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EP 2269558 A1 **EP 1068850 A2**
US 6294178 B **US 20100145297 A1**
US 20020162769 A1
Epi-Essentials Mini Liquid Antihistamine Containers

(58) Field of Search:
INT CL **A61J**
Other: **EPODOC, WPI, Internet**

(54) Title of the Invention: **Container**
Abstract Title: **Container for liquid antihistamine**

(57) A container 20 suitable for housing a single dose of orally administrable liquid antihistamine is described. A kit comprising the container and a single dose of an orally administrable liquid antihistamine contained within the container, as well as use of the kit to treat allergic reactions which may otherwise lead to anaphylaxis, is also described. The container may have a body 22 with a frangible neck (18, see figure 1) or a lid 24 with frangible seals 28a, 28b, 28c, 28d broken by the user upon twisting off the lid. The anti-histamine may be chlorphenamine, cetirizine, levocetirizine or promethazine.

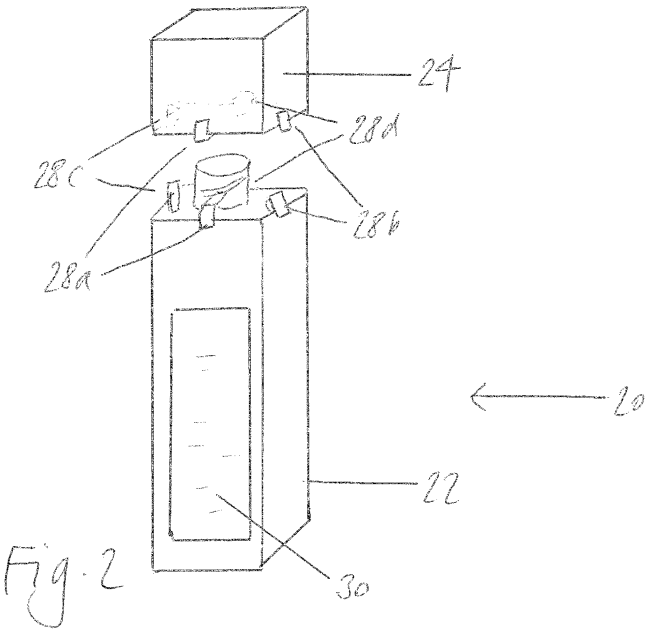

Fig. 2

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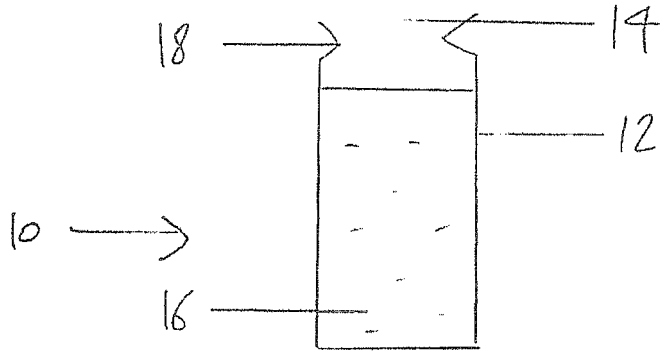
Fig. 1



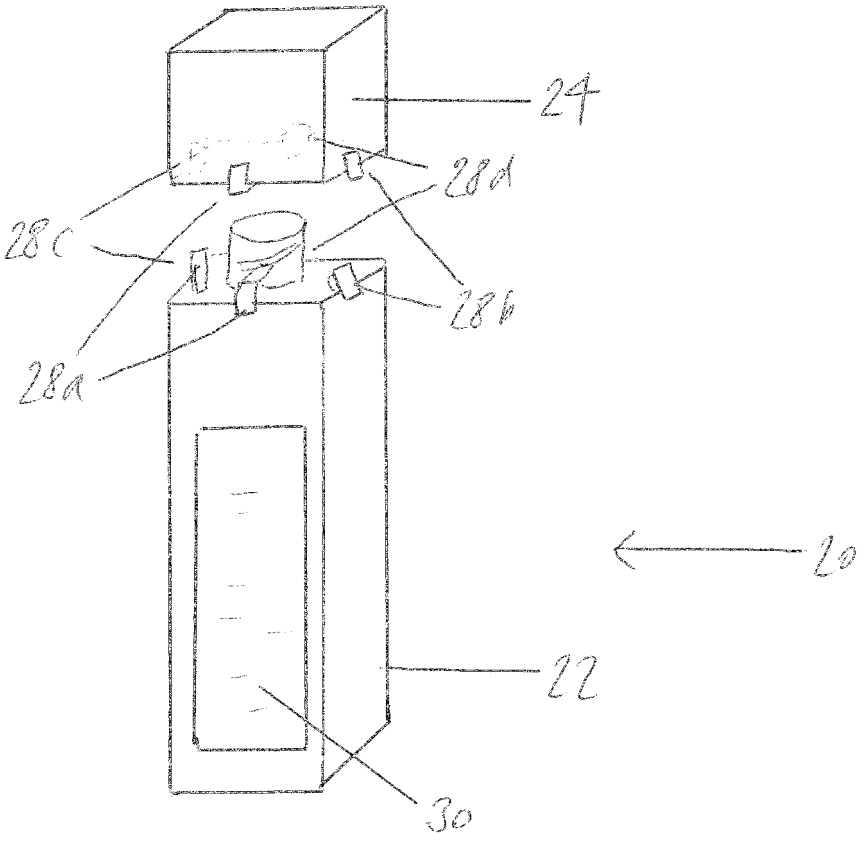


Fig. 2

Container

Field of the Invention

This invention relates to a kit comprising a single unit dosage form of a medicine, particularly an antihistamine. It also relates to a container for housing the medicine and therapeutic uses of the dosage form.

