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(54) Title: A CARTRIDGE FOR A MEDICAL INJECTION DEVICE

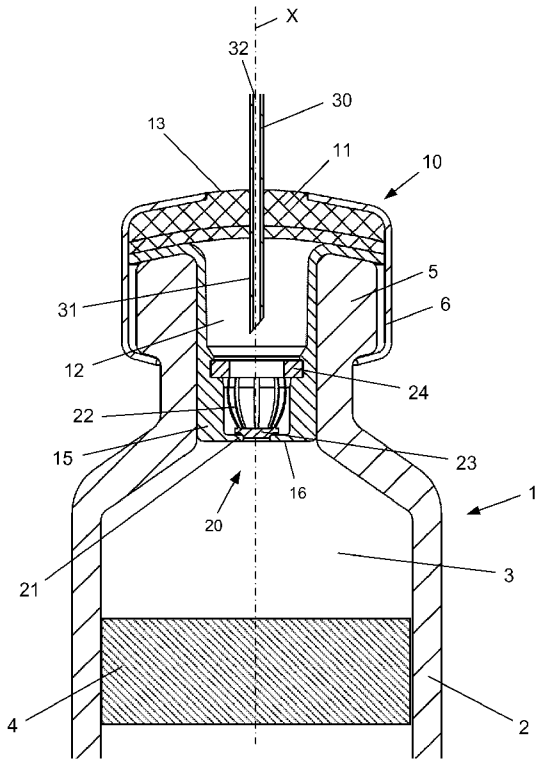

Fig. 1

(57) Abstract: The present invention concerns a cartridge (1) for a medical injection device having an injection needle (30) mounted thereon. The cartridge has a first variable volume reservoir (3) containing a liquid drug to be injected. Further the cartridge proximally comprises a movable plunger (4) and distally a septum unit (10). The septum unit comprises a first septum (11) being penetrable by a needle cannula, and a second septum (15). Further a one-way valve (20) is provided as a part of the septum unit. The one-way valve controls the flow from the first variable volume reservoir and into a second reservoir which is formed between the first septum and the second septum. The needle cannula penetrates into the second reservoir and the one-way valve allows liquid drug to flow from the first variable volume reservoir to the second reservoir only when a predetermined pressure is applied to the drug in the first variable volume reservoir.

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A Cartridge for a Medical Injection Device

THE TECHNICAL FIELD OF THE INVENTION:

The invention relates to a cartridge for a medical injection device. The invention especially refers to such cartridge having a one-way valve and especially a cartridge wherein the one-way valve is part of the cartridge unit.

DESCRIPTION OF RELATED ART:

A standard cartridge for a medical injection device is known from ISO standard No. 11608-3. Such cartridge comprises a hollow body which at the proximal end is closed by a membrane through which an injection needle can penetrate. The opposite end is sealed by a movable plunger which can be moved forward by the medical injection device. The variable volume reservoir between the outlet and the movable plunger contains the liquid drug which is pressed out through the lumen of the injection needle when a pressure is applied to the liquid drug.

A general problem with cartridges is that back-flow of bodily liquids are possible. During injection, the injection needle establishes a liquid communication between the body of the user and the interior of the cartridge. The injection needle is usually maintained inserted into the tissue of the user during the delivery of the required dose. At the end of delivery the pressure inside the cartridge has decreased and in some cases the pressure in the tissue of the user is higher and bodily liquids flow through the lumen of the injection needle and into the interior of the cartridge. This leads to contamination of the entire content of liquid drug in the variable volume reservoir which is undesired.

Various examples of one-way valves for medical injection devices are given in e.g. US 7,981,081 and EP 555,900. These known one-way valves are adapted to prevent back-flow into the drug chamber. However, they are constructed as external components that need to be attached to the injection device.

A cartridge assembly for a needle free jet injector having a one-way valve is further known from US 6,883,222. This cartridge assembly is however a complex construction and not suitable for a medical injection device using an injection needle.

DESCRIPTION OF THE INVENTION:

It is thus an object of the present invention to provide a simple and reliable cartridge design usable for needle based injections and wherein back-flow into the variable volume reservoir is prevented.

Further, the cartridge needs to be similar to standard cartridges as in ISO standard No. 11608-3 in order to fit into existing injection devices and in order to be usable with known double pointed pen needles. Henceforth, the cartridge including the one-way valve must be able to be handled as one unitary unit both in production, in storage and during sale.

