

# Application of aerosols

# Topics

- Types of aerosols
- Application of aerosols
- Biopharmaceutical aspects
  - Anatomy
- Preparations for inhalation
  - Liquid preparations
  - Solid preparations



# Aerosols

## Main types of aerosols:

- Solution-based
- Water medium
- Suspension or dispersion systems
- Foam-based systems
  - Water-based, stable foams
  - Non-aqueous, stable foams
  - Quick-breaking foams
  - Temperature sensitive foams



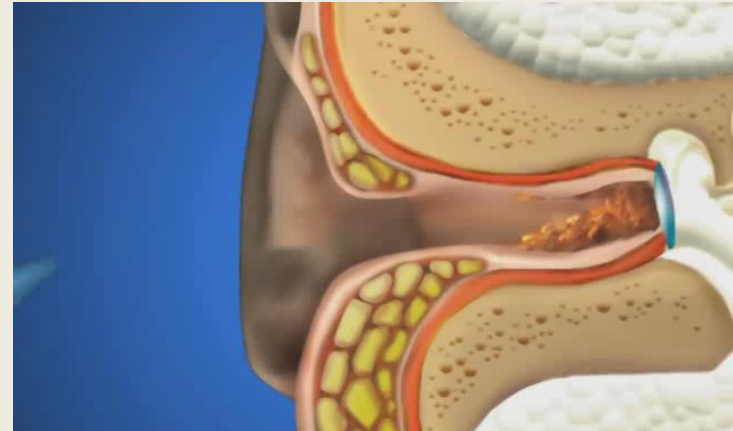
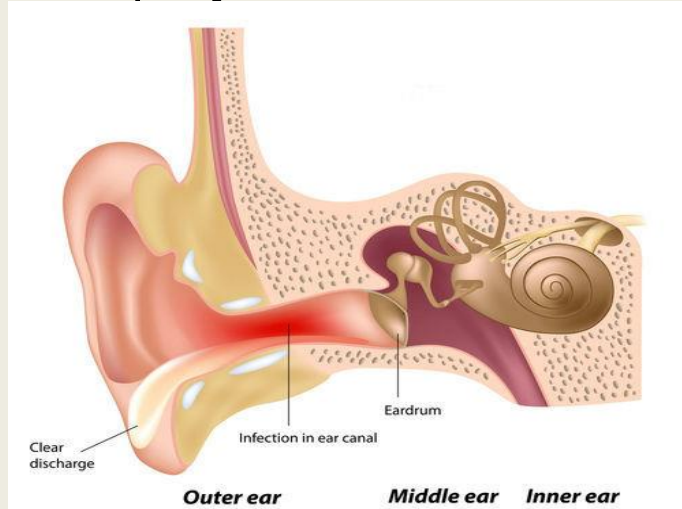
# Application of aerosols

Air fresheners



# Application of aerosols

## Ear spray



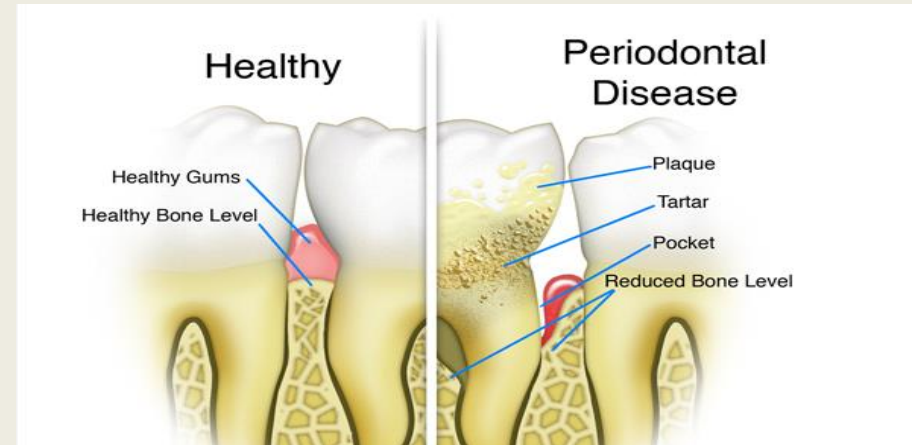
# Application of aerosols

## Nasal spray



# Application of aerosols

## Mouth spray



# Application of aerosols

## Throat treatment





# Application of aerosols

Skin therapy

Pigmentation



# Application of aerosols

Skin therapy

Sunburn



# Application of aerosols

Skin therapy

Skin burning



# Application of aerosols

## Skin therapy

### Eczema



# Application of aerosols

## Antianginal



# Application of aerosols

Body odour



# Application of aerosols

## Foot & nail antifungal spray



# Preparations for Inhalation (*Inhalanda*)





# Preparations for inhalation

## Definition

**Preparations for inhalation** are **liquid** or **solid** preparations intended for administration as **vapours** or **aerosols** to the **lungs** in order to obtain a **local** or **systemic** effect.

They contain **one** or **more active substances** which may be **dissolved** or **dispersed** in a suitable vehicle.

# Preparations for inhalation

## Definition

Depending on the type of preparation, inhalation preparations may contain:

- **propellants,**
- **co-solvents,**
- **diluents,**
- **antimicrobial preservatives,**
- **solubilizing and**
- **stabilizing agents, etc.**

These excipients **do not adversely affect the functions** of the mucosa of the respiratory tract or its cilia.

Preparations for inhalation are supplied in **single** or **multi-dose** containers.

