BASF Chemical Emergency Medical Guidelines

Aminonitrile C 1

Information and recommendations for doctors at hospitals/emergency departments

- **Patients exposed only to aminonitrile vapor do not pose a significant risk of secondary contamination. Patients whose clothing or skin is contaminated with aminonitrile-containing liquids may secondarily contaminate rescue and medical personnel by direct contact or through evaporation of aminonitrile and evolution of cyanide. Immediate skin and hair decontamination with water is crucial.**
- **Aminonitrile poisoning may lead to death within minutes. Given reason to believe that aminonitrile-containing material is present, severe hypoxic signs in the absence of cyanosis suggest the diagnosis.**
- **In case of suspected aminonitrile poisoning, immediate administration of 100% oxygen is crucial. If the patient is symptomatic/overexposed use the recommended cyanide antidotes.**

1. Substance information

2-amino-2,3-dimethylbutyronitrile
Synonym: aminonitrile
This product is composed of 2-amino-2,3-dimethylbutyronitrile (~ 80%) [CAS No. 013893-53-3] and Toluene (~ 20%) [CAS No. 000108-88-3]. It is colorless to amber oily liquid with a musty toluene odor. A small fraction dissociates to free cyanide (as HCN) under ambient conditions, whether as the neat (100%) liquid or in solution with non-reactive organic solvents such as toluene. HCN is in equilibrium with the aminonitrile and can be driven off simply by heating aminonitrile. Thermal decomposition of aminonitrile has been demonstrated, and it is known that the smoke from burning aminonitrile contains significant HCN. Within the body, metabolic processes can generate cyanide from the aminonitrile and cause cyanide toxicity. The odor of cyanide compounds does not provide adequate warning of hazardous concentrations. Since the compound is a solution in toluene, this product is flammable.

2. Routes of exposure

Inhalation

Airborne aminonitrile is readily absorbed via the lung. Intense exposure to airborne toluene is capable of significant irritation to the lungs.

Skin/eye contact

Aminonitrile is readily absorbed through skin or mucous membranes and causes systemic toxicity. Although the onset of toxic symptoms may be slightly delayed for skin exposures, a potentially lethal dose may occur from contamination of a very small area of skin by the aminonitrile. Exposure to aminonitrile may result in mild skin and eye irritation.

Ingestion

Unintentional ingestion of aminonitrile is unlikely. Aminonitrile is immediately absorbed from the gastrointestinal tract. Ingestion can lead to severe systemic toxicity.

3. Acute health effects

Initially the patient may experience flushing, tachycardia, shortness of breath, headache, and dizziness. This then may progress to agitation, stupor, coma, apnea, generalized seizures, bradycardia, hypotension and death.

BASF
We create chemistry

	Aminonitrile can lead to cyanide toxicity. Cyanide combines with the ferric iron in mitochondrial cytochrome oxidase, thus inhibiting oxidative phosphorylation and ATP production. The inhibition of oxidative metabolism places increased demands on anaerobic glycolysis, which results in lactic acidosis.
Central nervous system	CNS signs and symptoms usually develop rapidly. Initial symptoms are nonspecific and include excitement, dizziness, nausea, vomiting and headache. This then may progress rapidly to stupor, apnea, generalized seizures, and coma.
Cardiovascular	Abnormal heartbeat can occur in cases of severe poisoning. High blood pressure and a rapid heartbeat may be early, transient findings, followed by bradycardia, intractable low blood pressure, and death.
Respiratory	After systemic poisoning begins, victims may complain of shortness of breath and chest tightness. Pulmonary findings may include rapid breathing and increased depth of respirations. As poisoning progresses, respirations become slow and gasping; cyanosis may or may not be present. Pulmonary edema may develop.
Metabolic	An anion gap, metabolic acidosis occurs in severe poisoning from increased blood levels of lactic acid.
Dermal	Contact may cause skin irritation. Dermal absorption can occur, leading to systemic toxicity.
Ocular	When splashed in the eye, liquid aminonitrile can cause eye irritation and swelling. Aminonitrile is readily absorbed by this route.
Other	Burning sensation of the mouth and throat have occurred. Breath and vomitus may have a bitter almond odor to those who have the capability of smelling cyanide compounds. Aminonitrile is readily absorbed by the oral route.
Potential sequelae	Survivors of serious exposure should be evaluated for damage to the brain and heart. Patients who have serious cyanide poisoning may be at risk for CNS sequelae including memory deficits and Parkinson-like syndromes; they should be clinically monitored for several weeks to months afterwards.