The invention is defined in claim 1. Accordingly in one aspect the present invention relates to a cartridge and a needle cannula in combination. The needle cannula can either be removable attached to the injection device holding the cartridge or it can be permanent coupled to the injection device. Further, the cartridge can either be permanently secured in the injection device or it can be exchangeable.

The combined cartridge and needle cannula comprises:

- A cartridge with a first variable volume reservoir containing the liquid drug to be expelled. This first variable volume reservoir is distally sealed by a septum unit and proximally sealed by a movable plunger. A pressure “P” is generated inside the first variable reservoir by moving the movable plunger distally inside the cartridge.

- A septum unit, or septum assembly, with a first septum having a distal surface and a second septum having a proximal surface, provided such that a second reservoir is formed in the space between the first septum and the second septum. This second reservoir is preferably formed inside the boundaries of the cartridge and holds a small quantum of the liquid drug to be expelled.

- A needle cannula having a proximal end which is penetrated through the first septum and at least partly into the second reservoir such that liquid communication can be established between the second reservoir and a patient.

- A one-way valve provided between the first variable volume reservoir and the second reservoir. This one-way valve opens when the pressure ("P") inside the first variable volume reservoir reaches a pre-determined threshold value i.e. the one-way valve is a pressure actuated one-way valve.

The one-way valve is according to the invention located inside the boundaries of the cartridge and the one-way valve is located between the distal surface and the proximal surface of the septum unit.

The general idea thus being that the one-way valve is provided within the boundaries of the cartridge such that the cartridge can be handled as one unitary component in all matters and further that the one-way valve isolates a second reservoir i.e. the second reservoir is separated from the first variable volume reservoir by the one-way valve. One single unitary cartridge in which backflow is prevented is thus realized.

The first variable volume reservoir usually has an initiate capacity of 1,5 to 5 ml of liquid drug whereas the second reservoir has a significant smaller volume. The volume of the second reservoir can in one example be as small as 1/50 part of the first variable volume reservoirs initial volume.

The one-way valve is designed such that it opens when the pressure "P" in the liquid drug in the first variable volume reservoir reaches a predetermined threshold value referred to as the opening pressure. The one-way valve further shuts when the pressure decreases below a certain value referred to as the closing pressure.

During injection the medical injection device applies a pressure to the liquid drug which is larger than the opening pressure such that the liquid drug flow through the one-way valve into the second reservoir and further through the lumen of the injection needle and into the tissue of the user. When the intended dose has been injected, the pressure inside the first variable volume reservoir falls below the closing pressure and the one-way valve shuts off the flow into the second reservoir thereby preventing backflow into the first variable volume reservoir.

The opening pressure and the closing pressure does not necessarily have the same value, however, the closing pressure is usually set higher than the pressure normally occurring in

human tissue such that the one-way valve shuts off before bodily liquids starts to flow into the first variable volume reservoir.

Once the pressure has decreased to a value below the closing pressure and the valve shuts off, no dripping will occur since the flow is shut off. Further, there will be less waiting time before the injection needle can be removed from the tissue of the user.

The part of the cartridge forming the first variable reservoir is usually formed as a glass ampoule having a distal neck part. However, it could alternatively be manufactured from a suitable polymer.

The first septum and the second septum abut each other at the periphery such that the second reservoir is formed around a centre axis of the cartridge. Both septums are preferably attached to the cartridge by a metal cap beaded under the neck part.

The volume of the first variable volume reservoir is variable and decreases as the plunger is moved distally inside the first variable volume reservoir, however the volume of the second reservoir is fixed.

The one-way valve can be any kind of one-way valve which prevents backflow when the one-way valve is shut. The one-way valve is preferably a pressure valve which opens and closes in response to a pressure. The presence of such one-way valve would also prevent any other than the original producer from filling a liquid drug into the cartridge, at least via the distal opening.

The one-way valve can be a separate part or it can be part of the cartridge itself. In one example the one-way valve is an integrated part of the septum unit closing the distal end of the cartridge.

Preferably, the septum unit is formed as one single septum assembly, such that the septum assembly comprises both the first septum and the second septum and the one-way valve. When the cartridge is manufactured from glass the septum assembly can be easily secured to the glass cartridge using the well-known metal bead technology used today when securing a septum to a standard glass cartridge. The novel septum assemblies can thus be handled separately in the production facility.

