 1 to 10, preferably 1 to 5, in particular 2 to 4 mg per 100 ml of suspension are suitable.

The pH required is expediently adjusted by means of inorganic acids (hydrochloric acid, sulphuric acid, phosphoric acid), organic acids (for example citric acid, maleic acid), inorganic alkaline solutions (for example caustic soda or caustic potash solutions) or by means of salts which are usually used for this purpose (for example ammonium chloride, sodium citrate, sodium dihydrogen phosphate).

Besides water, other physiologically acceptable liquids may be used to prepare suspensions of azelastine embonate according to the invention. The type of liquid which is suitable is, for example, monohydric and polyhydric lower alcohols such as for example ethanol, propylene glycol, glycerol and polyglycols with molecular weights of 200 to 600 D. Mixtures of these liquids with each other and with water may also be used.

Liquid carriers which may also be used are, for example, natural oils (for example olive oil), synthetic and semi-synthetic oil-like pharmaceutical carrier liquids such as triglycerides of saturated vegetable acids with 8 to 12 carbon atoms and mixtures thereof.

The suspensions are preferably purely aqueous suspensions.

If mixtures of water and other liquids are used, the mixture is, for example, one in which the amount of the non-aqueous fraction is 1 to 60, preferably 10 to 40, in

particular 20 to 30 percent by weight, in 100 grams of suspension.

Wetting agents may also optionally be added to the suspensions according to the invention. Suitable wetting agents are, for example, anionic surfactants, for example soaps, fatty alcohol sulphates, non-ionic surfactants, for example polyethylene glycol - fatty acid esters (Myrj), polyethylene glycol - fatty alcohol ethers (Brij), sorbitan fatty acid esters (Span), polyethylene glycol - sorbitan fatty acid esters (Tween), polyethylene glycol - polypropylene glycol derivatives (Pluronics).

Sorbitan fatty acid esters (with saturated or unsaturated aliphatic C_{10} - C_{20} carboxylic acids), polyoxyethylene fatty alcohol ethers (C_{10} to C_{20} alcohols) and polyethylene glycol - sorbitan carboxylic acid esters (saturated or unsaturated aliphatic C_{10} to C_{20} carboxylic acids) are preferably used.

The amount of wetting agent used per 100 ml suspension may be e.g. 1 to 10^{-5}, preferably 0.5 to 0.001, in particular 0.1 to 0.01 g. The wetting agent is used to ensure optimal dispersion of the non-dissolved active substance. The amount required of any particular wetting agent may optionally be determined in a preliminary experiment.

Azelastine embonate suspensions according to the invention have viscosities, for example, in a range from 0.05 to 0.22. preferably 0.09 to 0.18, in particular 0.12 to 0.15 Pascal seconds (Pa.s) at a shear rate of 110 per second in a rotation viscometer.

In addition, supplementary embonic acid may be added to the azelastine embonate suspensions according to the invention. For example, 1 to 2000 mg, preferably 20 to 1000 mg, in

particular 50 to 150 mg of embonic acid per 100 ml of suspension may be added in addition to the azelastine embonate already present.

Surprisingly, the excess embonic acid produces an additional improvement in the taste.

To prepare suspensions with propellants (aerosols), conventional propellants (propane, butane fluorochlorohydrocarbons) are used in addition to or instead of the auxiliary substances mentioned. The azelastine embonate for such suspensions should have a particle size with diameters between 5 - 10 μm.

This type of aerosol is prepared, for example, by dispersing 3 to 3000 mg of azelastine embonate in 100 ml of a mixture of chlorinated fluorinated hydrocarbons and/or hydrocarbons at a temperature between -55°C and +55°C with the addition of 0.25 to 3 g sorbitan trioleate and optionally other auxiliary substances and placing the suspension obtained in this way into cans which are or will be sealed with metering valves which release 0.025 to 0.1 ml of suspension each time they are activated.

Azelastine embonate with this particle size is prepared by milling in a conventional micronising device.