Background to the Invention

An allergy is a hypersensitivity disorder of the immune system. Allergic reactions occur when the immune system reacts to normally harmless substances in the environment.

Substances that trigger allergic reactions are known as allergens. Allergens may be inhaled into the lungs, swallowed or ingested. Examples of typical allergens include pollen, food, or house dust mite.

Allergies are classified into IgE mediated and non-IgE mediated allergies. In IgE mediated allergies the immune system then begins to produce a class of antibodies known as IgE, specific for that particular allergen, which will later alert the fighting cells (mast cells and basophils) within the immune system every time that this substance is encountered. The mast cells bind with the IgE antibodies so that they can identify the allergen next time it comes into contact with the body. This is called sensitisation, and at this stage there are no physical symptoms of an allergy.

Mast cells are present in all the tissue that is in contact with the external environment, such as the skin, nose, eyes, mouth, throat, stomach and gut. The next time that the same allergen is encountered the mast cells identify it as an intruder and produce histamine and other chemicals. It is the release of the histamine and other chemicals and their effect on the body that cause allergic symptoms.

A mild allergy can therefore cause symptoms including the following:

- itchy, runny, or congested nose
- sneezing
- itchy or swollen lips or mouth
- hives or nettle rash, itchy rash, redness, swelling of face or other body parts
- nausea, stomach cramps, vomiting or diarrhoea

A mild allergic reaction may also progress into a severe allergic reaction also known as anaphylaxis which can be life-threatening.

Severe allergies can cause:

- tightness or a lump in the throat, hoarse voice, hacking cough
- short of breath, cough, not able to speak in full sentences, noisy breathing, wheezing
- feeling faint, weakness or floppiness, glazed expression, unconscious

The above symptoms may deteriorate rapidly.

Prolonged exposure to allergens can cause the immune system to also employ additional fighting cells to attack the invading substance. These release chemical substances that cause further discomfort to allergy sufferers and increase the severity of their symptoms.

However, the immune system can still respond to allergens without the production of the IgE antibody. In non-IgE mediated allergies multiple cells may inappropriately react to the presence of an allergen, and can cause many of the same symptoms as IgE mediated allergies.

Symptoms of IgE mediated allergies occur rapidly and soon after exposure to the allergen, whereas in non-IgE mediated allergies symptoms tend to appear much later after contact with the allergen. In these cases it can be much harder to identify which allergen is causing the problem.

Anaphylaxis is an acute, potentially life-threatening hypersensitivity reaction and can occur in response to almost any foreign substance. Common triggers include venom from insect bites or stings, foods, and medication. Foods, especially peanuts, are the most common trigger in children and young adults while medications, insect bites and stings are more common in older adults. On a pathophysiological level, anaphylaxis is caused by the release of mediators from certain types of white blood cells triggered either by immunological or non-immunological mechanisms.

Anaphylaxis is diagnosed based on clinical criteria. As described in Simons et al, "Anaphylaxis Guidelines", World Allergy Organization Journal (February 2011), anaphylaxis is highly likely when any one of the following three criteria (1) to (3) is fulfilled:

(1) Acute onset of an illness (minutes to several hours) with involvement of the skin, mucosal tissue, or both (eg, generalized urticaria, itching or flushing, swollen lips-tongue-uvula) AND at least one of the following A) or B):

A) Respiratory compromise (eg, dyspnea, wheeze-bronchospasm, stridor, reduced peak expiratory flow, hypoxemia)

B) Reduced blood pressure or associated symptoms of end-organ dysfunction (eg. hypotonia [collapse], syncope, incontinence)

OR

(2) Two or more of the following A) to D) that occur rapidly after exposure to a likely allergen for that patient (minutes to several hours)

A) Involvement of the skin-mucosal tissue (eg, generalized urticaria, itch-flush, swollen lips-tongue-uvula)

B) Respiratory compromise (eg, dyspnea, wheeze-bronchospasm, stridor, reduced peak expiratory flow, hypoxemia)

C) Reduced blood pressure or associated symptoms (eg, hypotonia [collapse], syncope, incontinence)

D) Persistent gastrointestinal symptoms (eg, crampy abdominal pain, vomiting)

OR

(3). Reduced blood pressure after exposure to known allergen for that patient (minutes to several hours)

A) Infants and children: low systolic blood pressure (age-specific) or greater than 30% decrease in systolic blood pressure

B) Adults: systolic blood pressure of less than 90 mm Hg or greater than 30% decrease from that person's baseline

Anaphylaxis can be rapid in onset and may cause death.

