Pharmacode

32.5 mm

Aetos

DissoNac Effervescent Tablet 200mg
DissoNac Effervescent Tablet 600mg

1. Name of the medicinal product
DissoNac Effervescent Tablet 200mg
DissoNac Effervescent Tablet 600mg

2. Qualitative and quantitative composition
Each effervescent tablet contains:

DissoNac Effervescent Tablet 200mg:
Acetylcysteine..... 200 mg

DissoNac Effervescent Tablet 600mg:
Acetylcysteine..... 600 mg

3. Pharmaceutical form
Effervescent tablet.

DissoNac Effervescent Tablet 200mg: Off-white to light yellow, round-shaped tablet, flat on both sides. When dissolved in water, the tablet effervesces to produce a light yellow solution.

DissoNac Effervescent Tablet 600mg: Light yellow, round-shaped tablet, flat on both sides. When dissolved in water, the tablet effervesces to produce a light yellow solution.

4. Clinical Particulars
4.1 Therapeutic indications
All respiratory tract diseases leading to the formation of thick secretions difficult to be expectorated, such as acute and chronic bronchitis, laryngitis, sinusitis, tracheitis, influenza, bronchial asthma and (as complementary treatment) mucoviscidosis.

4.2 Posology and method of administration
Administration
DissoNac Effervescent Tablet is administered orally.

Dosage
DissoNac Effervescent Tablet 200mg:
Children over 2 years: 100 - 200 mg 2 times a day. DissoNac Effervescent Tablet is contraindicated in children under 2 years of age.
Adults: 200 mg three times a day.

DissoNac Effervescent Tablet 600mg:
Adults: 1 effervescent tablet of 600 mg once daily. For patients with a reduced cough reflex (elderly and weakened patients) are advised to take the effervescent tablet in the mornings.

Dissolve DissoNac Effervescent Tablet in half a glass of water. This produces a solution that may be consumed immediately.

4.3 Contraindications
- Hypersensitivity to acetylcysteine or to any of the excipients.
- The tablet should not be used by children under 2 years of age.

4.4 Special warnings and precautions for use
- Bronchospasms may occur with the use of acetylcysteine. If bronchospasm occurs, the medicinal product should be discontinued immediately.
- Bronchial secretions may become more fluid and increase in volume, in particular at the start of the treatment with acetylcysteine. When a patient is unable to cough up the secretions effectively, postural drainage and bronchoaspiration should be performed.
- Caution is advised in patients with a history of peptic ulcer, especially when used concomitantly with other medicinal products known to irritate the mucous membrane of the gastrointestinal tract.
- Serious skin reactions such as such as Stevens-Johnson syndrome and Lyell's syndrome have been reported whilst taking acetylcysteine, but these occur rarely. For this reason, medical advice should be sought immediately, and the patient should stop taking acetylcysteine in the event of new-onset changes to the skin and mucous membranes.
- There are no studies on the efficacy and safety of acetylcysteine 600 mg effervescent tablet in adolescent population. However, mild, moderate or severe adverse reactions have been reported with the use of IV acetylcysteine in adolescents' population.
- This product should be used with caution by patients with histamine intolerance. They should avoid long-term therapy because acetylcysteine effervescent tablet affects the metabolism of histamine and can lead to symptoms of intolerance (e.g. headaches, rhinitis, itching).
- No specific studies have been performed in patients with renal or hepatic impairment. Hepatic and renal impairment reduce clearance and increase acetylcysteine plasma levels which may result in an increase in adverse drug reactions due to drug accumulation.
- DissoNac Effervescent Tablet contains sodium. Caution is advised in patients on a sodium-restricted diet.
- DissoNac Effervescent Tablet contains aspartame, which is a source of phenylalanine. This medicine is not suitable for phenylketonurics.
- A mild sulfur odour does not indicate a change in the medicinal product but is a property of the active substance itself.

4.5 Interaction with other medicinal products and other forms of interaction
- Simultaneous solution of DissoNac Effervescent Tablet with other medicinal products is not recommended.
- To date, the inactivation of antibiotics by acetylcysteine has been reported only in *in-vitro* tests, whereby the relevant substances were mixed directly with each other. However, if oral antibiotics are required, it is advised that these should be taken two hours before or after Acetylcysteine.
- Acetylcysteine should not be administered concomitantly with antitussive medicinal products because reducing the cough reflex may lead to a build-up of bronchial secretions.
- Simultaneous administration of acetylcysteine and nitroglycerin may increase the vasodilatory and platelet aggregation-inhibiting effect of nitroglycerin. If such combined treatment is considered necessary, the patient should be monitored for possible hypotension, which can be serious and may be indicated by headaches.
- Activated charcoal can decrease the effect of acetylcysteine due to reduced absorption.

Interactions with laboratory tests
- Acetylcysteine may have an effect on the values of salicylates by colorimetric analysis.
- Acetylcysteine may interfere with tests for ketones in urine.

4.6 Fertility, pregnancy and breast-feeding
Pregnancy
There are no data on the use of acetylcysteine in pregnant women. Animal studies do not indicate direct or indirect adverse effects on pregnancy, embryonic/foetal development, birth or postnatal development.

Lactation
There is insufficient information on the excretion of acetylcysteine or its metabolites in human milk. Use during breast-feeding should be subjected to careful consideration of the risk/benefit balance.

4.7 Effects on ability to drive and use machines
There are no data on the effect of acetylcysteine on the ability to drive. An effect is, however, not likely.