When preparing other oral preparations of azelastine embonate, conventional pharmaceutically and galenically acceptable auxiliary substances and carriers are used. In tablets, for example, the following auxiliary substances and carriers are used (amounts in percent by weight per tablet):

Filler (5-95%):	for example, starch, cellulose, lactose, saccharose, fructose, sorbitol, mannitol, calcium phosphate.
Binder (1-80%):	gelatine, cellulose ether, pectins, alginates, polyvinylpyrrolidone, lactose, microcrystalline cellulose.
Disintegrant (1-10%):	alginates, starch, pectins, carboxymethyl cellulose, polyvinylpolypyrrolidone, ultramylopectin, bentonite.
Lubricant (0.2-10%):	Stearic acid, stearates, polyglycols, talc, highly dispersed silicon dioxide.

Tablets may also contain: anti-adhesion agents, absorption accelerators, hydrophilisation agents, moisturisers and equivalent agents.

Coated tablets are often produced which then contain, for example, appropriate film-producers and coating materials as well as dyes, plasticisers and polishing agents.

The fillers, binders and lubricants mentioned may also be used in other oral pharmaceutical forms (capsules, granulates and the like).

Tablets and other oral preparations (capsules, granulates) contain, for example, between 0.5 and 30 mg, preferably 1 to 20 mg, in particular 1.5 to 12 mg of azelastine embonate.

Azelastine embonate according to the invention is prepared by reacting azelastine or an acid addition salt of azelastine with embonic acid or a salt of embonic acid in an appropriate solvent, wherein it is optionally heated.

Reaction takes place at temperatures of 18 to 150°C, in particular 20 to 100°C, preferably between 20 and 50°C.

Suitable solvents are, for example, lower aliphatic C_1-C_6 alcohols (methanol, ethanol, propanol, isopropanol, butanol), lower aliphatic ketones with 3 to 8 carbon atoms (acetone methylethyl ketone), glycol ethers, cyclic ethers (dioxan, tetrahydrofuran), esters of lower aliphatic carboxylic acids with lower aliphatic alcohols, amides and N-alkyl substituted amides of aliphatic C_1-C_4 carboxylic acids (dimethylformamide, dimethylacetamide), C_1-C_6 dialkylsulphones (dimethylsulphone, tetramethylsulphone), C_1-C_6 dialkylsulphoxides (dimethylsulphoxide) and other aprotic agents such as N-methylpyrrolidone, tetramethylurea, hexamethylphosphoric triamide, acetonitrile, mixtures of these agents with each other and mixtures with water. In the case of aqueous mixtures, the water fraction is generally not greater than 30 percent by volume. Furthermore, the reaction may also take place in alcohol/ether mixtures, wherein, for example, aliphatic C_2-C_6 ethers and cyclic ethers may be used. Likewise, reaction is possible in mixtures of lower aliphatic alcohols and halogenated aliphatic or aromatic hydrocarbons.

Azelastine and embonic acid are used in the ratio of 2:1. An excess of azelastine of 1 - 20 in particular of 1 - 5% with reference to the amount of embonic acid required for the ratio mentioned above, is preferably used.

If azelastine is used in the form of a salt, salts with the following acids, for example, are suitable: strong and moderately strong inorganic acids, (hydrohalic acids such as HCl, HBr, nitric acid, phosphoric acid, sulphuric acid), strong to weak organic acids such as aliphatic and aromatic sulphonic acids (methanesulphonic acid, toluenesulphonic acid), aliphatic saturated and unsaturated mono- and

polybasic carboxylic acids, aromatic carboxylic acids (benzoic acid, toluenecarboxylic acid).

Embonic acid may also be used in the form of a salt. Suitable salts of embonic acid are, for example, alkali metal salts (Na, K, Li), alkaline earth metal salts, magnesium salts, ammonium salts, alkylammonium salts.

Pharmaceutical azelastine embonate preparations are prepared by mixing or homogenising the azelastine embonate with the other auxiliary substances and carriers at temperatures between 10 and 80, preferably 18 to 40, in particular 20 to 30°C. They may be heated to 80 to 140, preferably 110 to 125°C, for 15 to 60 minutes in order to reduce the number of bacteria (sterilisation).

