SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Asist® 4% Acetylcysteine

For pediatric use

40 g Granules for preparing 100 mL Syrup

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 mL contains;

Acetylcysteine 200 mg

(Also contains, sodium methyl paraben, sodium propyl paraben as preservative; betacarotene (E160) as coloring agent; sorbitol as sweetener; orange essence as aromatic agent)

3. PHARMACEUTICAL FORM

Granules for syrup

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Acetylcysteine is indicated in reduction and excretion of viscous mucus, in conditions where expectoration is needed;

- Acute and chronic bronchopulmonary disorders
- Prevention of acetaminophen-induced hepatotoxicity

4.2 Posology and method of administration

Posology

Mucolytic uses

In diseases related with respirotary system for reducing the increased secretion and for ease of expectoration.

Adults and children older than 7 years: 600 mg/day (15 mL/day) is administered once a day or the total daily dose is divided into three equal doses and administered three times daily.

Children: Under 2 years of age: 200 mg/day (5 mL/day) is divided into two equal doses and administered - twice daily

2-7 years of age: 400 mg/day (10 mL/day) is divided into two equal doses and administered - twice daily

Acetaminophen overdosage

Loading dose is 140 mg/kg; Maintenance dose is 70 mg/kg every 4 hours (17 doses)

Method of administration

Method of administration is oral. IT Boiled and cooled water should be added until the mark on the bottle and shaken vigorously. After a half an hour, add water until marked level and shake well again. This process should be repeated until the whole granules are dissolved on the marked volume. Semitransparent syrup with orange flavored can be kept at refrigerator (2-8 ^{o}C) for 12 days.

4.3 Contraindications

It is contraindicated in patients known to be hypersensitive to acetylcysteine.

4.4 Special warnings and precautions for use

Following acetylcysteine administration, bronchial secretion may be markedly increased. Therefore, the airway should be open in the patients with cough reflex deficiency or cough insufficiency. Should be used cautiously in patients with asthma.

4.5 Interaction with other medicinal products and other forms of interaction

Drug interactions of acetylcysteine are rare.

Glutathione: Glutathione is a tripeptide, formed by glutamate, glycine and cysteine. Reduced glutathione plays a role in the detoxification of the oxygen radicals and several toxic agents in the organisms. Acetylcysteine may act as a cysteine donor and increases synthesis of glutathione.

Paracetamol (acetaminophen): Acetylcysteine involves in the structure of glutathione and conjugation with the reactive metabolite of paracetamol and may protect hepatotoxicity. There is no direct interaction of paracetamol with acetylcysteine.

4.6 Fertility, pregnancy and lactation

Risk Category in pregnancy is B. As there is not sufficient information whether acetylcysteine passes to the maternal milk or fetus, or not, during pregnancy and lactation it should be used only if it is clearly indicated.

4.7 Effects on ability to drive and use machines

Acetylcysteine has no negative influence on tool an machine use.

4.8 Undesirable effects

Gastrointestinal disturbances (i.e., nausea and vomiting), stomatitis, rinorrhea, urticaria, headache, tinnitus, and rarely allergic dermal reactions may occur. The agents that increase the mucus production should not be used concomitantly with antitussive antisecretive agents.
IN CASE OF AN UNEXPECTED SIDE EFFECT, CONSULT YOUR PHYSICIAN.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via EFDA yellow Card Scheme, online at https://primaryreporting.who-umc.org/ET or toll free call 8482 to Ethiopian food and drug authority (EFDA).

4.9 Overdose

Specific antidote is not available for Acetylcysteine. Symptomatic and supportive measures should be carried out.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Acetylcysteine having the capability of rupturing the disulfide bonds in mucus glycoproteins with its sulphydryl groups, causing mucolytic effect on mucoid and mucopurulent secretions. It rapidly decreases the density and the viscosity of the mucus collected in the respiratory tract.

It modifies the respiratory functions by facilitating expectoration, and excretion of bronchial secretions.

Acetylcysteine is an antioxidant agent.

As, Acetylcysteine is involved in synthesis of glutathione as a cysteine donor in the lung and liver cells, it increases synthesis of glutathione. Acetylcysteine and glutathione reacting with the free oxygen radicals, which formed by the neutrophils during lung infections and inhalation of tobacco smoke or toxic agent. Therefore acetylcysteine may protect cell injury and shows cytoprotective activity.

Acetylcysteine prevents or minimize acetaminophen-induced hepatotoxicity. Normally paracetamol is metabolized in the liver. Small quantities of acetaminophen are metabolized by the cytochrome P-450 microsomal enzyme system to a reactive intermediate metabolite, which is further metabolized via conjugation with glutathione and ultimately excreted in the urine. Those high doses of acetaminophen may deplete glutathione so that inactivation of this toxic metabolite is decreased and the level of intermediate metabolite increases. Acetylcysteine may protect the liver by maintaining or restoring glutathione levels or conjugation with the toxic intermediate metabolite.

5.2 Pharmacokinetic properties

Absorption: Acetylcysteine is stable in gastric and intestinal liquids and is well absorbed after oral administration. Bioavailability of 200 mg, used three times a day and 600 mg used once a day orally are similar. Its bioavailability does not change with the presence of the food. Peak plasma concentration is reached 30-60 minutes after the administration ,

Distribuition: Volume of distribuition (Vd) is between 0.33-0.47 L/kg. Primary distribuition sites are lungs, kidneys and liver. Following the oral administration 48% is found present in lung tissue. Acetylcysteine is detected free or reversibly bound to plasma proteins by disulphide bonds. It is %50 bound to plasma proteins.

Metabolism: Following deacetyllation in the liver, it enters the normal metabolic pathway of aminoacid cysteine. Increase of cysteine in the liver and blood, results in increase of glutathion level. Its plasma halflife is approximately 6 hours.

Excretion: Acetylcysteine is mainly excreted through urine and liver inmetabolites of sulphates and taurine.

5.3 Preclinical safety data

Acute toxicity studies in rats and mice, by oral, intraperitoneal and intravenous administration showed acetylcysteine to be of low toxicity. LD50 values greater than 7 g / kg in mice and 6 g / kg in rats have been reported. Chronic toxicity studies with acetylcysteine in rats at doses up to 2000 mg/ kg/ day and dogs at doses up to 300 mg/ kg / day for periods up to 52 weeks demonstrate that acetylcysteine is well tolerated, even at higher doses. In reproductive toxicity

studies in rats and rabbits, the oral administration of doses up to 2000 mg / kg / day did not show changes in reproductive capacity, teratogenic effects or peri/postnatal toxicity.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium citrate dihydrate

Sodium Methyl Parahydroxybenzoate

Sodium Propyl Parahydroxybenzoate

Disodium EDTA

Betacarotene 1% CWS

Orange essence (powder)

Sorbitol

6.2 Incompatibilities

Not applicable

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store below 30oC.

6.5 Nature and contents of container <and special equipment for use, administration or implantation>

Type III, amber coloured, marked at 100 mL, with white coloured LDPE packing, screwed, PE capped bottle containing 40 g of dry powder with 2.5 -5 mL scaled spoon in carton box with leaflet.

6.6 Special precautions for disposal <and other handling>

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

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8. MARKETING AUTHORISATION NUMBER(S)

Certificate No: 07177/08308/REN/2021

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Mar 4, 2022

10. DATE OF REVISION OF THE TEXT

September, 2023