The cartridge including the septum unit housing the second reservoir and the one-way valve thus makes up one single unitary unit which can be sold separately and used in a large variety of known medical injection devices. The cartridge could in one example be filled with insulin and accommodated in a pen system such as e.g. the FlexPen® currently sold by Novo Nordisk A/S.

Two different embodiments of a one-way valve are disclosed. In the first embodiment, the one-way valve comprises a dish which is pressed against a seat by a resilient member. The resilient member thus defines the opening and the closing pressure. When the pressure inside the cartridge is above a predetermined threshold value, the one-way valve opens to allow flow from the first variable volume reservoir and into the second reservoir. In the same manner, when the pressure drops below a certain value, the one-way valve shuts off the flow.

The seat is preferably formed as an integral part of the second septum. The resilient member is preferably provided to urge the dish into contact with the seat. Distally the resilient member abuts a part of the second septum, which can be either a recess moulded in the second septum or a separate part embedded in the second septum.

In a second embodiment, the one-way valve is an integral part of the second septum. The one-way valve is preferably moulded as a plurality of lips having an inherent resiliency pressing the lips together to close the flow. Once the pressure reaches the opening pressure, the lips are forced apart to allow flow. When the pressure in the first variable volume reservoir falls below the pressure applied inherently by the lips, the lips will close and shut off the flow.

DEFINITIONS:

An **"injection pen"** is typically an injection apparatus having an oblong or elongated shape somewhat like a fountain pen for writing. Although such pens usually have a tubular cross-section, they could easily have a different cross-section such as triangular, rectangular or square or any variation around these geometries.

As used herein, the term **"drug"** is meant to encompass any drug-containing flowable medicine capable of being passed through a delivery means such as a hollow needle in a controlled manner, such as a liquid, solution, gel or fine suspension. Representative drugs includes pharmaceuticals such as peptides, proteins (e.g. insulin, insulin analogues and C-peptide), and hormones, biologically derived or active agents, hormonal and gene based agents, nutritional formulas and other substances in both solid (dispensed) or liquid form.

"Cartridge" is the term used to describe the container containing the drug. Cartridges are usually made from glass but could also be moulded from any suitable polymer. A cartridge or ampoule is preferably sealed at one end by a pierceable membrane referred to as the **"septum"** which can be pierced e.g. by the back-end of a needle cannula. The opposite end is typically closed by a plunger or piston made from rubber or a suitable polymer. The plunger or piston can be slidable moved inside the cartridge. The space between the pierceable membrane and the movable plunger holds the drug which is pressed out as the plunger decreased the volume of the space holding the drug.

Further the term **"injection needle"** defines a piercing member adapted to penetrate the skin of a subject for the purpose of delivering or removing a liquid. For many pen systems, the needle cannula of the injection needle comprises a front part for penetrating the skin of the user and a back part for penetrating the septum of the cartridge thus creating a liquid flow between the interior of the cartridge and the subcutaneous layer of the user.

All references, including publications, patent applications, and patents, cited herein are incorporated by reference in their entirety and to the same extent as if each reference were individually and specifically indicated to be incorporated by reference and were set forth in its entirety herein.

All headings and sub-headings are used herein for convenience only and should not be constructed as limiting the invention in any way.

The use of any and all examples, or exemplary language (e.g. such as) provided herein, is intended merely to better illuminate the invention and does not pose a limitation on the scope of the invention unless otherwise claimed. No language in the specification should be construed as indicating any non-claimed element as essential to the practice of the invention.

The citation and incorporation of patent documents herein is done for convenience only and does not reflect any view of the validity, patentability, and/or enforceability of such patent documents.

This invention includes all modifications and equivalents of the subject matter recited in the claims appended hereto as permitted by applicable law.

BRIEF DESCRIPTION OF THE DRAWINGS:

The invention will be explained more fully below in connection with a preferred embodiment and with reference to the drawings in which:

Figure 1 show a cross sectional view of the distal end of the cartridge with the one-way valve in a closed condition.

Figure 2 show a cross sectional view of the distal end of the cartridge with the one-way valve in an open condition.

Figure 3 show a cross sectional view of a different embodiment with the one-way valve in a closed condition.

