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(54) **Improved containers for reactive pharmaceutical compounds.**

(57) There is provided a container including outlet means, which comprises plastics components and holds a pharmaceutically active compound having a primary or secondary amine group, in which some or all of the plastics components which come into contact with the pharmaceutically active compound during storage or release through the outlet means are made from polyester.

The container avoids the risk of interaction product formation which exists with conventional containers having non-polyester plastics components.

The container is particularly useful when the pharmaceutically active compound is an inhaled phenylethylamine derivative, such as reproterol.

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This invention relates to improved containers for reactive pharmaceutically active compounds, more particularly to improved containers for pharmaceutically active compounds having a primary or secondary amine group.

It has been found that when pharmaceutically active compounds having a primary or secondary amine group come into contact with certain plastics materials, including polyformaldehydes which are conventionally used for producing the plastics components of pressurized aerosol containers provided with valves, an interaction product may be formed. Thus, when such compounds are stored in or dispensed from containers where they come into contact with such plastics materials, there is a danger that the interaction product may contaminate the compound. This is highly undesirable, as the contaminant is potentially toxic.

We have now found that pharmaceutically active compounds having a primary or secondary amine group do not form interaction products when they come into contact with polyester materials, and that when such compounds are stored in or dispensed from containers in which some or all of the plastics components with which they come into contact are made from polyester, interaction product contaminants are not produced or their level is significantly reduced.

The present invention provides a container including outlet means, which comprises plastics components and holds a pharmaceutically active compound having a primary or secondary amine group; characterized in that some or all of the plastics components which come into contact with the pharmaceutically active compound during storage or release through the outlet means are made from polyester.

The pharmaceutically active compound may be present as a salt, including an acid addition salt formed with the amine group, for example a hydrochloride, hydrobromide or hydrosulphate.

It will be appreciated by those skilled in the art that the pharmaceutically active compound will often be present as a component of a pharmaceutical formulation.

It is particularly important that medicaments administered to sensitive organs such as the lungs should be as pure as possible. Because of the potential toxicity of the interaction product contaminant mentioned above, containers according to the present invention are particularly useful in the storage and administration to the lungs by inhalation of pharmaceutically active compounds having a primary or secondary amine group.

Inhalation devices for use in association with a pressurized aerosol cannister of medicament provided with a valve have been used in the administration of medicaments to the lung by inhalation for some time. A preferred type of container is therefore a pressurized aerosol cannister provided with a valve. Pressurized aerosol cannisters are often made from a metal, for example aluminium, in which case some or all of the components of the valve will be made of polyester.

Suitable valves for pressurized aerosol cannisters include metering valves, in particular those described in European Patent Application No 143577, which application is incorporated herein by reference.

When the container is a pressurized aerosol cannister provided with a valve, the pharmaceutically active compound is desirably dispersed in a pharmaceutically acceptable aerosol propellant, for example a chlorofluorocarbon or a hydrofluorocarbon such as trifluorochloromethane, dichlorotetrafluoroethane or dichlorodifluoromethane. Of course, a mixture of such propellants may be used, and conventional aerosol formulation components may also be present, including a surfactant, for example sorbitan trioleate.

Containers according to the invention are particularly useful in the storage and administration of pharmaceutically active phenylethylamine derivatives, including those in which the phenyl ring is substituted by hydroxy. Examples of such compounds include isoprenaline, salbutamol, orciprenaline and particularly reproterol.

When the pharmaceutically active compound is an inhalation medicament for administration to the lung, we prefer the container also to hold a prophylactic anti-asthma agent. Prophylactic anti-asthma agents include nedocromil sodium and sodium cromoglycate.

Suitable polyester materials for use in the invention include polyethylene terephthalate and particularly polybutylene terephthalate.

A specific example of a container according to the invention is a pressurized aerosol cannister provided with a valve, the cannister being made of aluminium and the valve being that described in EP 143577 with reference to Figures 1 and 2, but with the circular cup (1) and valve bush (3) being made of polybutylene terephthalate, and the cannister containing the following formulation:

sodium cromoglycate	1.4663 % w/w
reproterol hydrochloride	0.7331
sorbitan trioleate	0.5000
trifluorochloromethane	10.0000
dichlorotetrafluoroethane	13.0951
dichlorodifluoromethane	74.2055
	100.0000

Claims

1. A container including outlet means, which comprises plastics components and holds a pharmaceutically active compound having a primary or secondary amine group; characterized in that some or all of the plastics components which come into contact with the pharmaceutically active compound during storage or release through the outlet means are made from polyester.

2. A container according to claim 1, which is a pressurized aerosol cannister provided with a valve.

3. A container according to claim 2, wherein the pharmaceutically active compound is dispersed in a pharmaceutically acceptable aerosol propellant.

4. A container according to any one of the preceding claims, wherein the pharmaceutically active compound is for administration to the lung by inhalation.

5. A container according to any one of the preceding claims, wherein the pharmaceutically active compound is a phenylethylamine derivative.

6. A container according to any one of the preceding claims, wherein the pharmaceutically active compound is reproterol.

7. A container according to any one of claims 4 to 6, which also holds a prophylactic anti-asthma agent.

8. A container according to claim 7, wherein the prophylactic anti-asthma agent is sodium cromoglycate.

9. A container according to any one of the preceding claims, wherein the polyester is polybutylene terephthalate.

10. A medicament inhalation device comprising a container according to any one of the preceding claims.

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EUROPEAN SEARCH REPORT

Application Number

EP 91 30 6932

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int. Cl.5)
X	EP-A-0 196 288 (DRACO) * column 4, line 32 - line 33; claims 1,6 * * * page 5, line 9 - line 17 * *	1-10	A 61 M 15/00 A 61 J 1/00
A	US-A-4 451 641 (EASTMAN KODAK)		

TECHNICAL FIELDS SEARCHED (Int. Cl.5)

A 61 M
A 61 J
C 08 G

The present search report has been drawn up for all claims

Place of search	Date of completion of search	Examiner
The Hague	06 November 91	COUSINS-VAN STEEN G.

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
Y : particularly relevant if combined with another document of the same catagory
A : technological background
O : non-written disclosure
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T : theory or principle underlying the invention

E : earlier patent document, but published on, or after the filing date
D : document cited in the application
L : document cited for other reasons

& : member of the same patent family, corresponding document