

NATURAL MEDICINES

COMPREHENSIVE DATABASE



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N-ACETYL CYSTEINE

Also Known As:

Acetyl Cysteine, Acétyl Cystéine, Acetylcysteine, Acétylcystéine, Chlorhydrate de Cystéine, Cysteine, Cystéine, Cysteine Hydrochloride, Cystine, Hydrochlorure de Cystéine, L-Cysteine, L-Cystéine, L-Cysteine HCl, L-Cystéine HCl, L-Cystine, NAC, N-Acetil Cisteína, N-Acetyl-B-Cysteine, N-Acétyl Cystéine, N-Acetyl-L-Cysteine, N-Acétyl-L-Cystéine, N-Acetylcysteine, N-Acétylcystéine.

Scientific Name:

N-acetyl-L-cysteine.

People Use This For:

Orally, N-acetyl cysteine is used as an antidote for acetaminophen and carbon monoxide poisoning. It is also used for unstable angina, common bile duct obstruction in infants, lysosomal storage disorders, amyotrophic lateral sclerosis (ALS, Lou Gehrig's disease), Alzheimer's disease, phenytoin-induced hypersensitivity, and keratoconjunctivitis. It is also used for reducing lipoprotein (a) levels, reducing homocysteine levels, reducing risk of cardiovascular events in patients with end-stage renal disease, chronic bronchitis, chronic obstructive pulmonary disease (COPD), allergic rhinitis, fibrosing alveolitis, head and neck cancer, and lung cancer. N-acetyl cysteine is also used orally for myoclonus epilepsy; otitis media; hemodialysis-related pseudoporphyria; chronic fatigue syndrome (CFS); Sjogren's syndrome; preventing sports injury complications; radiation therapy; increasing immunity to flu and swine flu; and for detoxifying heavy metals such as mercury, lead, and cadmium. It is also used orally for preventing alcoholic liver damage; for protecting against environmental pollutants including carbon monoxide, chloroform, urethanes and certain herbicides; for reducing toxicity of ifosfamide and doxorubicin; as a hangover remedy; for preventing nonionic low-osmolality contrast agent-induced reduction of renal function in patients with renal insufficiency; for human immunodeficiency virus (HIV); and for trichotillomania (hair pulling).

Topically, N-acetyl cysteine is used for reducing dental plaque.

Intravenously, N-acetyl cysteine is used for acetaminophen overdose, acrylonitrile poisoning, amyotrophic lateral sclerosis (ALS, Lou Gehrig's disease), for hepatorenal syndrome, for decreasing mortality rate due to multisystem organ failure, for unstable angina in combination with nitroglycerin, and for acute myocardial infarction with nitroglycerin and streptokinase.

Rectally, N-acetyl cysteine is used for meconium ileus and meconium ileus equivalent.

By inhalation or intratracheal installation, N-acetyl cysteine is used as a mucolytic agent in acute and chronic lung disorders such as pneumonia, bronchitis, emphysema, cystic fibrosis, and others.

Safety:

LIKELY SAFE ...when used orally, intravenously, intratracheally, by inhalation, and appropriately. N-acetyl cysteine is an FDA-approved prescription drug (832, 1539, 1705, 1710, 2245, 2246, 2252, 2253, 2254, 2256, 2258, 2259, 2260) (5808, 6176, 6611, 7868, 10270, 10271, 16840).

PREGNANCY: POSSIBLY SAFE ...when used orally, intratracheally, or by inhalation. N-acetyl cysteine crosses the placenta, but has not been associated with adverse effects to the fetus or mothers (1711). However, N-acetyl cysteine should only be used in pregnant women when clearly indicated, such as in cases of acetaminophen toxicity.

LACTATION: Insufficient reliable information available; avoid using.

Effectiveness:

EFFECTIVE

Acetaminophen poisoning. Administering N-acetyl cysteine orally or intravenously is equally effective in decreasing mortality rate and preventing the permanent sequelae of acetaminophen poisoning (17).

Atelectasis. N-acetyl cysteine is helpful for atelectasis caused by mucus obstruction (15).

Bronchial diagnostic studies. N-acetyl cysteine is helpful when used for preparing people for bronchial diagnostic studies (15).

Bronchopulmonary disorders. Administering N-acetyl cysteine by inhalation is effective as a mucolytic for adjunctive treatment of acute and chronic bronchopulmonary disorders (15).

Cystic fibrosis. N-acetyl cysteine is effective for cystic fibrosis (15).

