

“Sterile or sterilized package for administration of medicinal or nutritional substances”.

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5 The present invention relates to a sterile or sterilized package (that it is sterile from the outset or sterilized at a later stage) for the delivery of medicinal or nutritional substances.

 Sterile or sterilized packages suitable for the administration of medicinal or nutritional substances are known. Examples of said packages are disclosed in EP 2962676 B1, EP3158987 B1, EP 3545935 A1, and in the
10 Italian utility model No. 2020160000582078.

 In said packages, an outer flexible bag with a sterile or sterilized inner chamber houses a bottle of medicinal or nutritional substance with a pierceable cap in an overturned position and an introduction and withdrawal device placed below, equipped with tools for coupling to the cap of the
15 bottle and the perforation of said cap, and with a tube with openable closure extending out of the bag.

 Said tube may either be inserted directly into a flexible bag placed below filled with a liquid diluent to be mixed with the substance withdrawn from the bottle (EP 2962676 B1 and EP 3158987 B1) or end with a (male or
20 female) connector, which may be coupled in turn with either a complementary (female or male, respectively) connector of a flexible bag placed below filled with a liquid diluent to be mixed with the substance withdrawn from the bottle, or a syringe for the withdrawal and/or reconstitution of the medicinal or nutritional substance contained in the
25 bottle, or a two-way tap which, depending on its adjustment, connects the connector of the upper bag to a syringe placed on one side of the bag, or said syringe to the connector of a bag placed below, in order to allow the substances in the bottle and lower bag to be mixed in dosed quantities (Italian utility model No. 202016000058207 and EP 3545935 A1).

30 For all the uses described above the same problem applies, i.e. to keep

a difference in pressure between the inside of the bottle – above the level of the liquid contained therein – and the outflow from the tube with the connector open such as to help the substance flow out of the bottle, even without exerting manual pressure from outside on the bag housing the bottle.

5 The object of this invention is to address the issue described above in a simple and safe manner, working in a closed system and under sterile conditions and without resorting to measures implying the use of further instrumental devices.

10 To this purpose, the present invention relates to a package for administration of medicinal or nutritional substances, comprising an outer bag with a sterile or sterilized inner chamber housing a bottle of medicinal or nutritional substance with a pierceable cap in an overturned position, and a device for the withdrawal and/or reconstitution of the substance contained in the bottle, which is placed below the cap of the bottle and may be hooked
15 to the neck of the bottle, said device including a needle for the perforation of the cap of the bottle which is axially movably with respect to the bottle, and an outflow tube with openable closure element extending out of the bag, said package being characterized in that said perforation needle is passed through
20 longitudinally by a first channel connecting - after perforation of the cap and with the closure element set open - the inside of the bottle to said outflow tube, and a second channel with a side opening and a hydrophobic filter configured to allow, after perforation of the cap, only air or other gaseous fluid to flow from inside the bottle into the inner chamber of the bag, or vice versa.

25 When the needle penetrates through the cap of the bottle and the closure element of the outflow tube is set open, the difference in pressure generated by the structure above triggers the outflow of the medicinal or nutritional substance from the bottle through the tube, and then to the bag or syringe which the tube has been connected to. At this stage, the channel with
30 a side opening equipped with hydrophobic filter ensures the proper air

pressure inside the bottle.

A possible embodiment and its application possibilities are shown and described – by way of non-limited example - in the appended drawings, in which:

5 Figure 1 illustrates a package according to the invention in an initially sealed condition;

 Figure 2 shows a withdrawal and/or reconstitution device used in the package of Fig. 1 for the coupling and perforation of the cap of a bottle of medicinal or nutritional substance set in an overturned position inside a
10 flexible bag;

 Figure 3 shows the package of Fig. 1 during administration of the medicinal or nutritional substance;

 Figure 4 illustrates different employment options for a package such as the one in Fig. 1;

15 Figures 5-9 show in greater detail the processing sequence for the mixing of the substance contained in the bottle with the one contained in the lower bag by means of a two-way tap and a syringe.

 The package shown in Figure 1 features an outer sterile or sterilized flexible bag 1, wherein an inner chamber 2, sterilized for example by means
20 of a mixture of ozone or other sterilizing gas and oxygen delivered through a tube 3 equipped with a connector 4 (for example of the type with an airtight open/close cap as described in EP 2667839 B1), houses and shows an overturned bottle 5 of medicinal or nutritional substance 6 with a neck 7 and a sealed (openable and automatically airtight reasealable) cap 8 in a coupling
25 position, and a withdrawal and/or reconstitution device 9 which is hooked to the neck 7 of the bottle 5 and may be operated from outside bag 1 in order to perforate cap 8 of bottle 5. The dotted line L generically indicates the level of substance 6 inside bottle 5.