4.8 Undesirable effects
- *Immune system disorder*: Uncommon: Hypersensitivity; Very rare: Anaphylactic shock, anaphylactic/anaphylactoid reactions.
- *Nervous system disorders*: Uncommon: Headache.
- *Ear and labyrinth disorders*: Uncommon: Tinnitus.
- *Cardiac disorders:* Uncommon: Tachycardia.
- *Vascular disorders*: Very rare: Haemorrhages.
- *Respiratory, thoracic and mediastinal disorders*: Rare: Bronchospasm, dyspnoea.
- *Gastrointestinal disorders*: Uncommon: Stomatitis, abdominal pain, nausea, vomiting, diarrhea; Rare: Dyspepsia.
- *Diseases of skin and subcutaneous tissue*: Uncommon: Urticaria, rash, angioedema, pruritus, Exanthema.
- *General disorders and administration site conditions*: Uncommon: Fever; Not known: Oedema of the face.
- *Investigations*: Uncommon: Low blood pressure.
  The occurrence of serious skin reactions (SCAR) such as erythema multiforme, Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) have been reported in temporal association with the use of acetylcysteine. In most of these cases reported at least one other drug was administered at the same time, which may have possibly enhanced the described mucocutenous effects.
- In case of recurrence skin and mucosal lesions, medical advice should be sought at once and the use of acetylcysteine terminated immediately.
- A decrease in platelet aggregation in the presence of acetylcysteine has been confirmed in various studies. The clinical significance of this has not been determined.
- Acetylcysteine may have an undesirable effect on the gastric mucosa in patients with a history of peptic ulcer or peptic ulcer.

4.9 Overdose
To date no toxic overdose has been observed for the oral pharmaceutical forms of acetylcysteine.

Symptoms
Overdoses may lead to gastrointestinal effects such as nausea, vomiting and diarrhoea.

Management
Symptomatic treatment in the event of an overdose.

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5. Pharmacological properties
5.1 Pharmacodynamic properties
Pharmacotherapeutic group: Mucolytics
ATC code: R05C B01
Acetylcysteine belongs to the group of amino acid cysteine derivative.

Mechanism of action
Acetylcysteine is believed to break the disulfide bonds in mucoproteins and it depolymerizes DNA strands in purulent mucus.

Pharmacodynamics effects
The effect of this activity is a reduction in the viscosity of mucous secretions. Another possible effect is detoxification of free radicals by interaction with the active sulfhydryl group of acetylcysteine.
In addition, acetylcysteine increases synthesis of glutathione. Due to this mechanism of action, acetylcysteine is also indicated as a specific antidote in paracetamol poisoning.
There are no studies on the efficacy and safety of once daily acetylcysteine 600 mg effervescent tablet in adolescent population. However, mild, moderate or severe adverse reactions have been reported with the use of IV acetylcysteine including adolescents' population.

5.2 Pharmacokinetics properties
Absorption and metabolism
Acetylcysteine is absorbed rapidly and almost completely after oral administration. It is metabolized in the liver into a pharmaceutically active metabolite cysteine, inactive diacetylcystine and cystine and into the other disulfides. Due to the high first pass effect, the bioavailability of orally administered acetylcysteine is very low (approximately 10%). In human peak plasma levels of acetylcysteine are reached in approximately 1-3 hours after an oral dose. Plasma concentration of the active metabolite cysteine about 2µmol/l and binding with proteins is about 50%. No dosage adjustments are required in patients with impaired kidney or liver impairment.

Elimination
Acetylcysteine is excreted almost entirely as inactive metabolites (inorganic sulfates, diacetylcystine) through the renal route. The elimination half-life of the acetylcysteine is about 1 hour, which is primarily determined by the rapid biotransformation in the liver. In patients with liver dysfunction the elimination half-life of acetylcysteine increases to 8 hours.

Distribution
In a pharmacokinetic study, intravenously administered acetylcysteine in human showed a distribution volume of 0.47l/kg; the plasma clearance is 0.11 l/h/kg. The elimination half-life after oral administration is 6.25 hours. In a study with rats it was shown that acetylcysteine crosses the placenta. There is no information on whether acetylcysteine crosses the blood-brain barrier in humans. There are no data on whether acetylcysteine is excreted in breast milk.

Hepatic and renal impairment
There is evidence that clearance of acetylcysteine can be significantly reduced up to 90% in the subjects with end-stage renal disease. This could result in a marked increase in systemic exposure to acetylcysteine in the extreme case of patients with end-stage renal disease. It is not known to what extent the results can be extrapolated to the less severe forms of renal impairment that are more likely to be encountered during routine use of proposed product. The elimination half-life of acetylcysteine was found to increase to eight hours in one study of patients with chronic liver disease. The total clearance of acetylcysteine was found to be significantly reduced following an intravenous dose of 600 mg over three minutes in nine subjects with hepatic cirrhosis.

6. Pharmaceutical particulars
6.1 List of excipients
- Sodium hydrogen carbonate
- Citric acid
- Sorbitol
- Sodium carbonate
- Sodium benzoate
- Macrogol 6000
- Copovidone
- Aspartame
- Saccharin sodium
- Ascorbic acid
- Orange flavour 10888-71
- Orange flavour 12026-31
- Betacarotene 1%

6.2 Special precautions for storage
Store below 30°C. Protect from light and moisture.

6.3 Nature and contents of container
Blister of 4 tablets. Box of 4 strip blisters.

7. Manufacturer
Stellapharm J.V. Co., Ltd.- Branch 1
(A Joint Venture Company of Auxilto GmbH, Germany)
No. 40 Tu Do Avenue, Vietnam-Singapore Industrial Park,
An Phu Ward, Thuan An City, Binh Duong Province, Vietnam.

8. Marketing authorization holder
Aetos Pharma Sdn Bhd
66B, Tingkat 2, Jalan Cerdas, Taman Connaught,
56000 Kuala Lumpur, Malaysia.

9. Date of revision of the text
5 March 2025