Tracheostomy care. N-acetyl cysteine is effective when used as an adjunct for preventing endotracheal crusting in tracheostomy care (15).

POSSIBLY EFFECTIVE

Angina. Administering N-acetyl cysteine orally or intravenously seems to improve unstable angina pectoris in combination with nitroglycerin (2245, 2246). Concurrent intravenous administration of N-acetyl cysteine also seems to reduce development of nitroglycerin tolerance (832, 2245). However, severe headache can occur when N-acetyl cysteine and nitroglycerin are administered together and may limit feasibility of concomitant use (2245).

Bronchitis. Taking N-acetyl cysteine orally seems to reduce the risk of acute exacerbations of chronic bronchitis when used over a three to six month period (6176).

Chronic obstructive pulmonary disease (COPD). In patients with moderate to severe COPD, taking N-acetyl cysteine orally can decrease the number of acute exacerbations by about 40% when used in addition to standard therapy (10429).

Contrast agent-induced nephropathy. Taking N-acetyl cysteine orally seems to prevent nonionic low-osmolality contrast agent-induced nephropathy in patients with renal insufficiency. Oral N-acetyl cysteine, with hydration with intravenous saline, seems to prevent acute renal damage in patients with chronic renal insufficiency (serum creatinine greater than 2.4 mg/dL) receiving iopromide (Ultravist-300) administration for elective computed tomography (CT) or coronary angiography (6611, 10428). However, in patients

with reduced renal function (serum creatinine greater than 1.2 ml/dL, but less than 2.4 ml/dL), oral N-acetyl cysteine doesn't seem to reduce the risk of contrast agent-induced renal damage after coronary angiography (11430).

End-stage renal disease (ESRD). Taking N-acetyl cysteine orally seems to reduce the incidence of cardiovascular events such as ischemic stroke and myocardial infarction by about 40% in patients with ESRD. However, the risk of total mortality or mortality from cardiovascular causes is not decreased (10430).

Epilepsy. Taking N-acetyl cysteine orally seems to be helpful for treating myoclonus epilepsy (2259).

Fibrosing alveolitis. Taking N-acetyl cysteine orally seems to improve pulmonary function tests and decrease biochemical markers of disease in patients with fibrosing alveolitis (7868).

Hyperhomocysteinemia. Taking N-acetyl cysteine orally seems to reduce homocysteine levels (2256, 2258).

Ifosfamide (Ifex) toxicity. Taking N-acetyl cysteine orally seems to reduce ifosfamide-induced bladder toxicity (5808, 10270). However, mesna (Mesnex) seems to be more effective for preventing ifosfamide toxicity than N-acetyl cysteine (10748).

Influenza. Taking N-acetyl cysteine orally seems to reduce symptoms of influenza (2260).

Trichotillomania (hair pulling). Some clinical research shows that taking N-acetyl cysteine orally, in doses up to 2400 mg daily, significantly decreases the urge to pull hair, the amount of hair pulled, and patients' perception of their control over hair pulling as measured by a self-rating scale. After 12 weeks of treatment, scores decreased by 40% (16840).

POSSIBLY INEFFECTIVE

Amyotrophic lateral sclerosis (ALS, Lou Gehrig's disease). Administering N-acetyl cysteine intravenously doesn't seem to improve symptoms of ALS (2254).

Doxorubicin-induced cardiac toxicity. Taking N-acetyl cysteine orally doesn't seem to prevent or reverse doxorubicin-induced cardiac toxicity (2252, 2253).

LIKELY INEFFECTIVE

Alzheimer's disease. Taking N-acetyl cysteine orally doesn't improve symptoms of Alzheimer's disease (7870).

Head and neck cancer or lung cancer. Taking N-acetyl cysteine orally in patients with head and neck cancer or lung cancer doesn't prevent second primary tumors (1710). N-acetyl cysteine alone, or in combination with retinyl palmitate, has no effect on mortality or event-free survival in patients with head and neck cancer or lung cancer (1705, 1710).

Multisystem organ failure. Administering N-acetyl cysteine intravenously, greater than 24 hours after hospital admission, might increase mortality rate due to multisystem organ failure. The effect of N-acetyl cysteine given within 24 hours of hospital admission requires further study (7871).

Nitrate tolerance. Taking N-acetyl cysteine orally doesn't reduce nitroglycerin tolerance (2281, 2282).