The figures are schematic and simplified for clarity, and they just show details, which are essential to the understanding of the invention, while other details are left out. Throughout, the same reference numerals are used for identical or corresponding parts.

DETAILED DESCRIPTION OF EMBODIMENT:

When in the following terms as “upper” and “lower”, “right” and “left”, “horizontal” and “vertical”, “clockwise” and “counter clockwise” or similar relative expressions are used, these only refer to the appended figures and not to an actual situation of use. The shown figures are schematic representations for which reason the configuration of the different structures as well as there relative dimensions are intended to serve illustrative purposes only.

In that context it may be convenient to define that the term “distal end” in the appended figure is meant to refer to the end of the cartridge carrying the injection needle whereas the term “proximal end” is meant to refer to the opposite end carrying the plunger.

Figure 1 discloses the distal end of the cartridge 1. In this example of the invention the cartridge 1 is made from a cylindrical glass ampoule 2 forming the first variable volume reservoir

3. The glass ampoule 2 is proximally provided with a movable plunger 4 and distally with a septum unit 10. As the plunger 4 is moved distally the volume of the first variable volume 3 reservoir decreases. Distally the ampoule 2 has a neck portion 5 around which a metal cap 6 is beaded. The metal cap 6 secures the septum unit 10 to the ampoule 2.

In the disclosed embodiment, the septum unit 10 comprises a distal septum 11 and a proximal septum 15 which there between define a second reservoir 12. In one embodiment, the first septum 11 can be constructed of several layers. In the depicted embodiment, there are two layers of individual rubber sheets which are sandwiched together. However, any known kind of pierceable septum in any construction can be used.

The septum unit 10 is preferably manufactured as one unitary assembly housing the first septum 11 and the second septum 15 with the second reservoir 12 there between and thus also the one-way valve 20. This septum unit or assembly 10 can then be attached to the cartridge 1 with a metal cap 6 beaded to the neck portion 5 of the glass ampoule 2..

The distal septum 11 has a distal surface 13 which is in contact with the surroundings and the proximal septum 15 has a proximal surface 16 which is in contact with the liquid drug internally in the cartridge 1, preferably with the liquid drug in the first variable volume reservoir 3.

As disclosed in the figures, the first septum 11 and the second septum 15 are sandwiched together at the periphery whereby the second reservoir 12 is formed between the two septums 11, 15 around the centre line X.

Proximally this second reservoir 12 is sealed by a valve 20. This valve 20 basicly comprises;

- A seat 21
- A resilient member 22, and
- A dish 23.

The seat 21 is formed in the second septum 15 and the disc 23 rests against the seat 21 when no pressure is present in the first variable volume reservoir 3.

The dish 23 is actively pressed against the seat 21 by the resilient member 22 which is encompassed between the dish 23 and a ring-shaped member 24. This ring-shaped member 24 has a centre opening through which the liquid drug in the first variable volume reservoir 3 can flow and a peripheral solid part supporting the resilient member 22. The periphery of the ring-shaped member 24 is further secured to the second septum 15.

The ring-shaped member 24 can either be a separate part or it can be formed as an integral part of the distal septum 15.

A needle cannula 30 is also provided. This needle cannula 30 is preferably secured in a non-shown hub such that the needle assembly can be mounted on the injection device holding the cartridge 1. In an alternative, the needle cannula 30 can be a non-removable and integral part of the injection device. The needle cannula 30 has a proximal part 31 which penetrates the first septum 11 such that the proximal part 31 (or at least part of it) is located inside the second reservoir 12. Any liquid drug contained in the second reservoir 12 can thus escape through the lumen 32 of the needle cannula 30.

When the pressure inside the first variable volume reservoir 3 (indicated by arrow “P” in figure 2) is above a predetermined opening pressure (the threshold pressure), which is determined by the force of the resilient member 22, the disc 23 is pressed out of its engagement with the seat 21 and liquid drug is free to pass into the second reservoir 12 as depicted in figure 2. Once the valve 20 is open this pressure “P” presses the liquid drug from the first variable volume reservoir 3 into the second reservoir 12 and further through the lumen 32 of the injection needle 20 and into the tissue of a user.