Typically, patients with severe allergies are provided with an Allergy Management Plan by their doctor. The treatments prescribed manage the allergies, control the symptoms and reactions; they do not cure the condition. Improvements are seen because the treatment prevents the allergy symptoms from starting, or reduces the

severity of the symptoms. Stopping treatments or not administering treatment can cause a sudden escalation in symptoms.

The primary treatment for a mild allergic reaction is anti-histamines, for example, cetirizine. Antihistamines work by blocking the action of histamine. They work best when taken prior to exposure to the allergen. However, they can also be taken after an allergic reaction has started, and this is useful for blocking the release of further histamine, reducing new symptoms and possibly preventing the reaction becoming severe.

In the case of anaphylaxis, the primary treatment is adrenaline (also known as epinephrine). For this reason, people who are at risk of anaphylaxis are often prescribed adrenaline auto injection devices (for example, those sold under the trade marks Epipen®, Jext® or Anapen®) for use by themselves or others in an emergency. However some patients and carers, for a variety of reasons, which include fear of needles or injections and the size of the containers, are reluctant to use or carry the auto injectors even though they know they should do so in the event of anaphylaxis. In this instance, giving anti-histamine to help reduce new symptoms or possibly to slow the reaction down is a better and potentially life-saving alternative to giving no medication at all. Patients who may be susceptible to anaphylaxis or who have mild allergic reactions which may potentially escalate to anaphylaxis are advised, as part of the care plan, to carry antihistamines with them. In the case of mild allergic reactions it is hoped that if the antihistamine is given immediately then it will halt the reaction and prevent it becoming severe. However, the advice is frequently ignored for varying reasons.

Antihistamine medication may be carried in either liquid or tablet form. With liquid form, the antihistamine medicine is carried on the person contained in a glass bottle. The volume of medicine contained in the bottle varies, but is normally between 50 and 250ml, particularly 70 or 200 ml. The 70ml counter pack is seldom prescribed and its shelf life is short. . The typical dosage of medication is normally between 5 and 20 ml: this is usually dispensed using a spoon of the appropriate size.

However, a number of problems are associated with both of these dosage forms and also the containers used to house liquid antihistamines.

In the case where antihistamines are carried in oral liquid form:

- The bottle is large, heavy and bulky, so it is not easily portable.

- The bottle is made of glass, which is easily breakable, presenting a possible safety hazard.
- The size of the bottle may not meet the strict requirements for permission to pass through security checks at airports and the like (current security at EU airports generally permit liquids of a maximum volume of 100ml).

These difficulties discourage patients from carrying medication on their person. Furthermore, the following additional problems are associated with liquid medication, such as antihistamines, for oral administration:

- The contents of the bottle (the active ingredient, excipients or both) frequently degrades after the bottle has been opened and its contents exposed to the air, often requiring the contents to be thrown away before they have been fully used; this results in a significant amount of medicine being wasted (at a cost to the healthcare provider). Some leading pharmacies in the United Kingdom have a policy whereby, once a bottle is opened, the remainder of the liquid is discarded 6 months after opening. Some brands of medicine even require any remaining liquid to be discarded 3 months after opening.
- Bottles containing liquids must be fitted with childproof tops. Many people find these difficult to remove, especially if panicking during a medical emergency.
- Dispensing the medicine using a non-medical spoon, for example a teaspoon, can result in inaccurate and variable dosing.
- Patients also forget to carry a spoon. In this instance, patients may be tempted to drink medicine straight from the bottle rather than not take it at all, which can lead to concerns over having taken too much or too little antihistamine.

Furthermore, the following additional problems are associated with antihistamines in solid oral dosage forms, such as tablets:

- Solid oral dosage forms frequently require a liquid to aid swallowing and often this is not available.
- Solid oral dosage forms can be difficult to swallow, particularly in circumstances where symptoms include swelling of the mouth or throat.
- Solid dosage forms frequently have a slower onset of action than liquids or injections.

Containers such as ampoules are known in the art for containing single-use amounts of solutions, such as sodium chloride 0.9% w/v for injection, sterile normal saline for wound irrigation or carmellose sodium 0.5% w/v eye drops. While the ampoules for injection readily admit a needle to enable the sodium chloride 0.9% to be injected, the neck of the ampoule is narrow, making it unsuitable for rapid oral administration of a liquid to the patient. In the case of ampoules used for wound irrigation, the liquid is squirted out of the ampoule and requires a few squeezes to empty the ampoule fully. Again, the ampoule is not designed for rapid oral administration. An example of such a container is the normal sterile saline ampoule for wound irrigation, sold under the trade name Irripod®, typically in amounts of 20ml. In the case of ampoules for eye drops, the liquid is dispensed from the ampoule drop by drop and again is not intended for rapid oral administration.

EP2269558A describes a plastic ampoule comprising a body portion, a head portion formed continuously to a mouth portion via a cut-off portion, and a knob portion formed continuously to the head portion, wherein the plastic ampoule is unsealed by twisting the knob portion with fingers and cutting the head portion off the mouth portion, and a hollow portion formed to have a bowl shape. However, the ampoules described in this document are intended to house solutions for injection: the document nowhere discloses that the ampoule may contain an orally administrable liquid medicine, particularly an antihistamine. In particular, the neck of the ampoules described in this document is narrow, which restricts the speed at which the liquid could be delivered orally: the speed of delivery of the antihistamine is particularly important during anaphylaxis or other severe allergic reactions. The ampoules currently on the market are not designed for rapid oral administration of drugs.