When preparing suspensions, the following method, for example, may be used. The swelling agents (0.1 to 10, preferably 0.3 to 1.5 g per 100 ml of suspension and optionally some of the other auxiliary substances) are dissolved in water or the other specified liquids or mixture of liquids at 20 to 30°C, wherein the amount of water, or the amount of liquid, is measured out in such a way that the final suspension contains 0.03 to 30, preferably 0.4 to 6, in particular 0.8 to 1.2 l of water, or liquid, with reference to 1 g of azelastine embonate. The aqueous solution thus obtained may then be heated for, for example, 10 to 120, preferably 15 to 60 minutes at 80 to 134, preferably 20 to 30 minutes at 110 to 121°C.

After cooling to 25 to 35°C, a wetting agent is optionally added to this solution and then the mixture of azelastine embonate and optionally the preservative, sweetener, colorant and optionally flavouring and other auxiliary substances and/or carriers, prepared at temperatures of

20 to 30°C, is added and the whole mixture is homogenised (temperature 15 to 35, preferably 20 to 30°C).

Optional addition of flavourings and adjustment of the pH to 3 to 9 then follows.

Preparation of the azelastine embonate suspension mentioned above uses, for example, for each 1 gram of azelastine embonate:

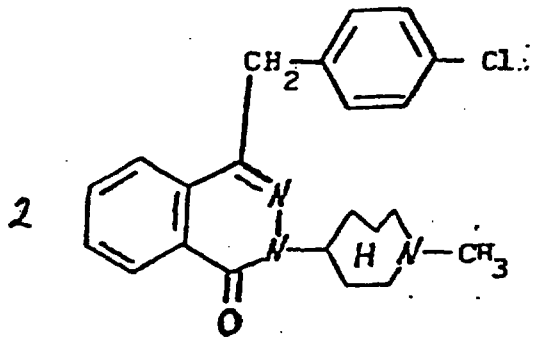
0.005 to 600 g, preferably 300 g to 400 g of sweetener

0.01 to 10 g, preferably 0.2 to 0.4 g of flavouring

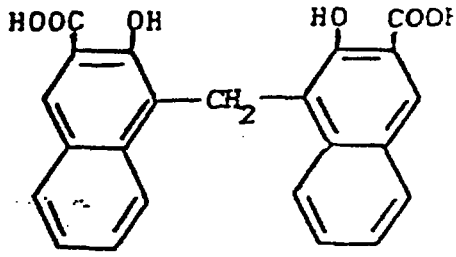
Some of the amount of flavouring stated here may optionally also be added to the suspension later.

Example 1

Azelastine embonate



x 1



Azelastine
(2 mol)

Embonic acid
(1 mol)

177.5 g (1.01 x 2 x 0.21 mol) of azelastine hydrochloride is dissolved in 4500 ml of 80% strength ethanol by stirring in a beaker. Following the addition of 90.6 g (0.21 mol) of the disodium salt of embonic acid, stirring is continued only until this has dissolved, ca. 4 minutes.

Afterwards, the mixture is immediately filtered through a fluted filter paper and the filtrate is left to stand overnight, untouched. Azelastine embonate rapidly precipitates. This is filtered under suction, washed with 80% strength ethanol and then with pure ethanol and dried under vacuum at 60°C for 20 hours. Yield 195 g (80% of theoretical).

The product thus obtained is further purified by stirring for 5 hours in ice-water, filtering under suction, washing first with ice-water and then with ethanol and drying under vacuum at 60°C for 20 hours. Yield 195 g (80% of theoretical). The azelastine embonate is obtained in the form of a crystalline, pale yellow coloured powder. Melting point: 197 to 201°C.

The IR spectrum is reproduced in Figure 1.

See Figure 2 for the nuclear magnetic resonance spectrum.

Example 2

Azelastine embonate suspension

3000 ml of suspension corresponding to 3300 g contains:

Azelastine embonate	3.600 g	
Xanthan gum	21.000 g	
Xylitol	1,200.000 g	
sodium propyl-4-hydroxybenzoate (Na salt of propyl 4-hydroxybenzoate)	1.200 g	
Sodium methyl-4-hydroxybenzoate (Na salt of methyl 4-hydroxybenzoate)	4.200 g	
1 N hydrochloric acid	21.000 g	(a)
Raspberry flavouring	0.900 g	
Amaranth (permitted red dye)	0.150 g	
Purified water	2,047.950 g	
	3,300.000 g	

a) The hydrochloric acid is required to adjust the pH to 6.5. Use of an amount of hydrochloric acid which is different from the cited value is compensated for by a corresponding decrease in the amount of purified water.