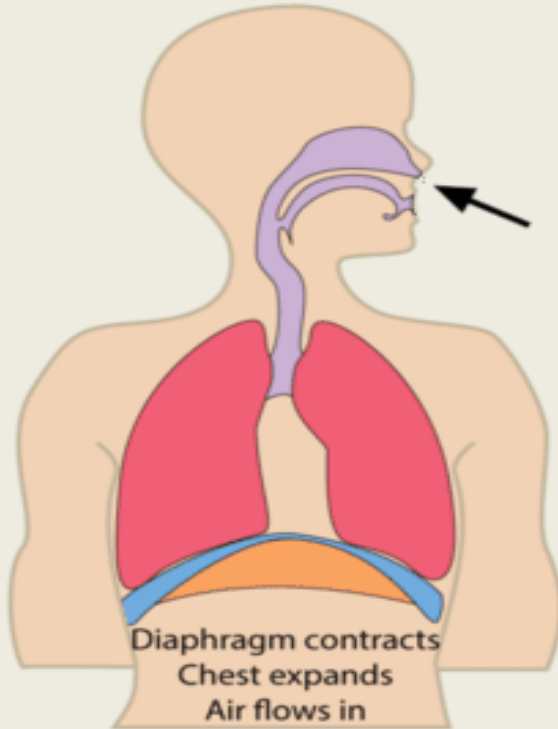
# Biopharmaceutical aspects



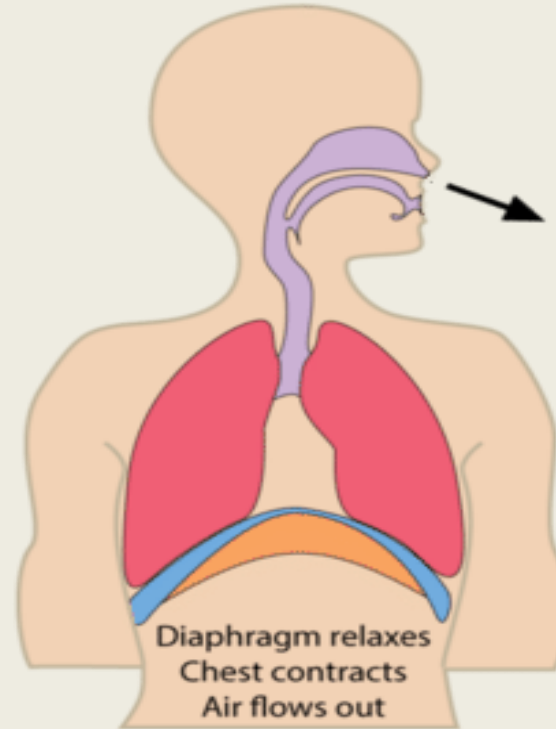
# Respiratory system

## The breathing

Inhalation

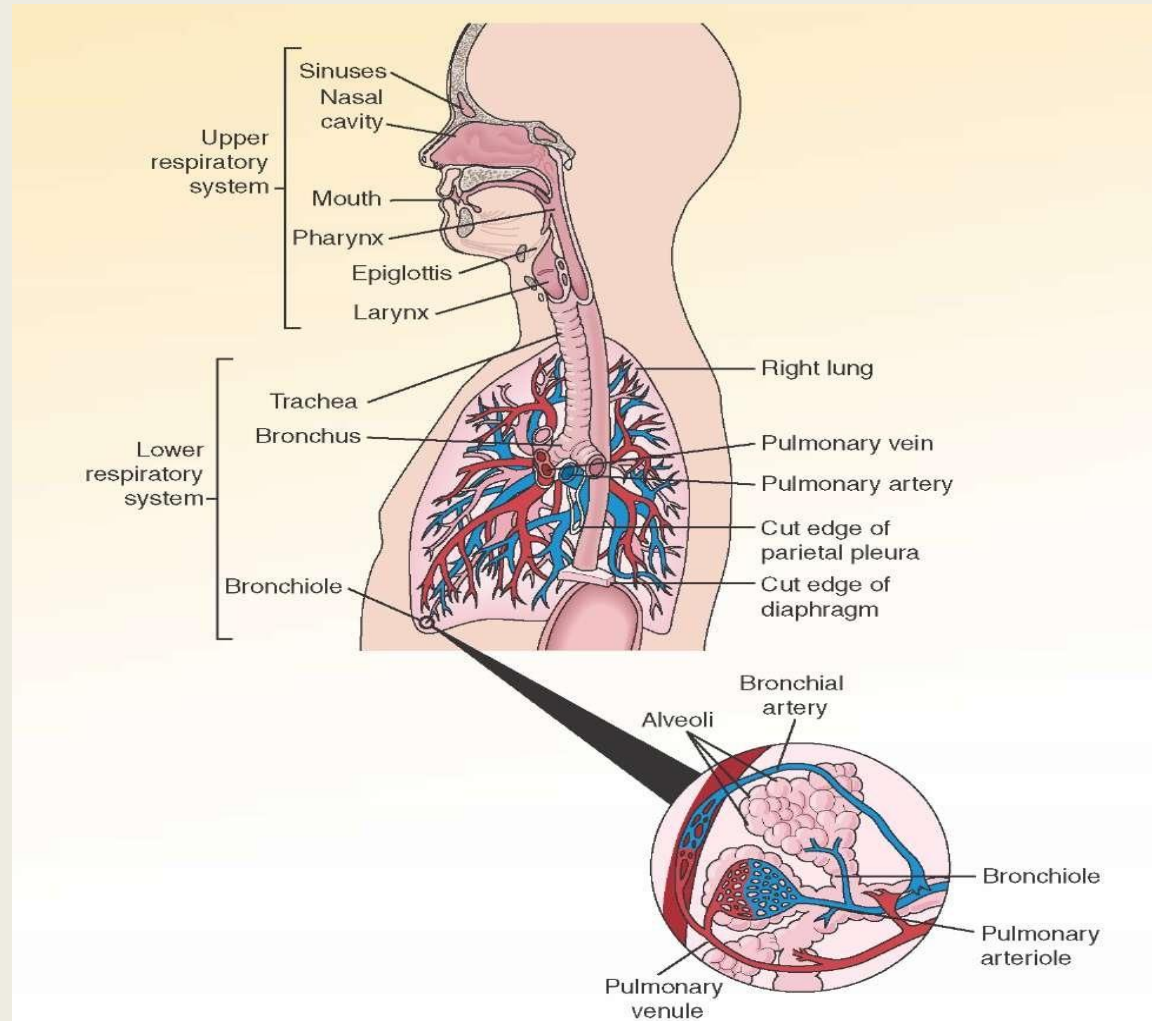


Exhalation



# Respiratory system

## Airway anatomy



# Respiratory system

## Anatomy of the airways

- Air enters the nostrils
- passes through the nasopharynx,
- the oral pharynx
- through the glottis
- into the trachea
- into the right and left bronchi, which branches and rebranches into
- bronchioles, each of which terminates in a cluster of
- alveoli.

**Only in the alveoli does actual gas exchange takes place.**

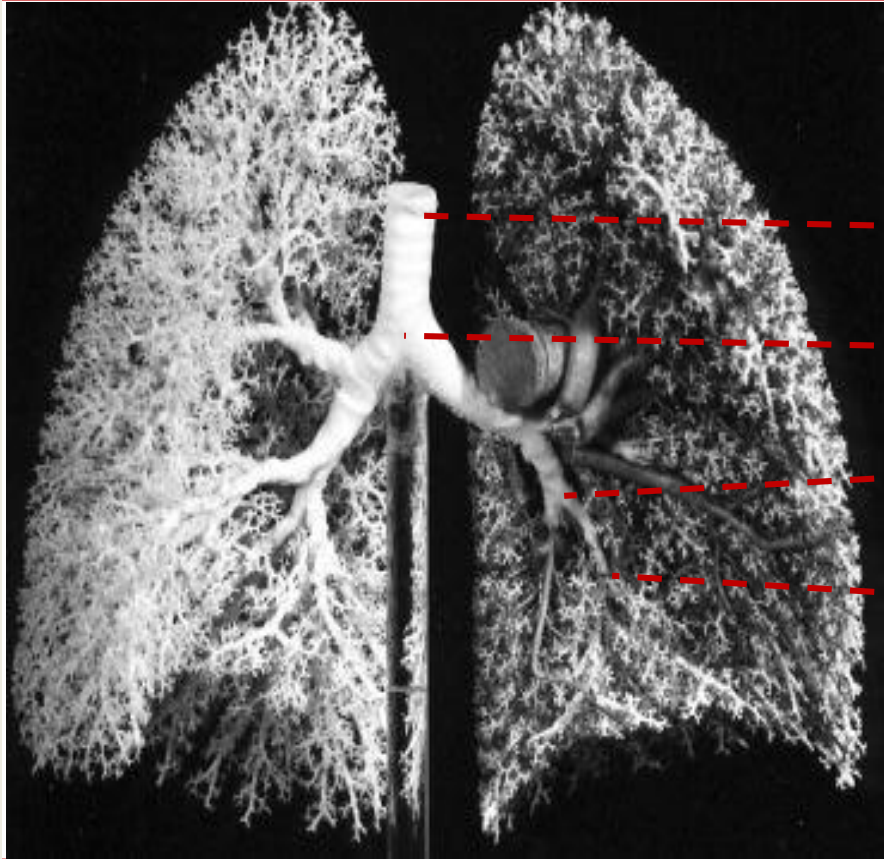
There are some **300 million alveoli** in adult lungs.

These provide a surface area of some 160 m<sup>2</sup>.

(Almost equal to the area of a tennis court and 80 times more than the area of our skin!).

# Respiratory system

## Anatomy of the airways



tracheas

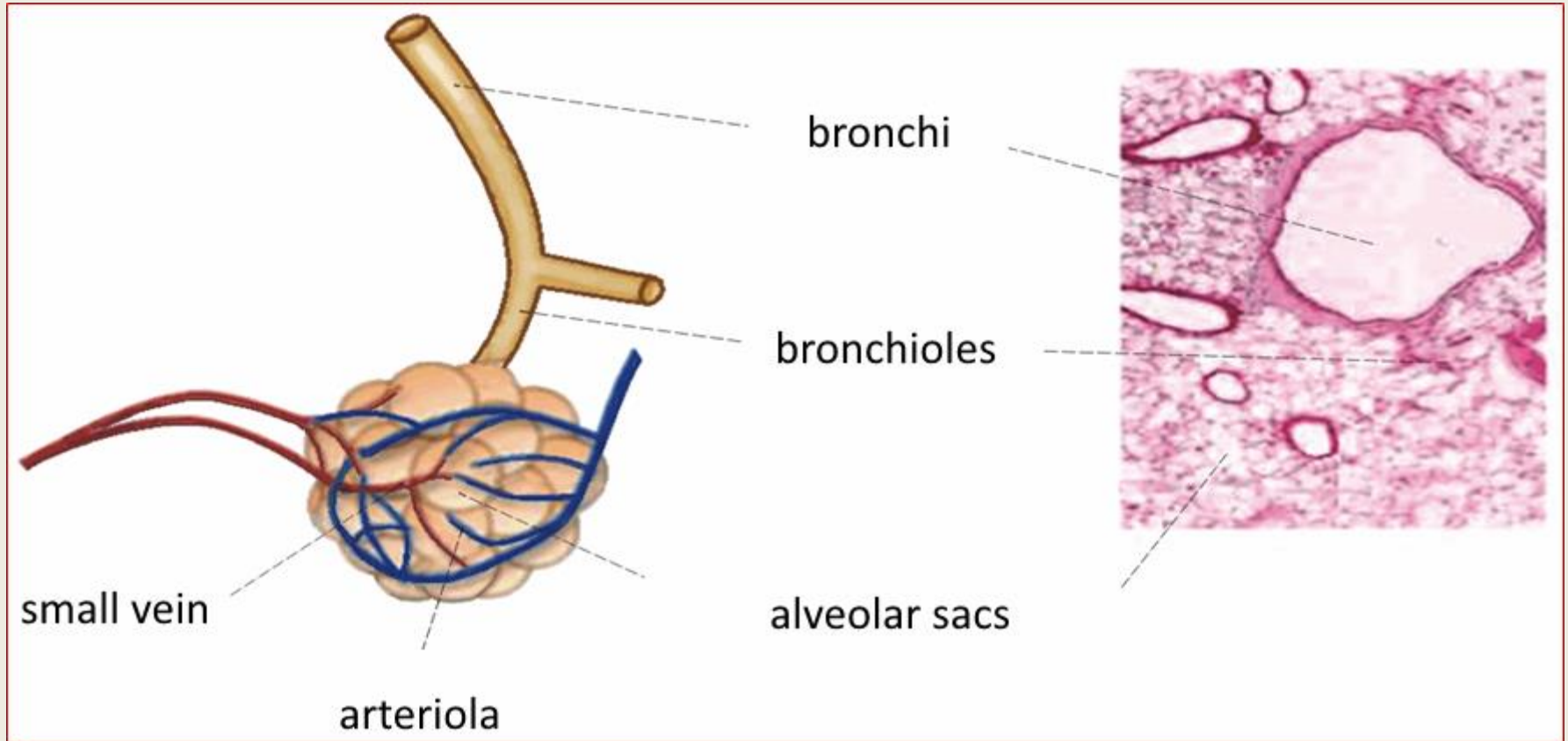
pulmonary hilum

bronchi

bronchioles




# Respiratory system

## Anatomy of the airways





# Particles in respiratory system

		Surface (m <sup>2</sup> )	Dumped particle sizes (μm)
trachea			
bronchus		0,03	5 – 20 μm
bronchiolus		5 – 7,5	1–5 μm
ductus alveolaris alveolus pulmonalis		100 – 150	

# Particles in respiratory system

The mechanism of **deposition** of inhaled particles affect the

- **size,**
- **sedimentation,**
- **density,**
- **shape,**
- **surface charge,**
- **surface tension,**
- **the particles hygroscopicity.**