Summary of the Invention

There is a significant unmet need for a single-use dosage form of an orally administrable liquid formulation of an antihistamine. Additionally, there is a need for a container housing the dosage form which can easily be carried on the person (preferably in a pocket) and be easily opened to allow rapid oral dispensing of a precise dose of the liquid antihistamine medicine at the first signs and symptoms of an allergic reaction especially if it has the potential to become a severe allergic reaction, such as anaphylaxis.

The above-mentioned problems are solved and needs are met by the present invention as defined herein.

According to a first aspect of the present invention, there is provided a kit comprising:
(a) a container suitable for housing a single dose, orally administrable liquid antihistamine; and
(b) a single dose of an orally administrable liquid antihistamine contained within the container.

According to a second aspect of the present invention, there is provided a container suitable for housing a single dose, orally administrable liquid antihistamine.

According to a further aspect of the present invention, there is provided a kit as defined above for use in treating an allergic reaction, especially severe allergic reactions which may lead to anaphylaxis.

These and other aspects of the invention are discussed in more detail below.

Brief Description of the Drawings

Fig. 1 illustrates a container according to one embodiment of the present invention; and
Fig. 2 illustrates a container according to another embodiment of the present invention.

Detailed Description of Preferred Embodiments

Definitions

In this specification, the terms below are defined as follows:

'Allergy' means a hypersensitivity disorder of the immune system in a human or animal.

'Allergic reaction' means a symptom which occurs in a human or animal allergy sufferer when the immune system reacts to allergens in the environment.

'Allergen' means a substance that triggers an allergic reaction. Allergens may be inhaled into the lungs, swallowed or ingested. Examples of typical allergens include pollen, foods (particularly nuts or dairy products) and house dust mite.

'Antihistamine' means a substance that blocks the action of histamine, particularly at the H_1 receptor sites. Histamine is responsible for immediate hypersensitivity reactions such as sneezing and itching. Members of this class of drugs may also be used for their side effects, including sedation and the prevention of nausea and vomiting.

'Anaphylaxis' is as defined above by the World Allergy Organisation criteria.

Container

The present invention provides a container suitable for housing a single dose, orally administrable liquid antihistamine. The nature of the container is not particularly limited provided it is capable of performing this function. Examples of suitable container types include vials, ampoules, bottles, cans and cartons.

The general shape of the container is not particularly limited: examples of suitable shapes include cuboid, prismatic and cylindrical. A generally cuboid shape is preferred.

Suitably, the container is dimensioned so as to be easily portable, thus overcoming the above-mentioned problems with the large glass bottles used to contain liquid oral antihistamines in the prior art. In one embodiment the container is dimensioned so as to be capable of fitting into a pocket of the user's clothing. In one embodiment, the maximum length of the container is 15, cm: preferably a maximum length of 14, 13, 12, 11, 10, 9, 8, 7, 6, 5, 4, 3 or 2 cm. In one embodiment, the maximum width of the container is not more than 5 cm: preferably no more than 4, 3, 2.5, 2, 1.5, 1 or 0.5 cm. In one embodiment, the maximum cross-sectional area of the container is 25 cm^2: preferably the maximum cross-sectional area of the container is 20, 15, 10, 7, 5, 3, 2 or 1 cm^2. A particularly preferred container has a maximum length of 5 cm (preferably a maximum length of 4, 3 or 2 cm) and a maximum width of 2 cm (preferably a maximum width of 1.5, 1 or 0.5 cm).

In one embodiment, the maximum length of the body portion of the container (i.e. excluding any removable top portion) is 15 cm: preferably a maximum length of 14, 13, 12, 11, 10, 9, 8, 7, 6, 5, 4, 3 or 2 cm.

Suitably, the length of the container is from 1 to 10 cm, preferably a length of 1.5 to 8, more preferably 2 to 6 cm. Suitably, the width of the container is from 0.5 to 5 cm: preferably 1 to 3 cm. Suitably, the cross-sectional area of the container is 1 to 25 cm^2: preferably, 2 to 10 cm^2. A particularly preferred container has a length of 1.5 to 8 cm (preferably 2 to 6 cm) and a width of 0.5 to 5 cm (preferably a width of 1 to 3 cm).

The container typically comprises a body portion and a mouth portion. The liquid oral antihistamine is housed in the body portion during storage and is dispensed via the mouth portion directly into the user's oral cavity during use. This both enables the medicine to be rapidly dispensed (preferably in a single movement) and avoids the need to dispense the medicine via a medical spoon and the problem of inaccurate dosing if a medical spoon is not used or is forgotten. It also avoids the issue of trying to swallow a tablet without a liquid or where there is swelling of the mouth or throat.

In some embodiments, the container may comprise a removable cap. The cap may be removed prior to use by any means commonly known in the art, such as torsion (twisting), flipping and pulling.