Preparation:

800.0 g of xylitol and 21.0 g of xanthan gum are dissolved in 2000 g of water in a 3000 ml beaker with stirring. The solution is then heated in an autoclave for 30 minutes at 115°C. After cooling to ca. 40°C, the solution is drawn

into the operational chamber of a homogenising apparatus under vacuum with recirculation.

400.0 g of xylitol, 1.2. g of sodium propyl-4-hydroxybenzoate, 4.2 g of sodium methyl-4-hydroxybenzoate, 0.15 g of amaranth and 3.6 g of azelastine embonate are mixed in a porcelain dish and introduced into the previously prepared solution in the operational chamber of the homogenising apparatus.

0.9 g of raspberry flavouring and 21.0 g of hydrochloric acid are introduced, under vacuum with recirculation, into the operational chamber of the homogenising apparatus. The solution is homogenised for 15 minutes.

The pH of the suspension thus obtained is adjusted to 6.5 by the addition of hydrochloric acid. The consumption of hydrochloric acid is compensated for by a decrease in the amount of purified water added. The formula to calculate the amount of water required is:

47.95 g - hydrochloric acid used in g = amount of water in g

The suspension thus obtained is a viscous, red-coloured juice (pH 6.3 to 6.7).
Active constituent per 100 ml: 0.1200 g azelastine embonate
Smell: like raspberries
Taste: raspberry flavoured
Viscosity: 0.1 0.15 Pascal seconds (Pa.s).

The juice (bulk goods) is placed, for example, into screw-topped bottles made from brown glass. The bottles should be filled with bulk goods in such a way that no air is entrapped due to pouring too fast.

The juice is stored, for example, at room temperature.

Example 3

Azelastine embonate suspension

5000 ml suspension corresponding to 5500 g contains:

Azelastine embonate	6.000 g (1)
Xanthan gum	32.500 g
Xylitol	1,500.000 g
Sodium propyl-4-hydroxybenzoate	2.000 g
Sodium methyl-4-hydroxybenzoate	7.000 g
Embonic acid	5.000 g
Raspberry flavouring	1.500 g
Amaranth (red dye)	0.250 g
Citric acid	64.000 g
Sodium hydroxide	32.500 g
Purified water	3,849.250 g (2)
	5,500.000 g

1) The azelastine embonate was passed through a 100 µm mesh sieve before processing.

2) The pH of the suspension is optionally adjusted to 6.5 with 1 N caustic soda solution. The consumption of caustic soda solution is subtracted from the amount of water.

Method of preparation:

I. 400 g of xylitol and 32.5 g of xanthan gum are ground together and this mixture is dissolved in 3000 g of water with stirring. The solution is heated in an autoclave for 30 minutes at 115°C. The water which evaporates during autoclaving is replaced. After cooling to ca. 30°C, the solution is then transferred,

under vacuum and recirculation, to the operational chamber of a homogenising apparatus.

II. In the sequence given, 64 g of citric acid, 5 g of embonic acid, 2 g of sodium propyl-4-hydroxybenzoate, 7 g of sodium methyl-4-hydroxybenzoate, 0.25 g of amaranth, 6 g of azelastine embonate, 1.5 g of raspberry flavouring and 1100 g of xylitol are introduced, under vacuum and recirculation, to the operational chamber of the homogenising apparatus. The pH is optionally adjusted to 6.5 using 1 N caustic soda solution.

Water is used to rinse out and make up the final volume to 5000 ml. The suspension is homogenised for 15 minutes under vacuum with recirculation.

The suspension thus obtained is a viscous, red juice.
Viscosity = 0.1 - 0.15 Pascal seconds (Pa.s)
pH = 6.3 - 6.7
Density = 1.09 - 1.11 g/ml
Smell: like raspberries
Taste: raspberry flavoured

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Patent Claims:

1. Azelastine embonate.

2. Pharmaceutical preparations which contain azelastine embonate as active substance optionally with other conventional physiologically acceptable auxiliary substances, carriers and/or diluents.

3. A stable aqueous suspension or aerosol containing 3 to 3000 mg parts by weight of azelastine embonate as active substance per 100 ml of suspension at a pH of 3 to 9.