These properties influenced by the

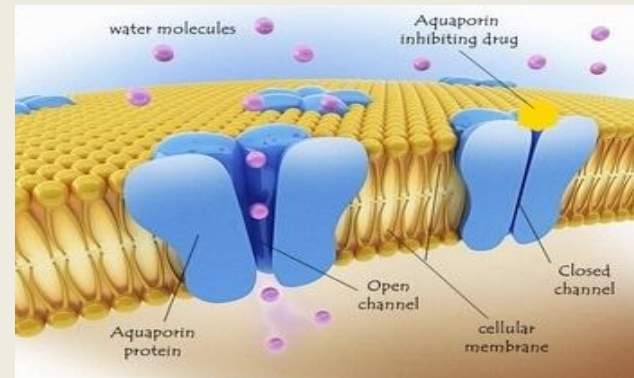
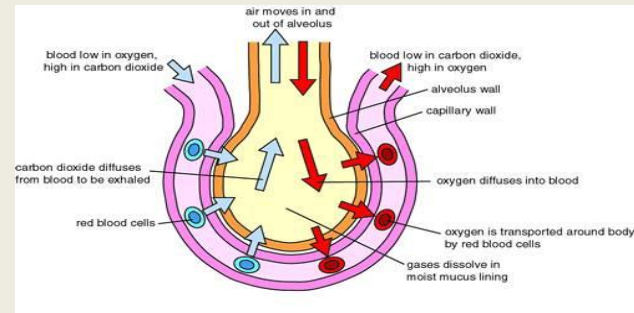
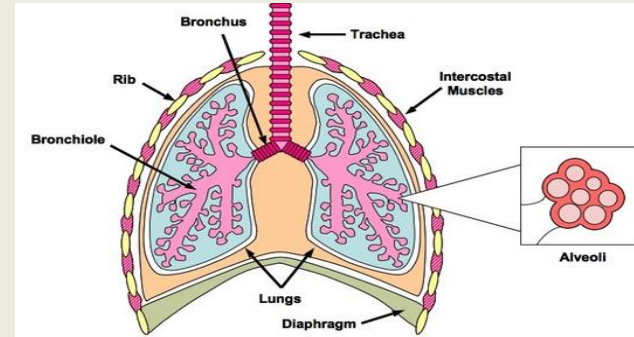
- **excipients,**
- **mode of administration and**
- **the atomizing parameters.**

# Particles in respiratory system

## Mechanism of drug absorption

The absorption of drugs may occur by:

- drug **diffusion** through alveoli,
- absorption through aqueous pores by **carrier mediated transport** (aquaporin channel),
- **phagocytosis** of **insoluble particles** allow absorption of compounds with low lipophilicity or high molecular weight.



# Preparations for inhalation

## Liquid preparations



# Liquid preparations

## Definition

Liquid preparations for inhalation are **solutions** or **dispersions**.

Liquid preparations for inhalation may be distinguished:

1. preparations intended to be **converted into vapour**,
2. liquid preparations for **nebulisation**,
3. **pressurised metered-dose** preparations for inhalation.



# Liquid preparations

## Preparations intended to be converted into vapour

Preparations intended to be converted into **vapour** are

- solutions,
- dispersions or
- solid preparations.

They are usually added to hot water and the vapour generated is inhaled.



# Liquid preparations

## Liquid preparations for nebulisation

Liquid preparations for inhalation intended to be converted into aerosols by continuously operating nebulisers or metered-dose nebulisers are

- solutions,
- suspensions or
- emulsions.

Suitable co-solvents or solubilisers may be used to increase the solubility of the active substances.

Liquid preparations for nebulisation in concentrated form for use in continuously operating nebulisers are diluted to the prescribed volume with the prescribed liquid before use.

Liquids for nebulisation may also be prepared from powders.

# Liquid preparations

## Liquid preparations for inhalation

### A. Preparations for steaming

- they may be solutions, dispersions or solids. Such formulations are usually added to hot water and the vapour formed must be inhaled.

### B. Liquid for nebulization

- aerosolized with a continuous nebulizer or metering valve nebulizer, in the form of solutions, suspensions or emulsions. The solubility of the active ingredient may be increased by the use of a suitable co-solvent or solubilizer.

### C. Pressurized inhaled metered dose

- solutions, suspensions or emulsions in dosing valves marketed in special containers which are pressurized with a suitable mixture of propellants or liquefied propellants, whether or not they may be used as solvents. Addition of cosolvents and solubilizers is permitted.



# Liquid preparations

## Liquid preparations for nebulization

### Continuously operating nebulizers

The pH of the liquid preparations for use in **continuously operating nebulizers** is not **lower than pH 3** and **not higher than pH 8.5**.

Suspensions and emulsions are readily dispersible on shaking and they remain sufficiently stable to enable the correct dose to be delivered.

Aqueous preparations for nebulization supplied in **multidose** containers may contain a suitable **antimicrobial preservative** at a suitable concentration except where the preparation itself has adequate antimicrobial properties.

Continuously operating nebulizers are devices that **convert liquids into aerosols** by **high-pressure gases, ultrasonic vibration** or other methods. They allow the dose to be inhaled at an appropriate rate and particle size which ensures deposition of the preparation in the lungs.

# Liquid preparations

Liquid preparations for nebulisation  
Continuously operating nebulisers

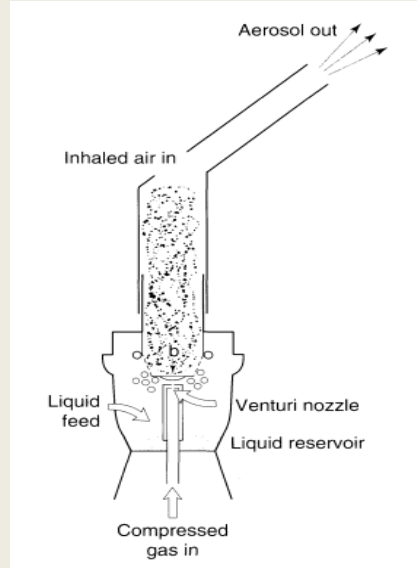
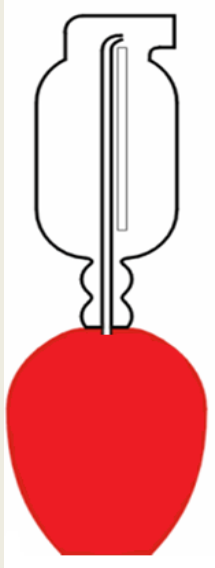


The power injectors with oxygen, compressed air, or ultrasonically produced spray.

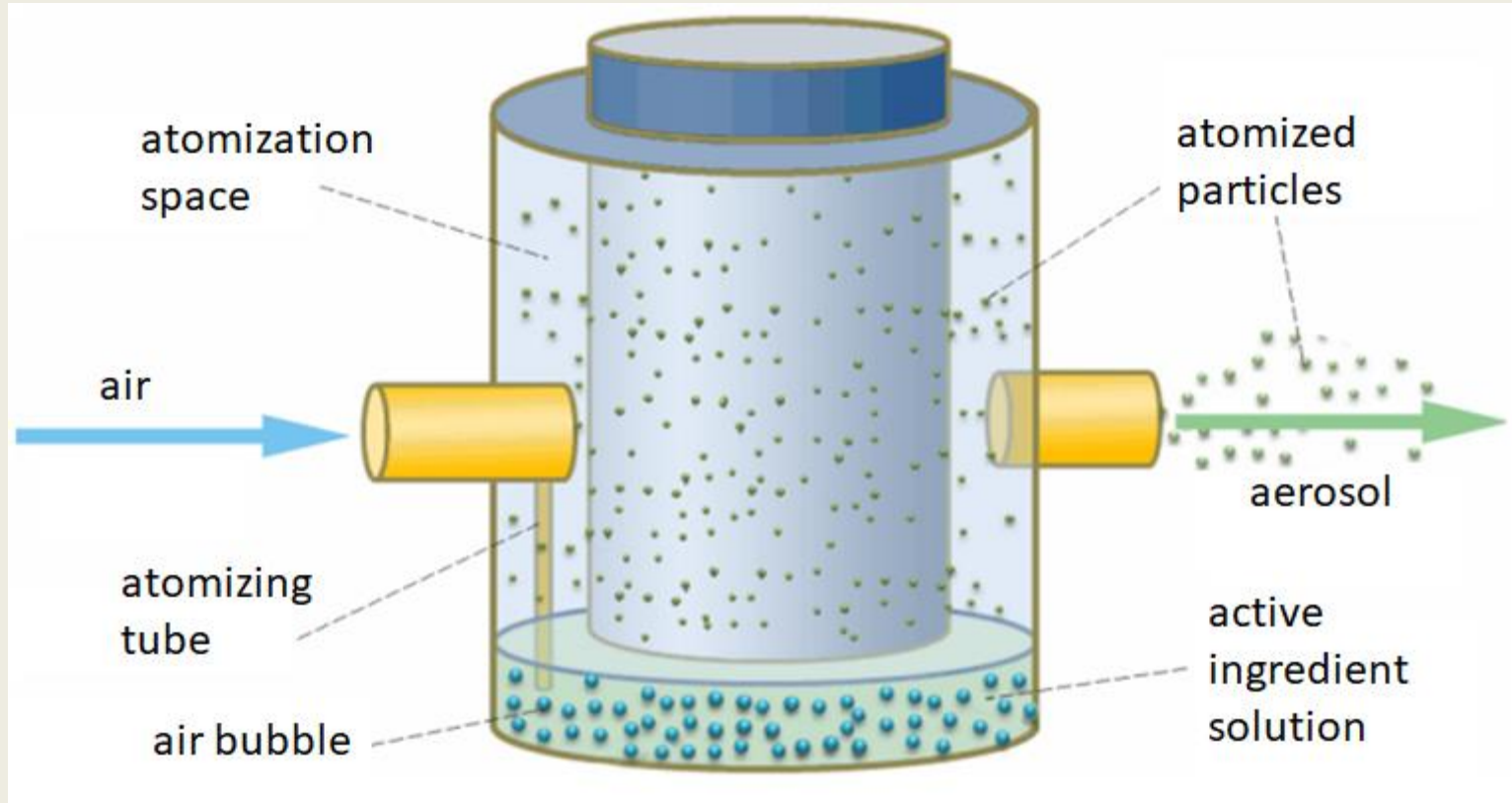
# Liquid preparations

Liquid preparations for nebulisation

Handy nebulizer



# Liquid preparations



Inhalation nebulizer equipment

# Liquid preparations



Jet nebulizer

Machine sprayers produce spray with oxygen, pressurized air, or ultrasound.

# Liquid preparations

## Pressurised metered-dose preparations for inhalation

**Pressurised metered-dose preparations** for inhalation are

- **solutions,**
- **suspensions or**
- **emulsions**

supplied in special containers equipped with a metering valve and which are held under pressure with suitable propellants or suitable mixtures of liquefied propellants, which can act also as solvents.

# Liquid preparations

## Pressurised metered-dose preparations for inhalation

Suitable **co-solvents**, **solubilisers** and **stabilisers** may be added.