4. Actions

Rescuer self-protection	**If the zone which has to be entered by the rescuer is suspected of containing aminonitrile, pressure-demand, self-contained breathing apparatus and recommended chemical-protective clothing shall be worn; do not use equipment that is contaminated itself. The environmental presence of HCN is immediate.** Where respiratory protection is required, skin protection is also required. Patients whose clothing or skin is contaminated with aminonitrile-containing liquids may secondarily contaminate rescue and medical personnel by direct contact or through liberation of HCN gas. Aminonitrile is a solution in toluene, so observe prudent precautions for handling a flammable liquid.
Patient recovery	Patients should be removed from the contaminated zone immediately. If patients can walk, they should walk. Patients who are unable to walk may be removed on backboards or stretchers; if these are not available, carefully carry or drag patients to safety. Immediate priorities must follow the **"A, B, C's"** of resuscitation.

Initial treatment

Speed is critical. For symptomatic patients, provide treatment - 100% oxygen - and prepare specific antidotes. **Treatment should be given simultaneously with decontamination procedures.** If trained, use amyl nitrite perles while waiting for intravenous antidotes (see below).

In case of ingestion do not induce emesis. If possible, immediately administer a slurry of activated charcoal. Avoid aspiration of the product into the lungs. Isolate gastric washings and vomitus; hydrogen cyanide may off-gas.

Intubation of the trachea or an alternative airway management should be considered in cases of respiratory compromise. When the patient's condition precludes this, consider cricothyrotomy if equipped and trained to do so.

Decontamination

All patients with suspected exposure to cyanide-containing solutions such as aminonitrile require decontamination. Do not decontaminate personnel or items without recommended protective gear including butyl rubber or Viton® gloves, chemical splash proof goggles, etc. Decontaminate equipment with 5.25% hypochlorite.

Patients who are able and cooperative may assist with their own decontamination. Rapidly remove and double-bag contaminated clothing while flushing exposed skin and hair with plain water for 5 minutes, then use soap and water for further decontamination. Protect patient's eyes during flushing of skin and hair.

Irrigate exposed or irritated eyes with plain water or saline for 5 minutes. Continue eye irrigation during other basic care or transport. Remove contact lenses if present and easily removable without additional trauma to the eye.

Antidotal treatment

The following treatment with antidotes should be given under medical supervision to patients who have known or suspected aminonitrile poisoning. Be prepared for immediate intravenous administration if early symptoms develop; e.g., after significant (> 10 squares cm area) skin contamination with likelihood of continuing absorption through the skin. The availability of antidotes may vary due to statutory and regulatory differences among different countries. The doctor who approaches an exposed patient for treatment should know what, if any, antidotes have been administered, the status of decontamination, and other relevant medical information.

The antidote regimen usually has two steps – (1) a methemoglobin former (amyl and/or sodium nitrite **or** 4-dimethyl aminophenol) to attract the cyanide from the affected enzymes, that is (2) followed by an agent to detoxify and enhance excretion of cyanide (sodium thiosulfate).

Before amyl and/or sodium nitrite **or** 4-dimethyl aminophenol (4-DMAP) is used in a patient it should be quite certain that he/she is poisoned by cyanide. It should only be used if the patient is in coma. It should not be used in smoke poisoning as carbon monoxide hemoglobin and methemoglobin together would not leave enough oxygen carriers.

An alternative antidote is hydroxocobalamine, the adult dose of which is 5 grams in 100 ml saline. A commercially available hydroxocobalamine preparation in the US is one mg/ml preparation for intramuscular injection. It would require 4-5 liters of this preparation for an adequate antidote dose, and therefore the US preparation should not be used. Protocols and preparations are different in various countries, however.