4. A process for the preparation of azelastine embonate, characterised in that 1 mole of embonic acid (which may also be present in the form of a salt) is reacted with 2 to 2.4 moles of azelastine or 2 to 2.4 moles of an acid addition salt of azelastine in a hydrophilic solvent, or mixture of solvents, an alcohol/ether mixture or an alcohol/halogenated hydrocarbon mixture at a temperature of 18 to 150°C.

5. A process for the preparation of pharmaceutical preparations containing azelastine embonate, characterised in that the azelastine embonate is processed with pharmaceutical carriers or diluents or other auxiliary substances at a temperature between 15 and 80°C to produce pharmaceutical preparations or is made into a therapeutically applicable form, wherein solid preparations contain 0.5 - 30 mg of azelastine embonate in the dosage unit and suspensions contain 3 to 3000 mg parts by weight of azelastine embonate in 100 ml of suspension.

6. A process for the preparation of a suspension containing azelastine embonate as active substance, characterised in that 3 to 3000 mg of azelastine embonate is homogenised with swelling agents, optional wetting agents, preservatives, sweeteners and flavourings, as well as colorants in water or mixtures of water and other physiologically acceptable liquids which are miscible with water at a temperature between 15 and 80°C, wherein the resultant suspension contains the amount of azelastine embonate given above in 100 ml of suspension, and optionally the suspension is adjusted to a pH between 3 and 9.

7. A process for the preparation of an aqueous suspension containing azelastine embonate as active substance, characterised in that a homogeneous mixture is prepared at a temperature between 15 and 80°C, this containing 3 to 3000 mg of azelastine embonate (per 100 ml of suspension) as well as preservatives, sweeteners, colorants and flavourings, wherein 0.001 to 30 g of preservatives (total amount), 0.005 to 60 g of sweetener, 0.001 to 1.0 g of colorant and 0.001 to 10 g of flavouring are used per 100 ml of suspension and this mixture is homogenised at a temperature between 15 and 80°C with a solution of 0.1 to 10 g of swelling agent in water (per 100 ml of final solution), wherein up to 60 percent by weight of the water may be replaced by other physiologically acceptable liquids which are miscible with water, optionally the suspension obtained in this way is adjusted to a pH of 3 to 9 by the addition of acid, an alkaline solution or acid salts and optionally the remainder of the flavourings and/or sweeteners which has not already been added is added.

8. A process for the preparation of a suspension containing azelastine embonate as active substance according to Claim 7, characterised in that 1 to 10^{-5} g of wetting agent (per 100 ml of final solution) are added during preparation of the suspension.

9. A process for the preparation of a suspension containing azelastine embonate as active substance, characterised in that 3 to 3000 mg of azelastine embonate is dispersed in 100 ml of a mixture of chlorinated fluorinated hydrocarbons and/or hydrocarbons, at temperatures between -55°C and +55°C, with the addition of 0.25 to 3 g of sorbitan trioleate and optionally other auxiliary substances, and the resultant suspension is dispensed into cans which are or will be sealed with metering valves which release 0.025 to 0.1 ml of suspension each time they are activated.

10. A process for the preparation of a solid preparation, containing 0.5 - 30 mg of azelastine embonate as active substance in the dosage unit, characterised in that the azelastine embonate is mixed with at least one of the auxiliary substances starch, cellulose, cellulose ether, sugar, hexitol, calcium hydrogen phosphate, calcium phosphate, modified starch, alginate, pectin, carboxymethyl cellulose, ultraamylopectin, bentonite, polyvinylpyrrolidone, granulated with an aqueous gelatine solution or starch solution or an aqueous vinylpyrrolidone/vinylacetate copolymer and the granulate obtained is compressed into tablets optionally with the addition of stearates, stearic acid, talcum, polyglycols and/or silicon dioxide and optionally also starch and/or cellulose or capsules are filled therewith, or optionally after the addition of soybean lecithin is

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suspended or homogenised in molten hard fat at temperatures between 33 and 37°C and then the mixture is poured into hollow cells, wherein optionally in addition conventional anti-adhesion agents, absorption accelerators, hydrophilising agents and/or humectants may also be added to the solid preparations during the preparation process.

11. Use of azelastine embonate for the preparation of medicaments.