 Figure 2 provides a magnified view of device 9 consisting of an upper
30 body 10 equipped with flaps 11 that may be hooked to neck 7 of bottle 5,

and a lower body 12 which is coupled to upper body 10 in an axially sliding mode and comprises a perforation needle 13 with a piercing tip 14 protruding upwards and a bottom shank 34 which is hermetically accommodated within a flexible outflow tube 15 ending with an airtight openable and automatically resealable end connector 16 (for example of the type with an airtight open/close cap as described in EP 2667839 B1), and terminates with a frangible closure element 17.

The perforation needle 13 is passed through longitudinally by two channels 18 and 19 running alongside each other, the former being open at the top end and closed at the lower end by the frangible element 17, and the latter being open at the top end and in permanent communication with inner chamber 2 of bag 1 through a side opening 20 equipped with a hydrophobic filter 21 allowing the passage of air or other gaseous fluids, but preventing any liquids from passing through.

In the initial condition described in Figure 1, with lower body 12 of device 9 set downward from upper body 10 of said device 9, the air or other sterile mixture contained inside inner chamber 2 of bag 1 is left outside bottle 5, which in turn contains medicinal or nutritional substance 6 in a sealed environment.

Pushing bottle 5 down from outside bag 1 towards lower body 12 of device 9, tip 14 of needle 13 perforates cap 8 of bottle 5, whereby channels 18 and 19 are put in communication with the inside of bottle 5, as shown in Figure 3.

This allows the passage of air or another sterile mixture through hydrophobic filter 21, side opening 20, and up channel 19 till inside bottle 5, forcing medicinal or nutritional substance 6 – once the frangible closure 17 is broken – to flow out of bottle 5 and down outflow tube 15 through channel 18 till connector 16, and from there to the external user device (syringe for withdrawal and/or reconstitution, further collection bag or other) by differential pressure. Filter 21 prevents substance 6 from flowing out

from the side opening 20.

As described in Figure 4, the user device may consist in a syringe for injection or withdrawal 22 with a luer 23 for the opening of connector 16, or a similar syringe for injection or withdrawal 24 with a luer 25 and a luer-lock device 26, or a simple input or collection bag 27 with a connector 28 shaped to complement connector 16 (or otherwise connected to outflow tube 15 of bag 1), as well as a two-way flow-diverting tap 29 placed between connector 16 and a complementary connector 30 of a lower bag, and which may be coupled to a syringe for withdrawal and reconstitution.

This latter application is detailed in Figures 5-9, where items corresponding to those in Figures 1-4 are referenced with the same numbers.

As shown in Figure 5, between the two bags 1 and 31 – the former containing a medicinal or nutritional substance 6 and the latter filled with a suitable liquid diluent 35 (or other liquid substance that may be mixed with medicinal or nutritional substance 6) and equipped with an inlet tube 51 with a connector 53 and an outlet tube 52 with an openable cap 54 – a two-way tap 29 is placed, which comprises three nozzles with a connector each (36, 38, 32), the first of which may be coupled to connector 16 of bag 1, the second to connector 30 of bag 31, while the third is normally sealed but may be opened and perforated with a syringe 40 with sliding plunger 41 and a luer 42 at the end. Tap 29 is adjustable into two positions by operating a rotating component 39. Connections between tap 29 and bags 1 and 31 may be permanent rather than through connectors 16, 36, and 30, 38.

In this case tap 29 is adjusted before use so as to inhibit any communications with lower bag 31, while tube 15 is closed with closure 17, as shown in Figure 5.

In order to mix a dosed quantity of pharmaceutical or nutritional substance 6 with diluent 35, syringe 40 with plunger 41 pushed all the way in as in Figure 5 is connected to tap 29 by inserting luer 41 inside connector 32, then the rotating component 39 of tap 29 is turned into a position so as to

inhibit communications with tube 15 and open connections to the inner chamber of bag 31; then, plunger 41 of the syringe is pulled backwards until a dosed quantity of diluent 35 is withdrawn from bag 31 (Figure 6).

5 Tap 29 is then adjusted so as to stop communications with the inner chamber of bag 31, the frangible closure 17 is broken to open connections between internal channel 18 of needle 13 and tube 15, and bottle 5 is pushed downwards, thereby forcing the tip of needle 13 into cap 8 of bottle 5 (Figure 7). Plunger 41 of syringe 40 is then pushed in in order to deliver the quantity of diluent withdrawn from bag 31 inside bottle 5, thus forming
10 therein a mixture 50 of medicinal or nutritional substance 6 and diluent 35 (Figure 7). At this stage, the air inside bottle 5 is forced to flow out of bottle 5 into inner chamber 2 of bag 1 through channel 19 and side opening 20. Hydrophobic filter 21 allows the passage of air while preventing substance 6 or mixture 50 from passing through.