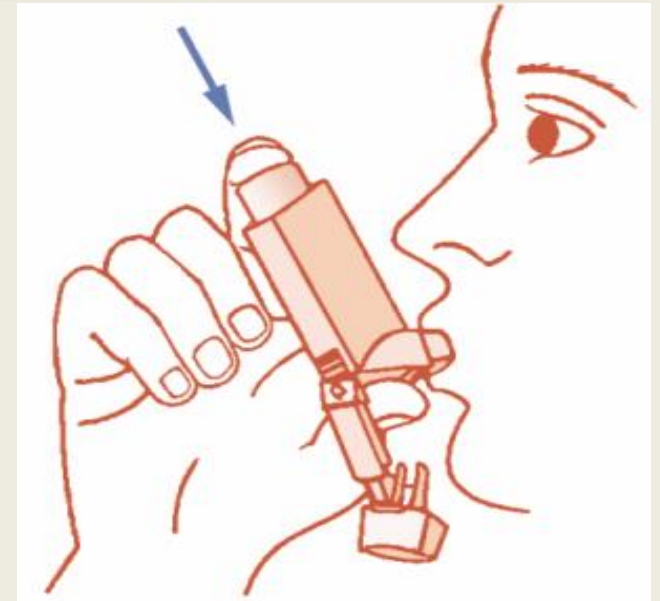
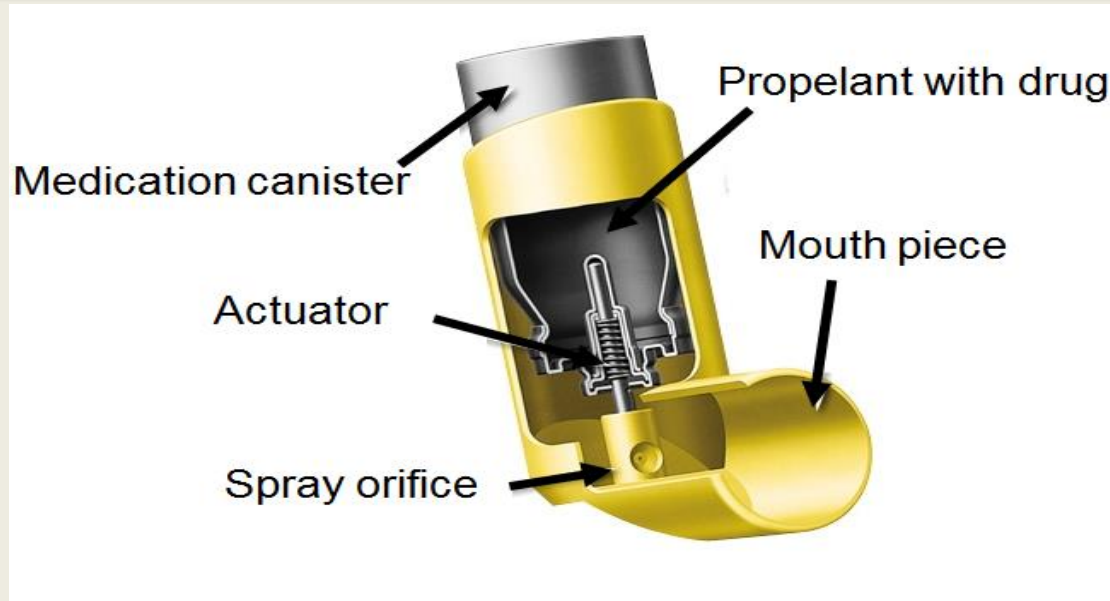
The delivered dose is the dose delivered from the inhaler to the patient.

For some preparations, the dose has been established as a **metered-dose**.

The metered-dose is determined by adding the amount deposited within the device to the delivered dose. It may also be determined directly.

# Liquid preparations

## Pressurised metered-dose preparations for inhalation



**Metered-dose nebulisers** are devices that convert liquids into aerosols by **high-pressure gases, ultrasonic vibration or other methods**.

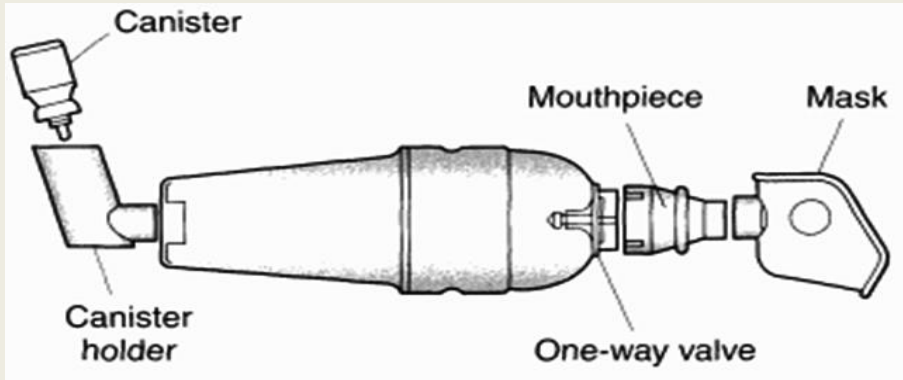
The volume of liquid to be nebulised is metered so that the aerosol dose can be inhaled with one breath.



# Liquid preparations

Pressurised metered-dose preparations for inhalation

## Spacer device

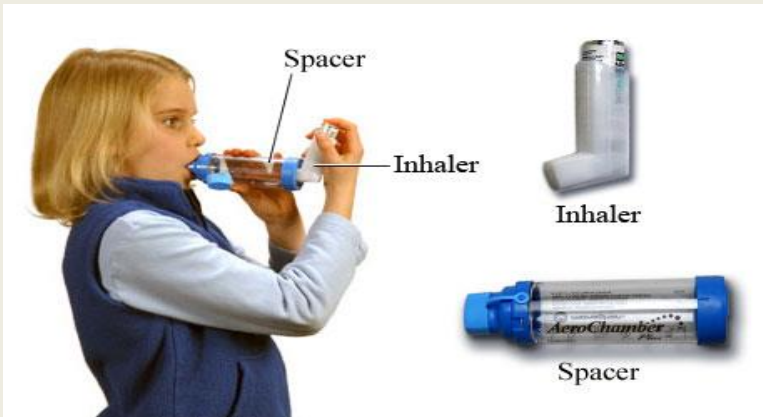


The Nebuhaler® spacer device fitted with a facemask for use by a child

# Liquid preparations

## Pressurised metered-dose preparations for inhalation

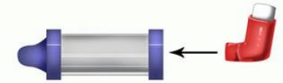
### Spacer device



### How to Use a Metered-Dose Inhaler with a Spacer



1. Shake the medicine.



2. Insert the mouthpiece of the inhaler into the rubber-sealed end of the spacer.



3. Breathe all of the air out of your lungs. Then put the spacer into your mouth between your teeth. Make a tight seal around the mouthpiece with your lips.



4. Press the metered-dose inhaler down once to release a spray of medicine. The medicine will be trapped in the spacer. Breathe in slowly and deeply.



5. Hold your breath for at least 5 to 10 seconds. Breathe out slowly.

# Liquid preparations

## Pressurised metered-dose preparations for inhalation

One of the most crucial components of a **metered-dose inhaler (MDI)** is its **propellant**. The propellant provides the force to generate the aerosol cloud and is also the medium in which the active component must be suspended or dissolved. Propellants in MDIs typically make up more than 99% of the delivered dose, so it is the properties of the propellant that dominate more than any other individual factor.

**Suitable propellants** must:

- have a boiling point in the range -100 to +30°C
- have a density of approximately 1.2 to 1.5 g cm<sup>-3</sup> (approximately that of the drug to be suspended or dissolved)
- have a vapour pressure of 40 to 80 psig
- have no toxicity to the patient
- be non flammable
- be able to dissolve common additives.

**Active ingredients should be either fully soluble or fully insoluble.**

# Liquid preparations

## Advantages of metered-dose pressurized preparations

- Easy to carry
- Easy to use
- It does not contaminate during use
- It is aseptically rechargeable and maintains its purity
- Protection from light, oxygen and moisture
- The goal is not-contact during application

# Liquid preparations

## Disadvantages of pressurized preparations

- Risk of explosion
- Output may be reduced during use
- Limited security
  - *Flammable*
  - *Overpressure*
  - *Unintentional inhalation*
- Insufficient application - in some cases
- Local and nasal sprays can not be water based systems

# Pressurised inhalation solutions

- ALVESCO 160  $\mu\text{g}$
- ATROVENT N 21  $\mu\text{g}/\text{dose}$
- ATIMOS 12  $\mu\text{g}/\text{dose}$
- FOSTER 100  $\mu\text{g}/6 \mu\text{g}$