In some embodiments, the container is dimensioned such that, in use, the majority of the full cross-sectional area of the container (suitably more than 70%, preferably more than 80%, more preferably more than 90%, even more preferably more than 95% of the cross-sectional area of the container) is exposed on opening the container. This enables the medicine to be poured directly into the user's oral cavity for rapid administration, and avoids the need for the medicine to be squeezed out of the container. In one embodiment, the container is provided with a mouth portion having a substantially similar cross-sectional area as the body portion. Suitably, the cross-sectional area of the mouth portion is more than 70%, preferably more than 80%, more preferably more than 90%, even more preferably more than 95% of the cross-sectional area of the body portion.

In other embodiments, the container is manufactured such that delivery of the contents is facilitated by squeezing the container. Typically, this is done by

manufacturing the container from a pliable material, such as one of the thermoplastic organic polymers listed below.

The volume of the container may vary depending on the amount of oral liquid antihistamine formulation to be delivered. Typically, the volume of the container is such that one, and only one, dose of the oral liquid antihistamine can be contained therein. In one embodiment, the volume of the container is in the range of about 0.1 ml to about 30 ml, in one embodiment about 0.5 ml to about 25 ml, in one embodiment about 1 ml to about 20 ml, in one embodiment about 2 ml to about 15 ml. Particular volumes of containers include 1, 2, 5, 10, 15, 20 and 25 ml. A particularly preferred container volume is 10 ml.

The fill level of the container may vary depending on the amount of oral liquid antihistamine formulation to be delivered. Typically, the fill level of the container is such that the majority of the volume of the container is filled with the oral liquid antihistamine. This enables the maximum volume of the dose to be present in a single use form. In one embodiment, more than 70%, in one embodiment more than 80%, in one embodiment, more than 90%, in one embodiment, more than 95% of the total volume of the container is filled with the oral liquid antihistamine.

The container may be provided with means to facilitate the opening thereof, particularly means which enable opening of the container to expose the majority of its cross-sectional area as outlined above. Such means may include frangible (break-off or snap-off) portions, torsionable (twist-off) portions, and the like.

In one embodiment, the container is provided with a frangible portion disposed between the body and mouth portions, particularly at or near the mouth portion. In use, the user opens the container by bending, breaking or snapping it at the frangible portion such that the majority of the cross-sectional area of the body container is exposed.

In a preferred embodiment, in use the user opens the container by holding the body portion and twisting off a removable cap portion, revealing a neck portion having substantially the same cross-sectional area as the body portion. This will allow the liquid present in the body portion to be poured through the neck portion straight into the mouth of the user.

The container may be made from any material suitable to enable it to contain the liquid antihistamine formulation. Typically, the material should be inert to the liquid antihistamine formulation. Preferably, the container is made from a material light enough so as to be easily portable by the user. Examples of suitable materials are well known to those skilled in the art and include: metals and alloys thereof (such as iron, steels, aluminium, copper, zinc, and brasses); glasses (such as silicate glass, fluoride glasses, aluminosilicates, phosphosilicate glasses, borosilicate glasses, and particularly safety glasses such as shatterproof glasses); paper or card (suitably treated to make it liquid-impermeable); and organic polymers (particularly thermoplastic organic polymers), including polyolefins such as polyethylenes, polypropylenes, polyisoprene, polychloroprene, poly(vinyl chloride); poly(acrylonitrile); poly(vinylidene fluoride); poly(tetrafluoroethylene) (Teflon®), poly(vinyl acetate), polystyrene; polyamides (nylons), polyesters, polycarbonates, polyimides, polyurethanes, saccharide-based polymers and mixtures thereof.

The container of the present invention may be provided with markings to indicate particular dosage volumes, such as markings every 5 or 10ml of dosage.

The container of the present invention may be produced and filled by a number of means well known to those skilled in the art, depending on the material and particular dimensions of the container.

In particular, when the container is an ampoule, the container may preferably be produced and filled by the "blow-fill-seal" method commonly used in the art. Since its introduction into the North American pharmaceutical market more than 40 years ago, blow-fill-seal (BFS) aseptic processing has established itself as a highly efficient and safe system for the filling and packaging of sterile pharmaceutical liquids and other healthcare products. BFS enables a container to be moulded from plastic, aseptically filled and hermetically sealed in one continuous, integrated and automatic operation, without human manipulation. The process provides flexibility in container design and system changeovers, high volume product output, low operational costs and a high assurance of product sterility. The inherent safety of the process – packaging sterile products under aseptic conditions without human intervention – has led the FDA, and the United States Pharmacopoeia, to characterize BFS technology as an "advanced aseptic process", indicating its use as a preferred technology.

In one embodiment, the container may be produced as part of a connected series of containers. The containers may be separated from one another by breaking along a suitable frangible portion.

Antihistamine

The active ingredient of the formulation used in the present invention is a histamine antagonist, commonly known as an antihistamine. In this specification the terms "histamine antagonist" and "antihistamine" are synonymous. The antihistamine may be any compound known in the art to act as a histamine antagonist. The antihistamine is typically capable of treating or preventing allergic reactions in humans. In one embodiment, the antihistamine is capable of treating or preventing anaphylaxis in humans.