INSUFFICIENT RELIABLE EVIDENCE to RATE

Colorectal cancer. Oral N-acetyl cysteine may reduce the likelihood of colorectal cancer in patients with a history of adenomatous colon polyps (7873).

Hepatorenal syndrome. There is some preliminary clinical evidence that intravenous N-acetyl cysteine might improve renal function in hepatorenal syndrome (1752).

Lamellar ichthyosis. There is some evidence that topical N-acetyl cysteine might be useful for lamellar ichthyosis, a congenital skin disease (3974, 3975).

Myocardial infarction (MI). Early evidence shows that intravenous N-acetyl cysteine, when given with nitroglycerin and streptokinase, in patients with evolving MI, may preserve left ventricular function and reduce oxidative stress (7872).

More evidence is needed to rate N-acetyl cysteine for these uses.

Mechanism of Action:

N-acetyl cysteine is the N-acetyl derivative of the amino acid L-cysteine (1705). N-acetyl cysteine is a precursor of glutathione, which is a potent antioxidant. Glutathione can not cross the cell membrane, but N-acetyl cysteine easily crosses the cell membrane where it is converted to cysteine and, subsequently, glutathione. Reactive oxygen species (ROS) such as hydrogen peroxide and hydroxyl-free radicals reduce intracellular and extracellular concentrations of glutathione. N-acetyl cysteine is a very efficient way to replenish glutathione and reduce damage caused by ROS (7874, 1761).

The antioxidant effects of N-acetyl cysteine may explain its apparent ability to prevent adverse effects caused by toxic chemicals, drug reactions, and nonionic low-osmolality contrast agents (1762, 6611). The antioxidant and free radical properties might also make N-acetyl cysteine useful in the treatment of pulmonary and cardiac disease (1705, 1765).

N-acetyl cysteine also appears to reduce cellular production of pro-inflammatory mediators such as tumor necrosis factor-alpha, TNF-alpha, and interleukin 1, IL-1 (1763). There is also interest in using N-acetyl cysteine for prevention and treatment of drug- and noise-induced hearing loss, where these effects may reduce cochlear and hair cell damage in the ear. Preliminary data from animal model research shows that intravenous N-acetyl cysteine might prevent or reduce hearing loss associated with cisplatin treatment or prolonged exposure to loud noise, or exposure to sudden loud pulses of noise, such as that caused by gunfire. Protection seems to be dependent on the dose used and the timing of doses in relation to noise exposure (15528, 15529, 15531, 15532, 15533).

N-acetyl cysteine is effective for acetaminophen hepatotoxicity because it restores glutathione levels in the liver and acts as an alternative substrate for conjugation of toxic acetaminophen metabolites (15). N-acetyl cysteine might be helpful in the congenital skin disease lamellar ichthyosis due to antiproliferative effects on skin cells (3975). N-acetyl cysteine may also have anticarcinogenic properties by inhibiting the invasive activity of tumor cells and angiogenesis of tumor cells (1767).

N-acetyl cysteine might decrease bladder toxicity caused by ifosfamide. The exact mechanism is not understood, but it probably involves binding of the thiol-sulfhydryl groups in N-acetyl cysteine to ifosfamide and its metabolite acrolein. N-acetyl cysteine does not appear to affect the anticancer activity of ifosfamide (10268, 10269).

Preliminary evidence indicates that N-acetyl cysteine can impair platelet aggregation. N-acetyl cysteine appears to increase synthesis of nitric oxide, a potent inhibitor of platelet function (10272).

In patients with human immunodeficiency virus (HIV) disease, N-acetyl cysteine can increase levels of glutathione. Increased concentration of glutathione seems to reduce oxidative stress associated with HIV disease and to improve the number and activity of

CD4 T-lymphocytes (1539).

There is interest in using N-acetyl cysteine for improving compulsive behaviors. N-acetyl cysteine appears to increase the uptake of cystine. Uptake of cystine activates a reverse transport of glutamate into the extracellular space. Restoring glutamate to the extracellular space inhibits further release of glutamate which improves compulsive behaviors (16840). Assessing the pharmacokinetics of N-acetyl cysteine is difficult because it binds to cysteine and other sulfhydryl molecules. Because these compounds are widely available in tissues, N-acetyl cysteine is rapidly removed from plasma. After oral administration of N-acetyl cysteine, the time to maximum plasma concentration (T_{max}) is approximately 0.72 hours. With a dose of 250 mg/m², the maximum plasma concentration (C_{max}) is about 1.75 mcg/mL. The half life (T_{1/2}) of N-acetyl cysteine is about 2 hours (10268).