# Pressurized inhalation suspensions

ECOSAL

VENTOLIN Evohaler

SEREVENT EVOHALER 25 µg/dose

FLIXOTIDE EVOHALER 125 µg/dose

FLIXOTIDE EVOHALER 250 µg/dose

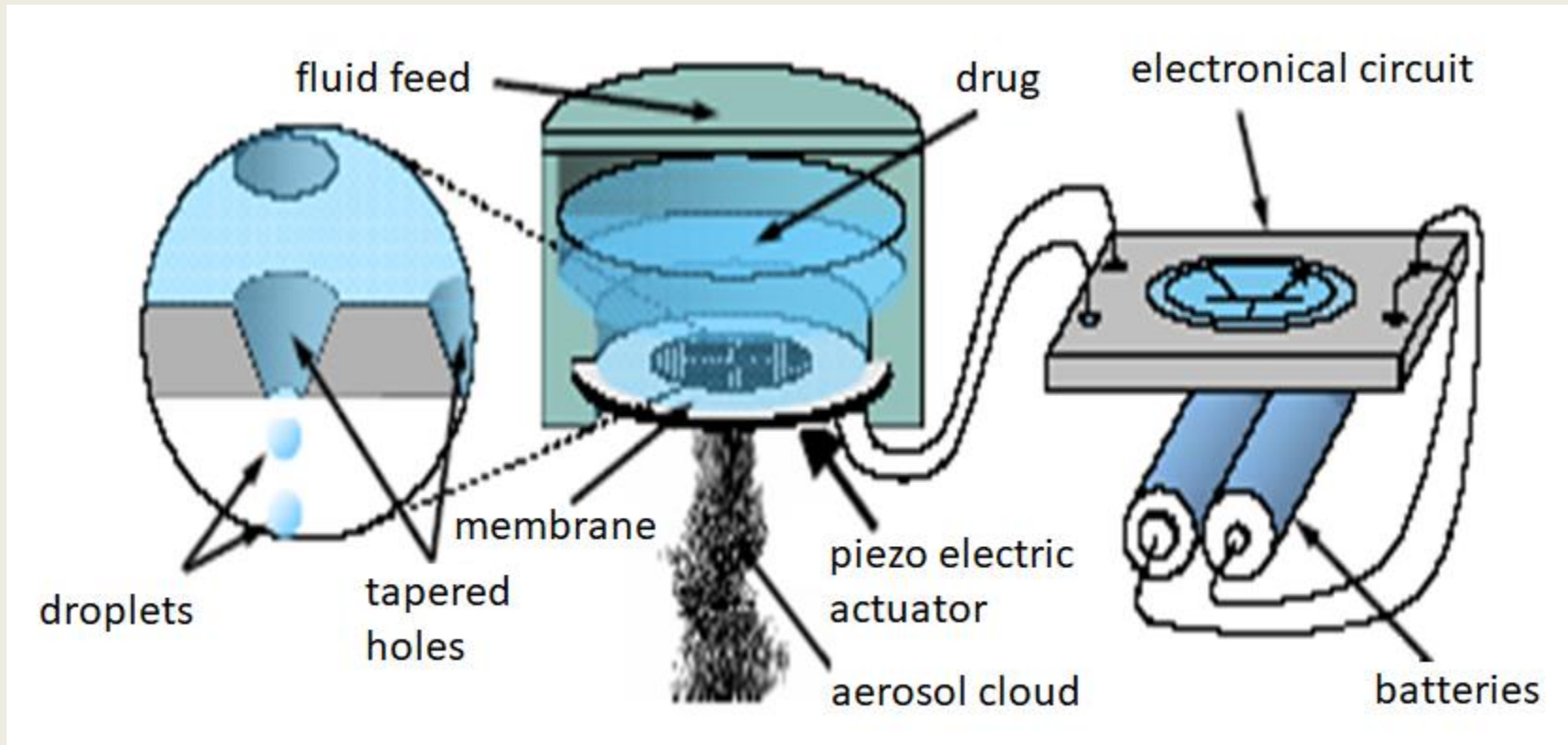
SYMBICORT forte SERETIDE Evohaler 25/50 µg/dose

SERETIDE Evohaler 25/125 µg/dose

SERETIDE Evohaler 25/250 µg/dose

# Special atomizing

Process:  
piezoelectric - membrane - atomized droplets

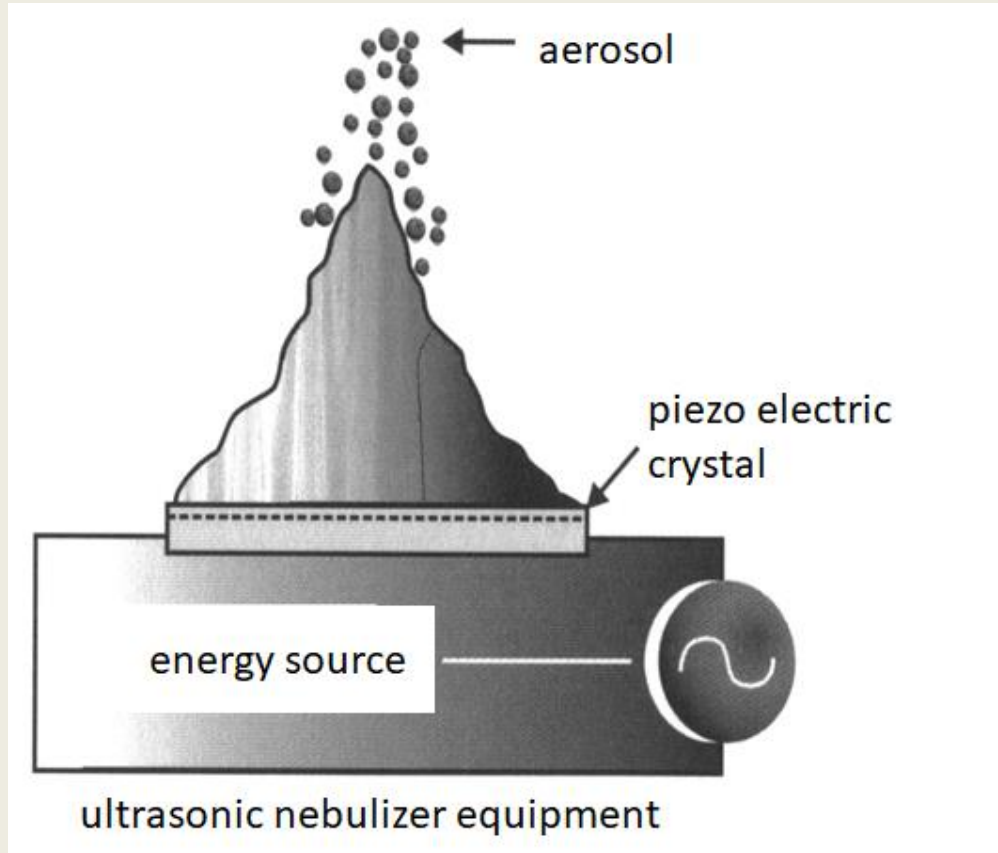




# Special atomizing

Process:

Ultrasonic nebulizer – Propellant free



# Preparations for Inhalation

*Solid preparations*

*Inhalation powders*

# Powder inhalation

DPI= dry powder inhalers

## SINGLE-DOSE DPIs



Aerolizer



HandiHaler

## MULTI UNIT-DOSE DPI



Diskhaler

## MULTI-DOSE DPIs



Twisthaler



Flexhaler



Diskus



Tudorza Pressair

# Solid preparations

## Powders for inhalation

**Dry powder inhaler** is drug is inhaled as a cloud of fine particles. Powders for inhalation are presented as **single-dose** powders or **multidose** powders. To facilitate their use, active substances may be combined with a suitable carrier.

In **pre-metered systems**, the inhaler is loaded with powders pre-dispensed in capsules or other suitable pharmaceutical forms.

For devices using a **powder reservoir**, the dose is created by a metering mechanism within the inhaler. The delivered dose is the dose delivered from the inhaler.

# Solid preparations

## Powders for inhalation

### Ideal preparation:

- Effective dosing
  - uniform dose
  - targeted delivery
  - operable at low inhalation flow rates
- Efficient device
- Easy to use

# Solid preparations

## Powders for inhalation

### Advantages:

- Propellant free design
- Less need for patient coordination
- Less potential for formulation problems
- Environmental sustainability
- Less potential for extractable from device components

# Solid preparations

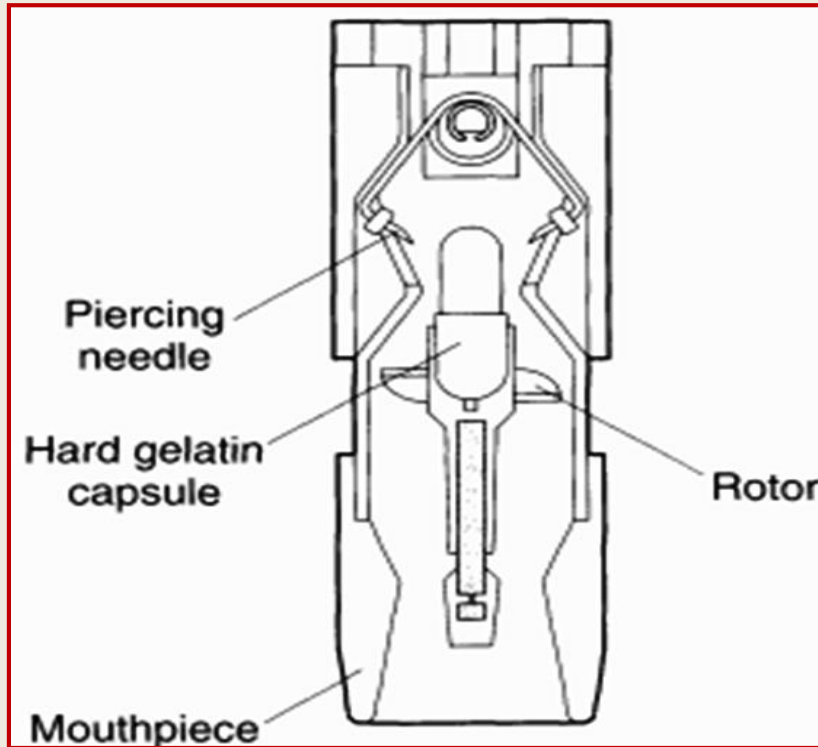
## Powders for inhalation

### Disadvantages:

- Dependency on patient inspiration flow rate and profile
- Device resistance and other device issues
- More expensive than pressurized MDI
- Complex development and manufacture
- Not available world wide
- Greater potential problems in dose uniformity

# Solid preparations

## Powders for inhalation - Spinhaler

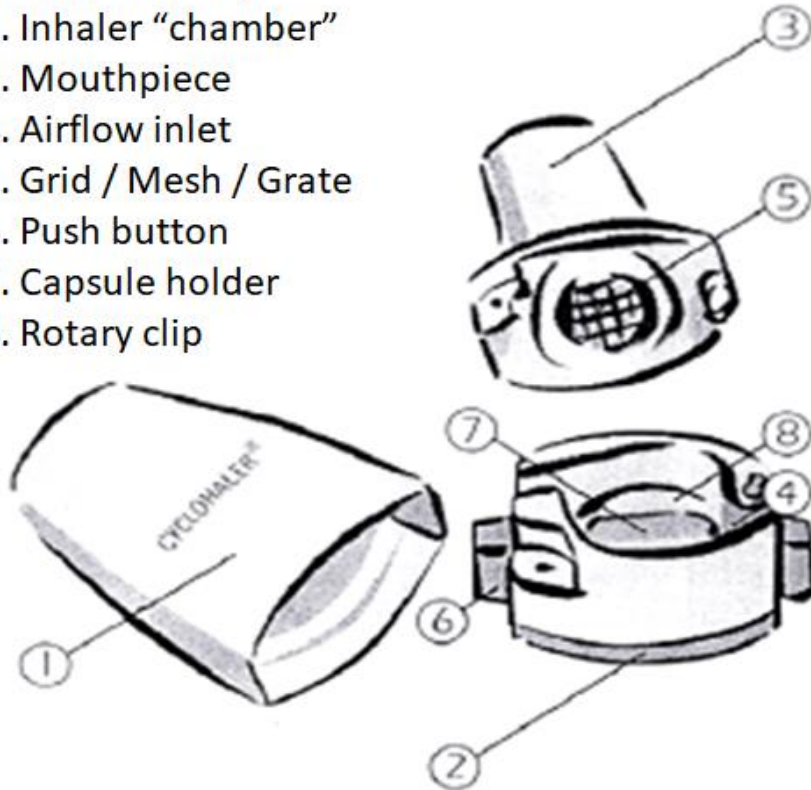




# Solid preparations

## Powders for inhalation - Aerolizer

1. Protective cap
2. Inhaler "chamber"
3. Mouthpiece
4. Airflow inlet
5. Grid / Mesh / Grate
6. Push button
7. Capsule holder
8. Rotary clip