15 With tap 29 still set in the position described above, a dosed quantity of mixture 50 is then withdrawn from syringe 40 by pulling plunger 41 backwards, as illustrated in Figure 8. The air previously forced into inner chamber 2 of bag 1 may flow back into bottle 5 through opening 20 with hydrophobic filter 21 and channel 18 of needle 13.

20 Tap 29 is then set back into a position of closure of tube 15 and opening of communications with the inner chamber of bag 31, and plunger 41 is pushed in to deliver the dosed quantity of mixture 50 previously withdrawn from bottle 5 into bag 31 (Figure 9). Bag 31 is then ready for use.

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CLAIMS

1. A package for administration of medicinal or nutritional substances, comprising:
 - an outer bag (1) with a sterilized inner chamber (2),
 - 5 a bottle (5) of medicinal or nutritional substance (6) set in an overturned position and disposed within the inner chamber (2) of the outer bag (1), the bottle (5) comprising a neck (7) and a pierceable cap (8),
 - a device (9) configured to withdraw or reconstitute substance (6) contained in the bottle (5), the device (9) is hooked to the neck (7) of the bottle (5), and the device
 - 10 (9) comprises a perforation needle (13) configured to move in an axial direction relative to the bottle (5) and to perforate the cap (8) of the bottle (5) and a bottom shank (34) extending from a base of the needle (13), and
 - an outflow tube (15) extending out of the outer bag (1) and comprising an openable closure element (17) disposed in a passage of the outflow tube (15),
 - 15 characterized in that said perforation needle (13) comprises:
 - a first channel (18) extending longitudinally through the perforation needle (13) such that first channel (18) establishes fluid communication between an interior of the bottle (5) and the passage of the outflow tube (15) when the
 - 20 perforation needle (13) perforates the cap (8) and the closure element (17) is opened,
 - a second channel (19) extending from a side opening (20) of the perforation needle (13) to a tip of the perforation needle (13), wherein the side opening (20) is disposed at the base of the needle (13) above the bottom shank (34) and opens directly into the inner chamber of the outer bag (1), and
 - 25 a hydrophobic filter (21) disposed within the perforation needle (13) at the side opening (20) and configured to allow only air or other gaseous fluid to flow between the interior of the bottle (5) and the inner chamber (2) of the bag (1) when the perforation needle (13) perforates the cap (8).
- 30 2. The package according to claim 1, characterized in that the reconstitution device (9) comprises an upper body (10) equipped with flaps configured to be hooked to the neck (7) of the bottle (5) and a lower body (12) slidably coupled to the upper body (10) the lower body (12) comprises said perforation needle (13) and a bottom shank (34) housed

hermetically within said outflow tube (15), and the first channel (18) extends in a longitudinal direction through the bottom shank.

5 3. The package according to claim 1 or 2, characterized in that said outflow tube (15) includes an end connector (16) disposed at an end of the outflow tube (15) and configured to open and close the end of the outflow tube (15).

 4. The package according to claim 3, characterized in that said end connector (16) configured to be coupled to an opening syringe (22, 24).

10 5. The package according to any one of the preceding claims, characterized in that said bag (1) is made of a flexible material.

 6. The package according to any one of claims 1-5, characterized in that said bag (1) comprises a tube (3) with an airtight connector (4) configured to open and close to introduce a mixture of ozone or any other sterilizing gas into said inner chamber (2) of the bag (1).

15 7. The package according to any one of claims 1-6, characterized by comprising: a second bag (31) positioned below said outer bag (1) and designed to contain a liquid substance (35) to be mixed with said medicinal or nutritional substance (6), and a two-way tap (29) disposed between the outer bag (1) and the second bag (31), the two-way tap (29) comprising a side open/close connector (32) configured to be coupled to an opening syringe (40) with a sliding plunger (41), characterized in that said tap (29) is configured to be adjusted between a first position inhibiting communications between said side connector (32) and said second bag (31), and a second position inhibiting communications between said side connector (32) and said outflow tube (15) of said outer bag (1).

20 8. The package according to claim 7, characterized in that said two-way tap (29) comprises a first connector (36) secured to an end connector (16) of the outflow tube (15) of the outer bag (1) and a second connector (38) secured to an end connector (30) of a second outflow tube of the second bag (31).

9. The package according to claim 7, characterized in that said tap (29) is permanently secured to the outflow tube (15) of the outer bag (1) and a second outflow tube of the second bag (31).

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10. The package according to any one of claims 1-3 and 5-6, further comprising a collection bag (27) positioned below said outer bag (1) and in communication with the outer bag (1).

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