The antihistamine active ingredient used in the present invention may have other pharmacological effects in addition to its antiallergenic effect. Examples of additional pharmacological effects include antiemetic, antidepressant, antipsychotic, sedative and muscle relaxant effects. In one embodiment, the antiallergic effect is the principal pharmacological effect of the antihistamine. In one embodiment, the antiallergenic effect is the sole pharmacological effect of the antihistamine.

In one embodiment, the antihistamine is an H_1 antagonist. In particular, the antihistamine is an H_1 antagonist capable of treating or preventing allergic reactions in a human or non-human (preferably a human) subject. Examples of suitable H_1 antagonists include azelastine, brompheniramine, buclizine, bromodiphenhydramine (also known as bromazine), carbinoxamine, cetirizine, cyclizine, chlorphenamine, chlorodiphenhydramine, clemastine, cyproheptadine, desloratadine, dexbrompheniramine, deschlorpheniramine, dexchlorpheniramine, dimetindene, diphenhydramine, ebastine, embramine, fexofenadine, levocetirizine, loratadine, meclozine, orphenadrine, pheniramine, phenyltoloxamine, promethazine, pyrilamine (also known as mepyramine), rupatadine, tripelennamine and triprolidine, or a pharmaceutically acceptable salt of any thereof.

The active ingredient used in the present invention may be present either as the free base or acid, or as a pharmaceutically acceptable salt, solvate or hydrate thereof. These salts include acid addition salts (including di-acids) and base salts. Pharmaceutically acceptable acid addition salts include nontoxic salts derived from

inorganic acids such as hydrochloric acid, nitric acid, phosphoric acid, sulfuric acid, hydrobromic acid, hydroiodic acid, hydrofluoric acid, and phosphorous acids, as well nontoxic salts derived from organic acids, such as aliphatic mono- and dicarboxylic acids, phenyl-substituted alkanoic acids, hydroxy alkanoic acids, alkanedioic acids, aromatic acids, aliphatic and aromatic sulfonic acids, etc. Such salts include acetate, adipate, aspartate, benzoate, besylate, bicarbonate, carbonate, bisulfate, sulfate, borate, camsylate, citrate, cyclamate, edisylate, esylate, formate, fumarate, gluceptate, gluconate, glucuronate, hexafluorophosphate, hibenzate, hydrochloride/chloride, hydrobromide/bromide, hydroiodide/iodide, isethionate, lactate, malate, maleate, malonate, mesylate, methylsulfate, naphthylate, 2-napsylate, nicotinate, nitrate, orotate, oxalate, palmitate, pamoate, phosphate, hydrogen phosphate, dihydrogen phosphate, pyroglutamate, saccharate, stearate, succinate, tannate, tartrate, tosylate, trifluoroacetate and xinofoate salts. Pharmaceutically acceptable base salts include nontoxic salts derived from bases, including metal cations, such as an alkali or alkaline earth metal cation, as well as amines. Examples of suitable metal cations include sodium (Na^+), potassium (K^+), magnesium (Mg^{2+}), calcium (Ca^{2+}), zinc (Zn^{2+}), and aluminium (Al^{3+}). Examples of suitable amines include arginine, *N*,*N*'-dibenzylethylenediamine, chloroprocaine, choline, diethylamine, diethanolamine, dicyclohexylamine, ethylenediamine, glycine, lysine, *N*-methylglucamine, olamine and procaine. The degree of ionization of the salt may vary from completely ionized to almost non-ionized.

In a preferred embodiment, the antihistamine is selected from clorphenamine, cetirizine, levocetirizine or promethazine or a pharmaceutically acceptable salt of any thereof. In a preferred embodiment, the antihistamine is selected from cetirizine or levocetirizine or a pharmaceutically acceptable salt of either thereof.

The antihistamine medicine used in the present invention may contain a single active ingredient or a mixture of active ingredients. Preferably, the antihistamine used in the present invention contains a single active ingredient.

The antihistamine in the kit of the present invention is formulated to be administered orally. Oral administration may involve swallowing in which case the compound enters the bloodstream via the gastrointestinal tract. Alternatively or additionally, oral administration may involve mucosal administration (e.g., buccal, sublingual, supralingual administration) such that the compound enters the bloodstream through the oral mucosa.

The antihistamine used in the present invention is formulated as a liquid. Liquid formulations include suspensions, solutions, syrups and elixirs. Such formulations typically comprise a carrier (such as water, ethanol, polyethylene glycol, propylene glycol, or a suitable oil carrier). Preferably, the antihistamine used in the present invention is formulated in aqueous solution.

The container contains a single dose of the liquid, orally available antihistamine. This solves the problems of the prior art, in that the user can simply open the container and self-administer the single dose of the antihistamine by ingesting the entire contents of the container. This makes the kit simple to use and easily portable by subjects of all ages. Rapid ingestion of the liquid contents of the container allow the product to reach the bloodstream quickly while avoiding the problems associated with solid dosage forms or the need for painful injections.