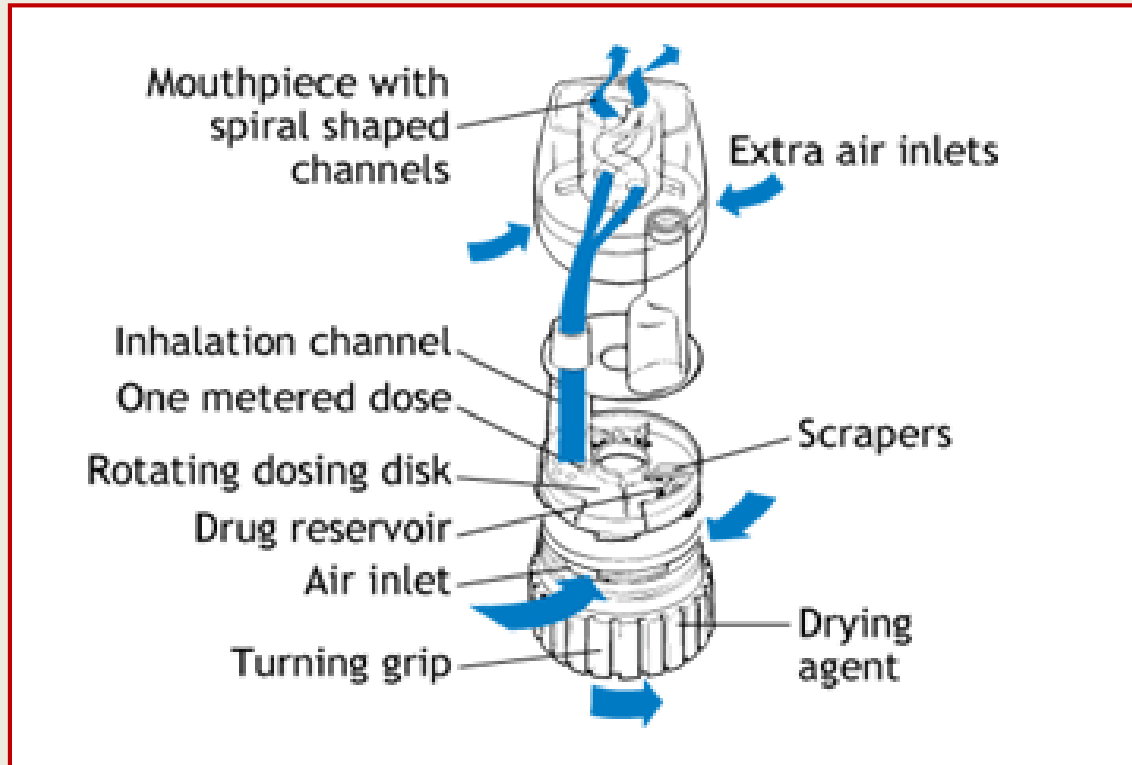


Aerolizer®



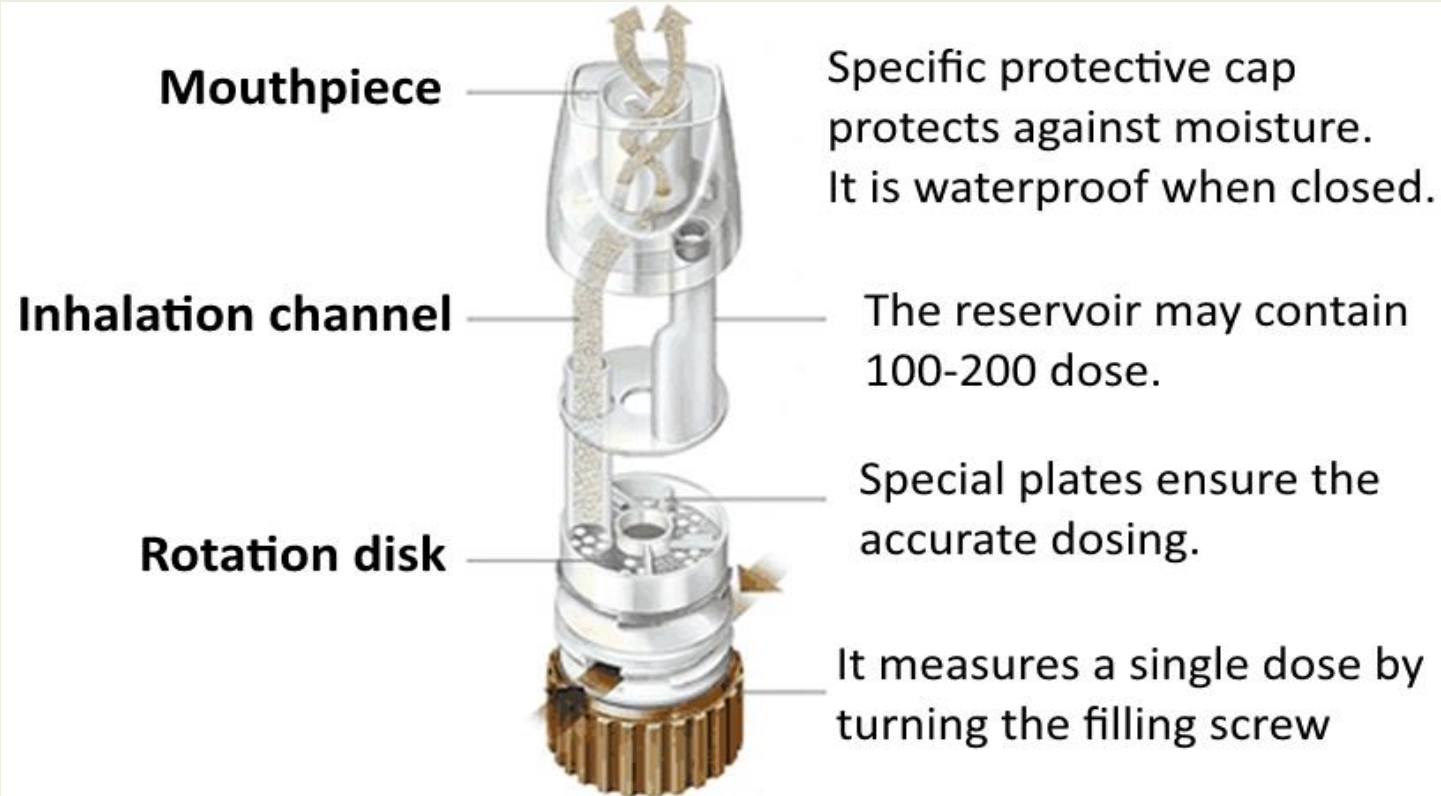
# Solid preparations

## Powders for inhalation - Turbuhaler



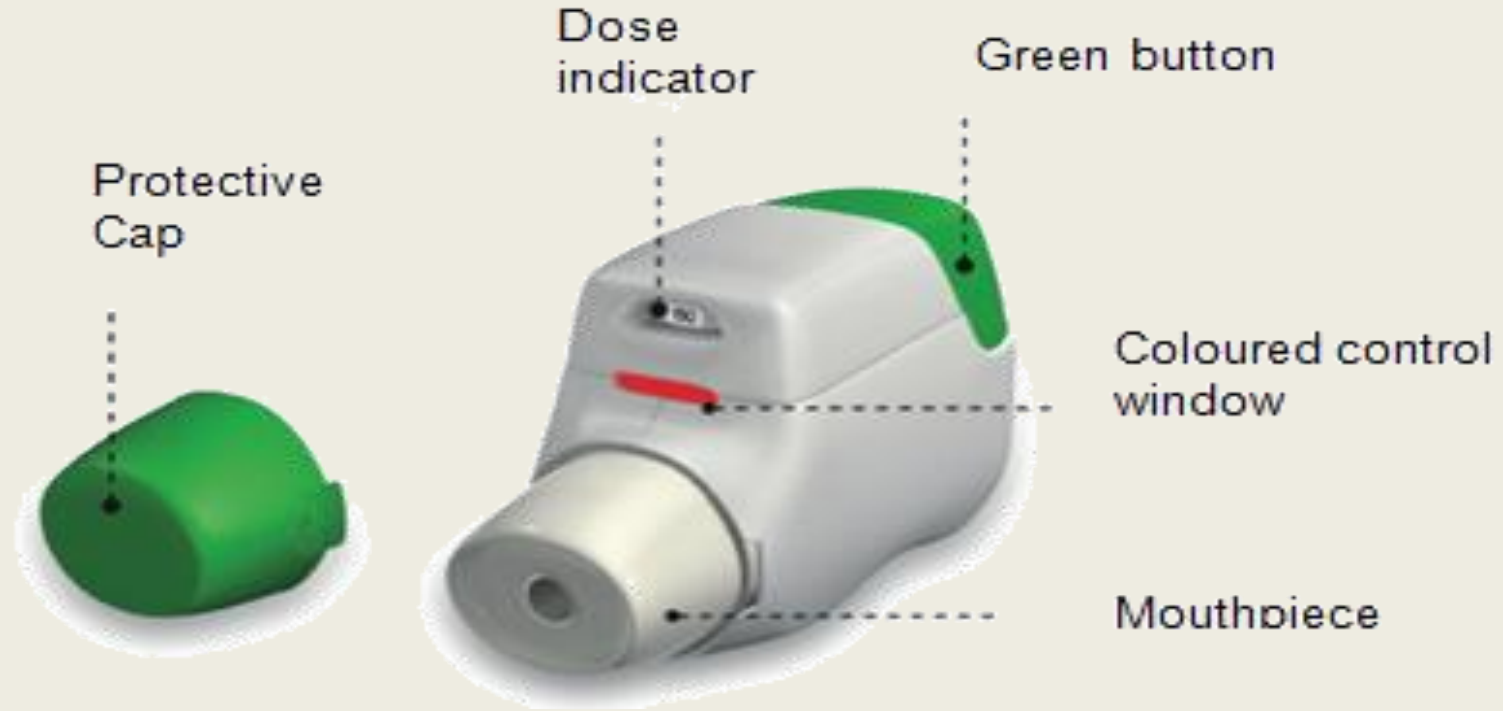
# Solid preparations

## Powders for inhalation - Turbuhaler



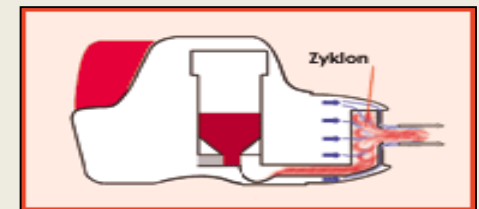
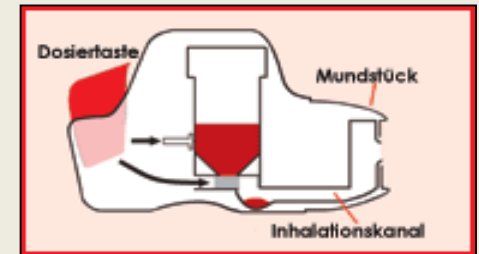
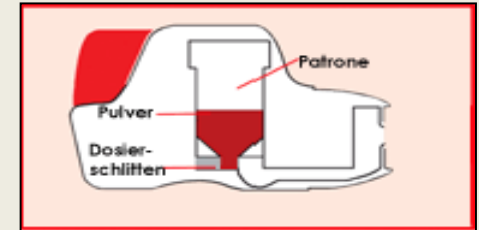
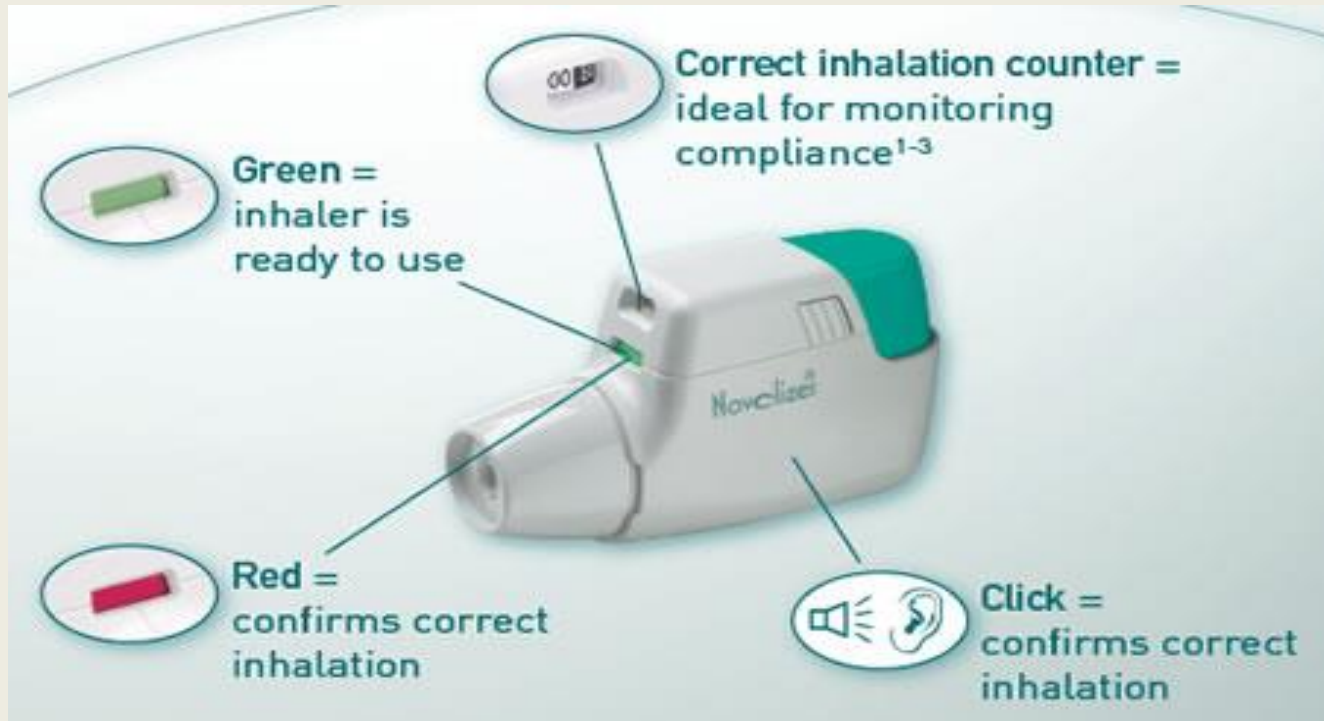
# Solid preparations