Adverse Reactions:

Orally, N-acetyl cysteine can cause gastrointestinal adverse effects including nausea, abdominal pain, vomiting, constipation, and diarrhea, particularly when used in high doses (1539, 10270, 10271, 11430, 16840). N-acetyl cysteine has an unpleasant odor that sometimes makes it difficult for patients to take orally. Using a straw to drink N-acetyl cysteine solutions can improve tolerability (17). In some cases, placement of a nasogastric or duodenal tube and administration of metoclopramide or ondansetron can also be helpful for patients unable to tolerate oral N-acetyl cysteine (17). Rarely, generalized urticaria with mild fever, sulfhemoglobinemia, headache, hypotension, rash, and hepatotoxicity has occurred (17).

Intravenously, N-acetyl cysteine can sometimes cause allergic reactions including anaphylactoid reactions (1716). For less severe allergic reactions, diphenhydramine can be administered and the N-acetyl cysteine infusion can be continued. For more severe reactions (e.g., angioedema, respiratory symptoms), the infusion should be temporarily discontinued and resumed an hour after diphenhydramine administration (1716).

By inhalation, N-acetyl cysteine has been associated with stomatitis, nausea, vomiting, drowsiness, clamminess, and severe rhinorrhea (15). Fever, chills, chest tightness, and bronchoconstriction have been reported rarely (15). Sensitization and dermal eruptions have also been reported. However, sensitization has not been confirmed by patch testing (15).

In cases of N-acetyl cysteine overdose, symptoms typically resemble a severe anaphylactoid reaction (17).

Interactions with Herbs & Supplements:

None known.

Interactions with Drugs:**ACTIVATED CHARCOAL**

Interaction Rating = **Moderate** Be cautious with this combination.

Severity = High • Occurrence = Possible • Level of Evidence = D

N-acetyl cysteine appears to reduce the capacity of charcoal to adsorb acetaminophen and salicylic acid (7869). But concomitant use of activated charcoal does not seem to reduce the effectiveness of N-acetyl cysteine (1755).

NITROGLYCERIN

Interaction Rating = **Major** Do not take this combination.

Severity = High • Occurrence = Probable • Level of Evidence = B

Concomitant administration of N-acetyl cysteine and intravenous nitroglycerin can cause severe hypotension (2246) and intolerable headaches (2245, 2280).

Interactions with Foods:

None known.

Interactions with Lab Tests:

BLOOD PRESSURE: Concomitant administration of intravenous NAC and nitroglycerin can lower blood pressure and reduce blood pressure readings (2246).

CHLORIDE: NAC can cause false-positive serum chloride test results measured with the Beckman Synchron CX3 analyzer (275).

CREATININE: Intravenous NAC can cause falsely low serum creatinine test results when measured by single-slide method on Kodak Ektachem systems (275).

CYSTEINE (FREE): Intravenous NAC can increase free cysteine plasma concentrations and test results (275).

GOLD: Intravenous NAC can increase urinary gold excretion (concentration) and test results in patients previously given gold (275).

KETONES: NAC can cause false-positive urine ketone test results when measured with Chemstrips (Boehringer Mannheim) or Multistix (Miles) (275).

LIPOPROTEIN A: Used orally, NAC might reduce serum lipoprotein A concentrations and test results in some patients (275).

LITHIUM: Very high serum NAC concentrations might cause falsely low serum lithium test results when measured with Kodak Ektachem systems (275).

LIVER FUNCTION TESTS: NAC might increase liver enzyme (AST, ALT) concentrations and test results. Liver function tests were markedly elevated on two occasions in a child with cystic fibrosis after receiving large NAC doses by rectal and naso-gastric tube administration (15).

PROTHROMBIN TIME (PT): Intravenous NAC can decrease PT and test results (1341).

SALICYLATE: Serum NAC concentrations of 50 mg/dL (occurring with intravenous NAC administration) can cause falsely low serum salicylate test results when measured with Kodak Ektachem systems. Serum NAC concentrations of 10 mg/dL (occurring with oral NAC administration) do not interfere with serum salicylate results measured with Kodak Ektachem systems (275).

Interactions with Diseases or Conditions:

ALLERGY: Contraindicated in individuals with acetylcysteine allergy (15).

ASTHMA: Oral NAC inhalation or intratracheal administration might cause bronchospasm, monitor closely (15).