At the end of dosing and as the injected liquid drug is dispersed in the tissue of the user, the pressure “P” inside the first variable volume reservoir 3 falls. Once this decreasing pressure falls below a certain closing pressure, the valve 20 closes and shut off further flow. The closing force of the one-way valve 20 is preferably set such that the one-way valves 20 closes before the pressure in the tissue of the user forces bodily fluids through the lumen 32 and into the first variable volume reservoir 3.

In a second embodiment disclosed in figure 3, the one-way valve 20 is formed integral with the second septum 15.

The second septum 15 is proximal provided with a plurality of lips 17 which are pressed together by the inherent resiliency. The second septum 15 and thus the lips 17 are preferably moulded from a rubber composition. When the pressure in the first variable volume reservoir 3 increases during performing an injection, these lips 17 are pressed apart which allows the liquid drug to pass through the one-way valve 20 and into the second reservoir 12. When the pressure decreases at the end of the injection the inherent resiliency moves the lips radially together thus closing passage through the one-way valve 20.

Some preferred embodiments have been shown in the foregoing, but it should be stressed that the invention is not limited to these, but may be embodied in other ways within the subject matter defined in the following claims.

Claims:

1. A cartridge and a needle cannula in combination, comprising:

- a cartridge (1) having a first variable volume reservoir (3) containing a liquid drug, which first variable volume reservoir (3) distally is sealed by a septum unit (10) and proximally sealed by a movable plunger (4), and wherein a pressure "P" is generated in the first variable reservoir (3) by moving the movable plunger (4) distally inside the cartridge (1), and

- which septum unit (10) comprises a first septum (11) having a distal surface (13) and a second septum (15) having a proximal surface (16), and wherein a second reservoir (12) is formed between the first septum (11) and the second septum (15),

- a needle cannula (30) having a proximal end (31) penetrated through the first septum (11) and at least partly into the second reservoir (12), and

- a one-way valve (20) provided between the first variable volume reservoir (3) and the second reservoir (12) which one-way valve opens when the pressure (P) is above a pre-determined threshold value, wherein

the one-way valve (20) is located inside the cartridge (1) between the distal surface (13) and the proximal surface (16) of the septum unit (10).

2. A cartridge and needle cannula in combination according to claim 1, wherein the one-way valve (20) is an integrated part of the septum unit (10).

3. A cartridge and needle cannula in combination according to claim 2, wherein the one-way valve (20) is an integral part of the second septum (15).

4. A cartridge and needle cannula in combination according to claim 2 or 3, wherein the one-way valve (20) comprises a dish (23) abutting a seat (21).

5. A cartridge and needle cannula in combination according to claim 4, wherein the seat (21) is an integral part of the second septum (15).

6. A cartridge and needle cannula in combination according to claim 4 or 5, wherein the dish (23) is urged toward the seat by a resilient element (22) such as a spring.

7. A cartridge and needle cannula in combination according to any of the previous claims, wherein the volume of the second reservoir (12) is fixed.

8. A cartridge and needle cannula in combination according to any of the previous claims, wherein the cartridge (1) comprises an ampoule (2) made from a glass material.