## Powders for inhalation - Novolizer



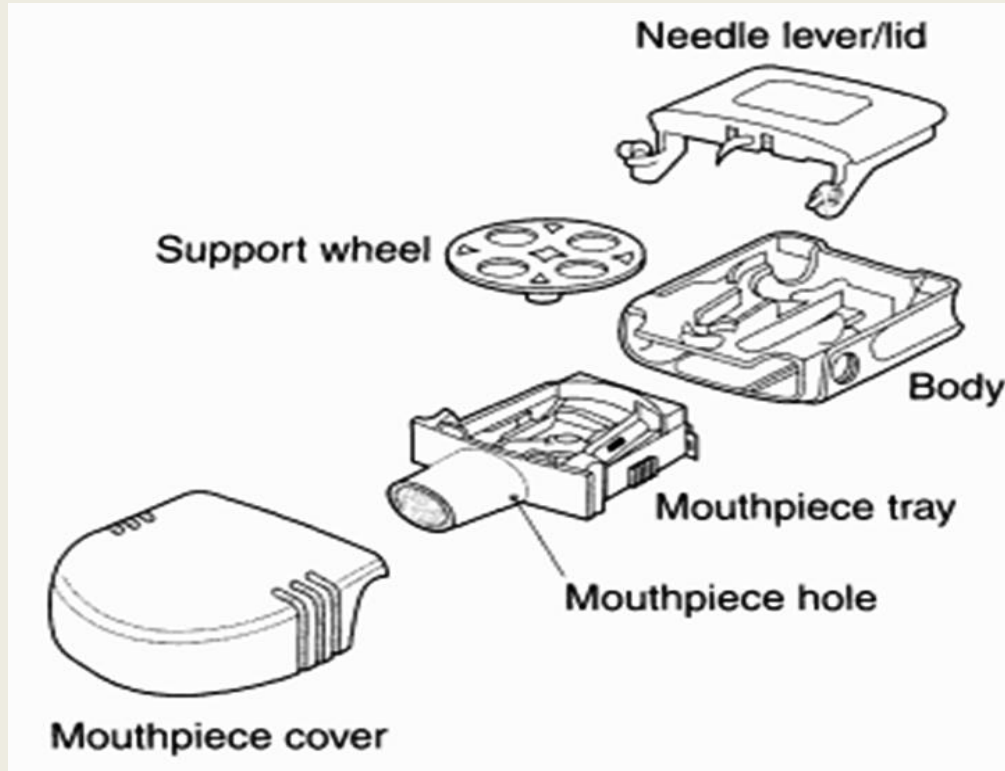
# Solid preparations

## Powders for inhalation - Novolizer



# Solid preparations

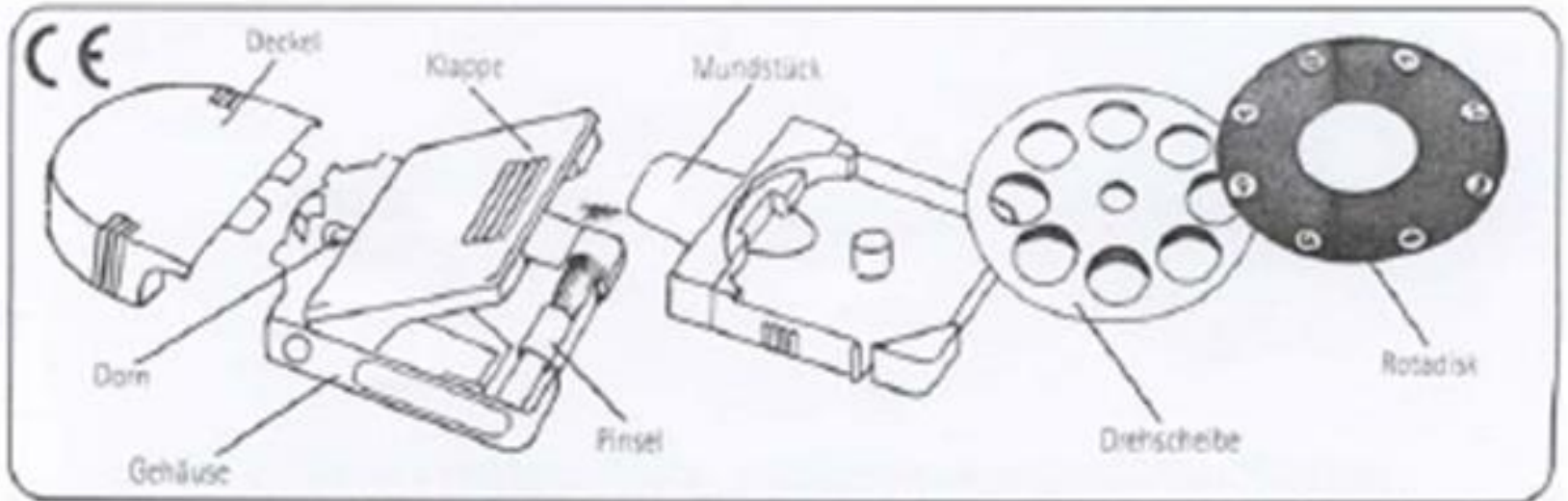
## Powders for inhalation - Dischaler



# Solid preparations

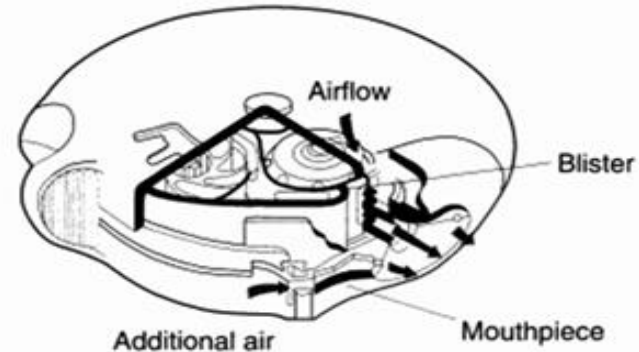
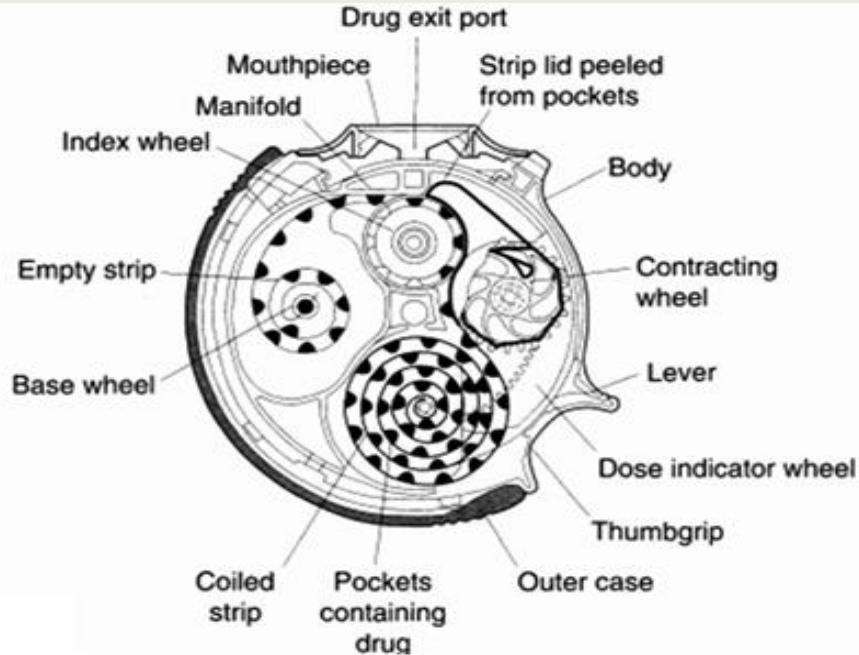
## Powders for inhalation - Diskhaler

### Diskhaler® (Rotadisk)



# Solid preparations

## Powders for inhalation - Accuhaler





# Solid preparations

## Powders for inhalation - NEXThaler



Open

Inhale

Close



**FOSTER<sup>®</sup>**  
**NEXThaler<sup>®</sup>**  
FOR PERSISTENT ASTHMA

Introducing  
the next generation  
of fixed combination  
powder inhalers



Read the package insert  
before use.  
120 doses. For inhalation use.

BECLOMETASONE DIPROPIONATE  
FORMOTEROL FUMARATE DI-HYDRATE

FOSTER<sup>®</sup> NEXThaler<sup>®</sup>  
100 mcg / 6 mcg per dose  
Powder for Inhalation  
ANTI-ASTHMA



0108002693/01

Chiesi

120

Chiesi

120

# Solid preparations

FORADIL 12 µg

SPIRIVA 18 µg

MIFLONIDE 200 µg

RELENZA 5 mg

SEEBRI BREEZHALER 44 µg

ONBREZ BREEZHALER 150 µg

IBUVENTOL Easyhaler 200 µg

FLIXOTIDE DISKUS 100 µg

BUDESONID EASYHALER 100 µg

FORMOTEROL EASYHALER 12 µg

RHINOCORT Turbuhaler 100 µg

BRICANYL TURBUHALER 0,5 mg

OXIS TURBUHALER 4,5 µg

SEREVENT Diskus 50 µg

THOREUS Diskus 50/100 µg

SERETIDE Diskus 50/100 µg

DIMENIO 50 µg/250 µg

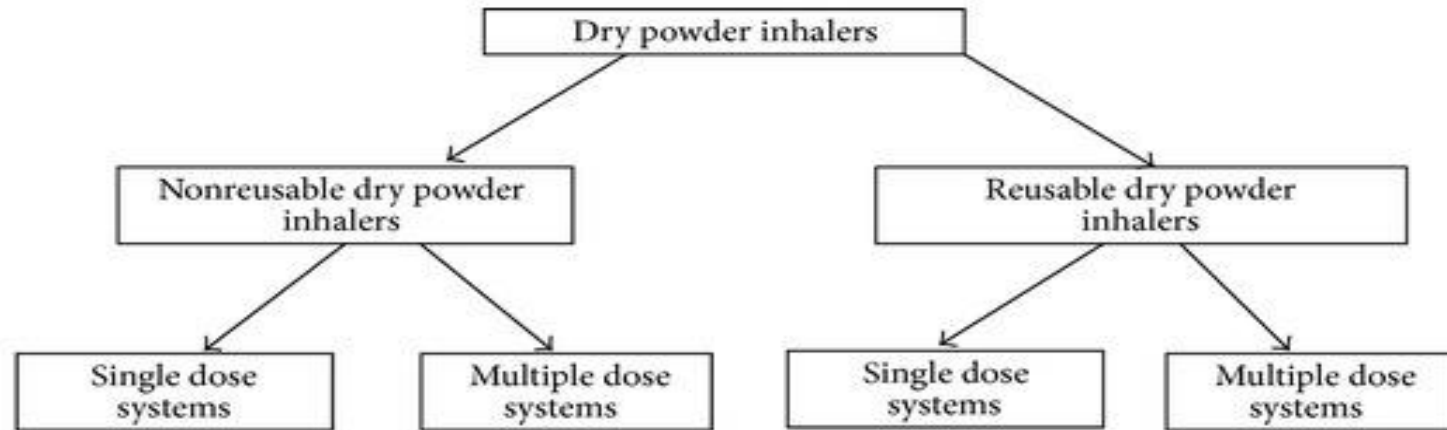
PULMICORT TURBUHALER 100 µg

SYMBICORT Turbuhaler 4,5 µg/160 µg

SYMBICORT forte Turbuhaler 9 µg/320 µg

SYMBICORT mite Turbuhaler 4,5 µg/80 µg

# Comparison of dry powder inhalers



Diskus

Turbuhaler

Easyhaler



Aerolizer

Rotadisk

Novolizer

Useable for

60 SD

200 SD

200 SD

50 SD

3 months

1 year

SD: single dose

# Advantages and disadvantages of inhalers

Device	Advantage	Disadvantage
pMDI	<ul style="list-style-type: none"> <li>• Compact</li> <li>• Portable</li> <li>• Multidose</li> <li>• Metered dose</li> <li>• Familiarity by patient</li> </ul>	<ul style="list-style-type: none"> <li>• Co-ordination required</li> <li>• High plume speed</li> <li>• High deposition in mouth and pharynx</li> <li>• 'Cold Freon' effect</li> <li>• Dose counter not always available</li> <li>• Contains propellants that are greenhouse gases</li> </ul>