The dosage of active ingredient used in the present invention will vary depending on the nature of the active ingredient and on factors such as the age, sex, weight and physical condition of the user. In one embodiment, the dosage of active ingredient used in the present invention is typically in the range of about 0.01 mg to about 3000 mg, in one embodiment about 0.05 mg to about 2000 mg, in one embodiment about 0.1 mg to about 2000 mg, in one embodiment about 0.2 mg to about 1000 mg, in one embodiment about 0.5 mg to about 500 mg, in one embodiment about 1 mg to about 300 mg. Although these dosages are based on an average human subject having a mass of about 60 kg to about 70 kg, a skilled clinician or pharmacist will be able to determine the appropriate dose for a patient such as a child or infant whose mass falls outside of this weight range.

The volume of liquid formulation present in the container will vary depending on the nature of the active ingredient and on factors such as the age, sex, weight and physical condition of the user. In one embodiment, the volume of liquid formulation used in the present invention is typically in the range of about 0.1 ml to about 30 ml, in one embodiment about 0.5 ml to about 25 ml, in one embodiment about 1 ml to about 20 ml, in one embodiment about 2 ml to about 15ml. Particular volumes of liquid formulation include 1, 2, 5, 10, 15, 20 and 25 ml. A particularly preferred volume is 10 ml.

The concentration of active ingredient present in the container is typically in the range of about 0.00033 mg/ml to about 3000 mg/ml, in one embodiment about 0.001 mg to about 1000 mg/ml, in one embodiment about 0.01 mg/ml to about 100 mg/ml, in one embodiment about 0.1 mg/ml to about 10 mg/ml, in one embodiment about 0.5 mg/ml to about 5 mg/ml.

In particular embodiments, when the active ingredient is cetirizine, a particularly preferred concentration is 1mg/ml. In particular embodiments, when the active ingredient is loratadine, a particularly preferred concentration is 1mg/ml. In particular embodiments, when the active ingredient is chlorphenamine, a particularly preferred concentration is 0.4 mg/ml.

The liquid antihistamine formulation used in the present invention may contain excipients such as salts, carbohydrates, sweeteners, flavourings, taste-masking agents, buffering agents, solubility-enhancing agents, surfactants, emulsifying agents. These are all well known to the person skilled in the art.

In an alternative embodiment, the active ingredient may be any pharmaceutically active substance. Examples of other possible classes of phamaceutically active substances include analgesics (painkillers), antibiotics, antivirals, antifungals, antiemetics, anticancer agents, antidiabetic agents, antidepressants, anxiolytics, antipsychotics, statins and antihypertensives. The container of the invention is particularly suitable for medicines capable of being formulated as a single-use, orally administrable liquid dosage form.

The container of the present invention may additionally or alternatively contain another liquid formulated to be taken orally in a single delivery. Examples include liquid foods and alcoholic and non-alcoholic drinks (such as energy drinks and isotonic drinks).

In one embodiment, the container has a label attached thereto, the label providing instructions regarding how to administer the orally available liquid medicine. Such a label is commonly known in the United Kingdom as a Patient Information Leaflet (PIL). In another embodiment, the container is provided together with an outer casing which also includes instructions regarding how to administer the orally available liquid medicine.

In one embodiment, the container is encased in wrapping materials. Such materials may encase the container on its own (the instruction label being outside the casing) or may encase both the container and the label. Single containers may be encased separately or multiple containers may be encased either separately or together.

Medical Uses, Subjects and Methods of Treatment

The antihistamine contained in the container of the invention is typically used to treat allergic conditions.

Therefore, the invention comprises in an additional aspect a kit as defined above for use in treating an allergy. Typically, the active ingredient treats the symptoms (i.e. the allergic reaction) rather than the underlying hypersensitivity.

Therefore, the invention comprises in an additional aspect a kit as defined above for use in treating an allergic reaction.

The invention comprises in a further aspect a method of treating an allergy in a subject in need thereof, the method comprising oral administration of a liquid antihistamine formulation contained in a container according to the invention.

The invention comprises in a further aspect a method of treating an allergic reaction in a subject in need thereof, the method comprising oral administration of a liquid antihistamine formulation contained in a container according to the invention.

Examples of allergic conditions treatable using antihistamines include asthma, eczema, hives (urticaria), allergic rhinitis, allergic contact dermatitis, allergic conjunctivitis and allergic fungal sinusitis. In one embodiment, the antihistamine contained in the container of the invention is used to treat allergies, especially those that may lead to anaphylaxis.

The source of the allergic condition (allergen) may be any known allergen, including foods (particularly nuts such as peanuts), animals, airborne allergens (such as dust or pollen), insect stings (such as stings of bees, wasps) and allergic reactions to medications like aspirin and antibiotics such as penicillin.

Where the active ingredient is another class of medicine suitable for being formulated as a single-use, orally administrable liquid dosage form, the kit of the present invention may be used to treat other conditions, non-limiting examples of which include pain, infections (such as bacterial, viral, or fungal infections), emesis, cancer, diabetes (such as Type I diabetes, Type II diabetes or gestational diabetes) depression, anxiety, psychotic disorders (such as schizophrenia), cardiovascular disorders and hypertension.