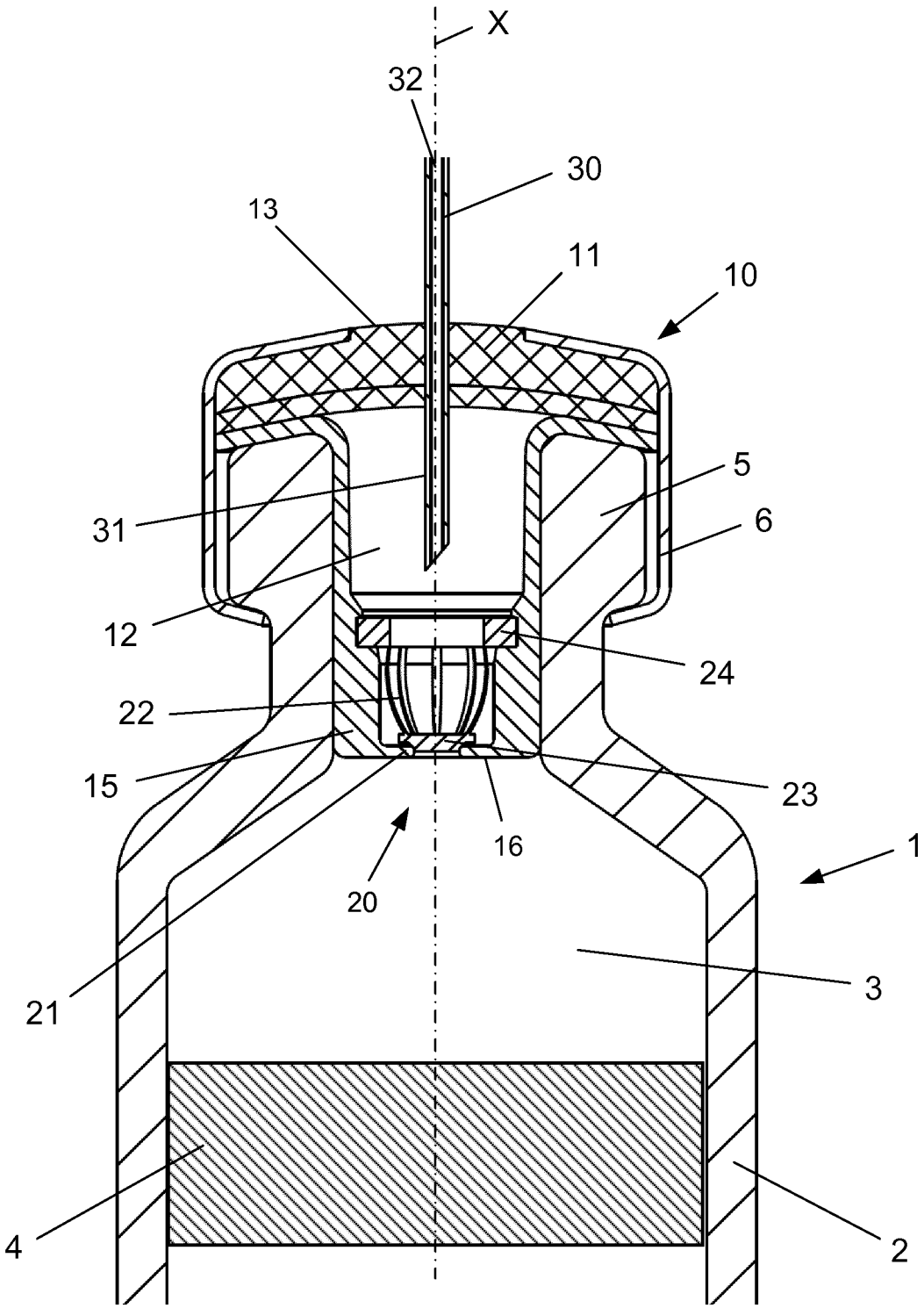

Fig. 1

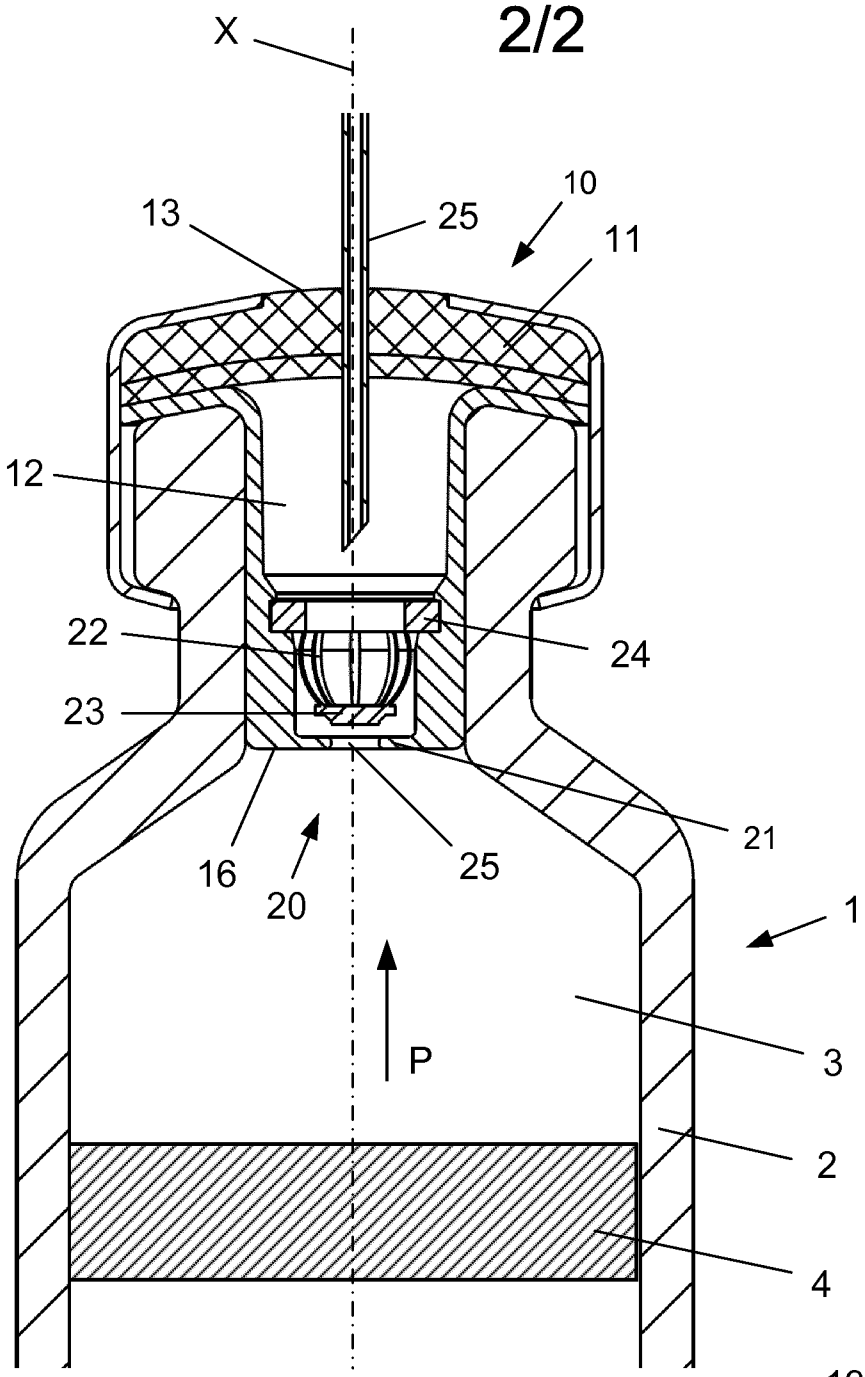

Fig. 2

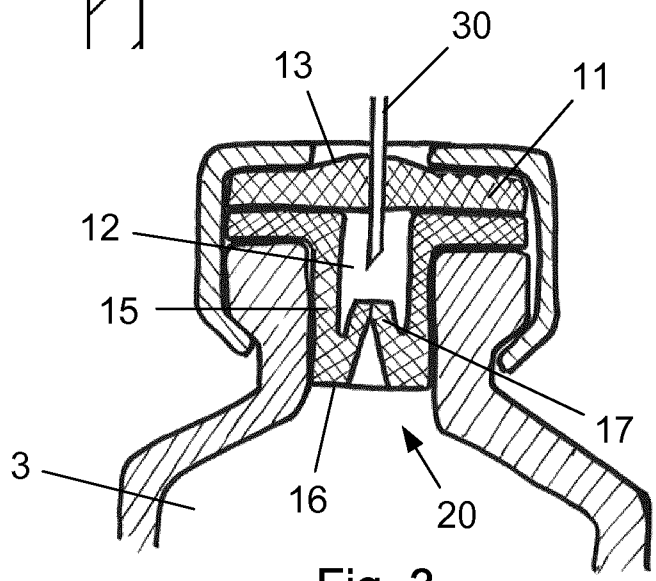

Fig. 3

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2015/057602

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61M5/24
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61M

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 3 091 240 A (MCCONNAUGHEY ROBERT K ET AL) 28 May 1963 (1963-05-28) claims 1,4 figures	1-8
X	US 2006/229562 A1 (MARSH RONALD W [US] ET AL) 12 October 2006 (2006-10-12) claims figures	1-6
X	US 2 828 742 A (ASHKENAZ DAVID M) 1 April 1958 (1958-04-01) claims figures	1-6
X	US 2013/085470 A1 (O'CONNOR SEAN M [US] ET AL) 4 April 2013 (2013-04-04) abstract figures	1-6

☐ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

* Special categories of cited documents :

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
6 August 2015	18/08/2015

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Türkavci, Levent

1

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/EP2015/057602

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