pMDI + spacer	<ul style="list-style-type: none"> <li>• No co-ordination necessary</li> <li>• Holds aerosol for short period prior to inhalation</li> <li>• Slows down aerosol plume</li> <li>• Reduces deposition in mouth and pharynx</li> <li>• Can improve lung deposition</li> </ul>	<ul style="list-style-type: none"> <li>• Bulky to carry around</li> <li>• Some dose lost in spacer</li> <li>• Static charge may be a problem</li> <li>• Requires regular cleaning</li> <li>• Contains propellants</li> </ul>
Breath-actuated pMDI	<ul style="list-style-type: none"> <li>• No co-ordination required</li> <li>• Compact</li> <li>• Portable</li> <li>• Breath-actuated</li> </ul>	<ul style="list-style-type: none"> <li>• 'Cold Freon' effect</li> <li>• Minimum required flow to trigger</li> <li>• Contains propellants</li> </ul>
DPI	<ul style="list-style-type: none"> <li>• Breath-actuated</li> <li>• Does not require propellants</li> <li>• Multiple dose devices available</li> <li>• Compact</li> <li>• Portable</li> <li>• Reproducible dose delivered</li> </ul>	<ul style="list-style-type: none"> <li>• Multiple designs (may be confusing to patients)</li> <li>• Requires patient to achieve a minimum inspiratory threshold to generate dose</li> <li>• Moisture-sensitive</li> <li>• May be complicated to load</li> <li>• Single capsule devices require loading each time</li> </ul>
Nebulisers	<ul style="list-style-type: none"> <li>• Can be used to dispense drugs not available as pMDI or DPI</li> <li>• Can deliver high doses of drug</li> <li>• Delivery by tidal breathing</li> <li>• Vibrating mesh devices are portable</li> <li>• Intelligent nebulisers allow more efficient delivery</li> </ul>	<ul style="list-style-type: none"> <li>• Jet and ultrasonic nebulisers require external energy source</li> <li>• Older designs are very inefficient at delivery</li> <li>• Long treatment times</li> <li>• Newer devices are expensive</li> </ul>
Soft mist inhaler	<ul style="list-style-type: none"> <li>• Portable</li> <li>• Multidose</li> <li>• Slow mist generated over 1.5 seconds</li> <li>• Fine aerosol droplets</li> <li>• Easy to use</li> </ul>	<ul style="list-style-type: none"> <li>• Only one device currently available</li> <li>• Some co-ordination necessary</li> </ul>

**Application problem... OMG!!!**



**Thank you  
for your attention!**