The subject treated with the orally available liquid antihistamine present in the container may be a human or a non-human animal. Examples of non-human animal subjects include companion animals such as cats, dogs, horses, rabbits, guinea pigs, hamsters and gerbils, and livestock such as cows, sheep, goats and pigs. Preferably, the subject is a human subject.

Example

The invention will now be described by the following, non-limiting examples.

Fig. 1 illustrates in cross-section at 10 an ampoule consisting of a body portion 12 and a mouth portion 14. The ampoule is filled with a liquid antihistamine 16. The ampoule is typically cylindrical and of dimensions 5cm (length) by 2cm (diameter), enabling it to be carried in the pocket of the patient's clothing. The ampoule is provided with a frangible neck portion 18, which the user can break in order to expose substantially the full cross-sectional area of the ampoule. This enables the liquid antihistamine to be poured quickly into the patient's oral cavity to ensure the most rapid delivery of the medicine.

Fig. 2 illustrates generally a container 20 according to another embodiment of the invention. The container comprises a body portion 22 which is generally cuboid in shape in the illustrated embodiment: other possible general shapes, such as cylindrical and prismatic, could be envisaged by the skilled person. The container also comprises a top portion 24: this is generally, not exclusively, the same shape as the body portion.

The container also comprises a mouth portion 26 in fluid communication with the body portion. In this example, the mouth portion is generally cylindrical in shape:

other possible general shapes, such as cuboid or prismatic, could be envisaged by the skilled person, but cylindrical is preferred to fit easily in the mouth of the user.

The container is provided with frangible seals 28a, 28b, 28c, 28d which connect the body portion 22 and top portion 24 to seal in the liquid prior to use. Such seals may be formed during manufacture of the container by any means known in the art: in particular, when the container is formed of a thermoplastic organic polymer, the container and seals may be formed by moulding. In use, the frangible seals are broken by the user, by twisting off the removable top portion. This exposes the mouth portion and allows delivery of the liquid.

The container may be provided with a label or similar instructions 30 on one side thereof. Such instructions may be printed on a self-adhesive label or alternatively may be present in a bag portion capable of enclosing an instruction leaflet.

All publications mentioned in the above specification are herein incorporated by reference. Various modifications and variations of the described kits, containers and methods of the present invention will be apparent to those skilled in the art without departing from the scope and spirit of the present invention. Although the present invention has been described in connection with specific preferred embodiments, it should be understood that the invention as claimed should not be unduly limited to such specific embodiments. Indeed, various modifications of the described modes for carrying out the invention which are obvious to those skilled in the art are intended to be within the scope of the following claims.

Claims:

1. A kit comprising:
   (a) a container suitable for housing a single dose, orally administrable liquid antihistamine; and
   (b) a single dose of an orally administrable liquid antihistamine contained within the container.

2. A kit according to claim 1, wherein the antihistamine is capable of treating or preventing anaphylaxis in a human or non-human animal subject.

3. A kit according to claim 1 or claim 2, wherein the antihistamine is selected from chlorphenamine, cetirizine, levocetirizine or promethazine or a pharmaceutically acceptable salt of any thereof.

4. A kit according to any one of claims 1 to 3, wherein the container is dimensioned such that, in use, substantially the full cross-sectional area of the container is exposed on opening the container.

5. A kit according to any one of claims 1 to 4, wherein the container is dimensioned so as to be capable of fitting in the pocket of a user's clothing.

6. A kit according to any one of claims 1 to 5, further comprising instructions for administration of the antihistamine.

7. A kit as defined in any one of claims 1 to 6 for use in treating an allergic reaction.

8. A kit for use according to claim 7, wherein the allergic condition may lead to anaphylaxis.

9. A container suitable for housing a single dose, orally administrable liquid antihistamine.

INTELLECTUAL PROPERTY OFFICE

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Claims searched:	1-9	**Date of search:**	13 March 2013

Patents Act 1977: Search Report under Section 17

Documents considered to be relevant:

Category	Relevant to claims	Identity of document and passage or figure of particular relevance
X	1-9	US 2002/162769 A1 (WEINSTEIN) See paragraph 34 and figure 2 at least
X	1-9	US 6294178 B (WEINSTEIN) See figure 2 and associated description, and column 2, lines 16-34
X	1-9	Epi-Essentials Mini Liquid Antihistamine Containers See http://web.archive.org/web/20120716111023/http://epi-essentials.com/catalog.php?item=20, dated 16-07-2012
X	1-9	EP 2269558 A1 (NAKANO) See figure 1 at least
X	1-9	US 2010/145297 A1 (AGUILO-PINEDO) See the whole document
X	1-9	EP 1068850 A2 (FONTANA) See the whole document

Categories:

X	Document indicating lack of novelty or inventive step	A	Document indicating technological background and/or state of the art.
Y	Document indicating lack of inventive step if combined with one or more other documents of same category.	P	Document published on or after the declared priority date but before the filing date of this invention.
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Field of Search:

Search of GB, EP, WO & US patent documents classified in the following areas of the UKC^{X} :

Worldwide search of patent documents classified in the following areas of the IPC

A61J

The following online and other databases have been used in the preparation of this search report

EPODOC, WPI, Internet

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International Classification:

Subclass	Subgroup	Valid From
A61J	0001/05	01/01/2006