HEMODIALYSIS-ASSOCIATED PSEUDOPORPHYRIA: NAC might improve pseudoporphyria skin lesions associated with hemodialysis. Two cases are reported in which pseudoporphyria skin lesions healed with oral NAC administration in patients on chronic hemodialysis (5052).

Dosage/Administration:

ORAL: For acetaminophen overdose, an oral loading dose of 140 mg/kg of a 5% solution should be administered. The commercially available 10% and 20% solutions may be diluted with water, carbonated, or non-carbonated beverages, and administered through a straw to lessen the disagreeable odor of N-acetyl cysteine. Seventeen additional doses of 70 mg/kg as a 5% solution should be given every 4 hours, for a total dose of 1330 mg/kg over 72 hours (17).

For unstable angina, a typical dose is 600 mg three times daily with transdermal nitroglycerin (2245).

For preventing acute exacerbations of chronic bronchitis, doses of 200 mg twice daily, 200 mg three times daily, 300 mg slow-release twice daily, and 600 mg controlled-release twice daily have been used (6176).

For treating chronic obstructive pulmonary disease (COPD), N-acetyl cysteine 600 mg once daily, in addition to standard care, has been used for up to 6 months (10429).

For treating fibrosing alveolitis, N-acetyl cysteine 600 mg 3 times daily has been used (7868).

For prophylaxis of urinary bladder toxicity due to ifosfamide, 1 to 2 grams every 6 hours has been used (5808, 10268, 10269, 10270, 10271).

For reducing plasma homocysteine levels, 1.2 grams daily has been used (2258).

For myoclonus epilepsy, 4-6 grams daily has been used (2259).

For reducing symptoms of influenza, 600 mg twice daily has been used (2260).

For reducing the risk of cardiovascular events in patients with end-stage renal disease, 600 mg twice daily has been used (10430).

For hemodialysis-associated pseudoporphyria skin lesions, 200 mg four times daily or 600 mg twice daily has been used (5052).

For preventing iopromide (Ultravist-300)-induced reduction of renal function in patients with chronic renal insufficiency, 400 to 600 mg N-acetyl cysteine twice daily on the day before and on the day of iopromide administration, with IV saline (0.45%) 1 mL/kg body weight per hour for 12 hours before and 12 hours after iopromide administration, has been used (6611, 10428).

In Alzheimer's disease, N-acetyl cysteine 50 mg/kg/day has been used (7870).

For trichotillomania (hair-pulling), N-acetyl cysteine 1200 mg to 2400 mg daily has been used (16840).

INTRAVENOUS: There are 2 dosage regimens for intravenous N-acetyl cysteine. For patients presenting 10 to 24 hours after acetaminophen ingestion, particularly if large doses were taken, the following 48-hour regimen should be used (17). Administer a loading dose of 140 mg IV N-acetyl cysteine as a 3% solution over 1 hour. The 3% solution is prepared by diluting the 20% IV solution with 5% dextrose. Twelve additional doses of 70 mg/kg IV N-acetyl cysteine should be administered over 1 hour every 4 hours thereafter. The alternative 20-hour regimen consists of IV administration of 150 mg/kg N-acetyl cysteine in 200 ml of 5% dextrose solution, administered over 15 minutes. Follow this dose with 50 mg/kg N-acetyl cysteine in 500 mL 5% dextrose over 4 hours and 100 mg/kg in 1 liter 5% dextrose over 16 hours. The total dose is 300 mg/kg over 20 hours. This regimen is most effective if begun within 8 hours of acetaminophen ingestion (17). In evolving acute myocardial infarction (MI), N-acetyl cysteine 20 mg/minute for 1 hour followed by 10 mg/minute for 23 hours, for a total of 15 grams/24 hours, has been used.

Intravenous nitroglycerin and streptokinase were also given (7872). For reducing mortality rate due to multisystem organ disease, N-acetyl cysteine 150 mg/kg bolus, followed by a continuous infusion of 12 mg/kg/hr for 3 to 5 days has been used; however, mortality rate was not significantly reduced (7871).

Editor's Comments:

None.

This monograph was last reviewed on 12/17/2012 and last updated on 09/13/2011. Monographs are reviewed and/or updated multiple times per month and at least once per year. If you have comments or suggestions on something that should be reviewed or included, please [tell the editors](#). For details about our evidence-based approach, see our [Editorial Principles and Process](#).

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