Step 1. In some countries, 0.2-0.4 ml amyl nitrite inhalant ampule (perle) is available and its administration is recommended while waiting for the intravenous treatment to commence. The victim should be lying down in case the nitrite lowers his blood pressure. Break an amyl nitrite perle in a cloth and hold lightly under the nose for 15-30 seconds. Administer oxygen for 15-30 seconds. Repeat amyl nitrite and oxygen administration alternatively. A new perle should be used every 3 minutes, and administer 100% oxygen alone when antidote is administered intravenously (see below).

If 4-DMAP is available, immediately administer 4-DMAP intravenously (IV), usually in a dose of 1 ampule of 250 mg 4-DMAP in an adult. A therapeutic level of methemoglobin will be formed.

If 4-DMAP is not available, infuse sodium nitrite intravenously as soon as possible. The victim should be lying down in case the nitrite lowers his blood pressure. The usual adult dose is 300 mg (10 ml of a 3% solution) infused over no less than 5 minutes (2 to 4 ml per minute). The usual dose for children without anemia is 0.15 to 0.33 ml/kg (up to 10 ml) of a 3% solution IV infused over no less than 5 minutes. It can be mixed in 50 to 100 ml of normal saline. Monitor blood pressure during sodium nitrite administration, and slow the rate of infusion if hypotension develops. To treat hypotension, infuse a fluid challenge of 10-20 ml/kg normal saline and place the victim in the Trendelenberg position. Consider administration of an adrenergic agent if shock occurs. One dose of sodium nitrite should raise the methemoglobin levels to no more than 20%.

Step 2. After either 4-DMAP or sodium nitrite administration, over ten minutes infuse sodium thiosulfate. The adult dose of sodium thiosulfate is 12.5 grams (50 ml of 25% solution) for adults, and for children the dose is 1.65 ml/kg of 25% solution.

Do not treat methemoglobinemia, unless 4-DMAP or nitrite was overdosed or the assumed diagnosis of cyanide poisoning is revised. If signs of poisoning persist or reappear, repeat injection of sodium thiosulfate one hour later at one-half of the original dose. For seizures give diazepam 5 mg intravenously, and this dose may be repeated one time 1 to 2 minutes later if needed.

Further evaluation and treatment

In addition to the standard intake history, physical examination, and vital signs, obtain arterial blood gas measurements, methemoglobin fraction, hemoglobin, venous O_2 and whole blood cyanide levels. Also obtain a posterior-anterior chest x-ray.

After treatment with 4-DMAP or sodium nitrite, serum methemoglobin levels should be monitored and should not exceed 30 to 40%, given anemia is not present. Cyanosis occurs with methemoglobin concentrations of approximately 15%. In cases of symptomatic overdose or mistaken use of methemoglobin former, treat the methemoglobinemia.

All patients who require systemic antidotes for treatment of aminonitrile exposure should be admitted to an intensive care unit for at least 24 hours.

Laboratory tests

The diagnosis of acute aminonitrile toxicity is primarily a clinical one, based on the rapid onset of CNS toxicity and cardiorespiratory collapse together with known or strongly suspected aminonitrile exposure. Laboratory testing is useful for monitoring the patient and evaluating complications. Routine laboratory studies include complete blood count, glucose, electrolytes and lactic acid. After treatment with 4-DMAP or sodium nitrite, serum methemoglobin levels should be monitored.

Arterial and venous blood gases should be performed to assess oxygenation, oxygen extraction, and acid-base balance. Pulse oximetry is not sufficient. Additional studies include ECG monitoring and determination of serum lactate.

Correct metabolic acidosis with bicarbonate when blood pH falls below 7.15. Also evaluate and treat electrolyte imbalance (e.g. hyperkalemia, hypercalcemia).

Patient release/follow-up

Patients who remain **asymptomatic for 2 hours after exposure by inhalation (4 hours by other routes) and have not received antidotes as well as patients who have a normal clinical examination and no signs or symptoms of toxicity may be discharged after an appropriate observation period in the following circumstances:**

a) The evaluating physician is experienced in the evaluation of individuals with cyanide exposure.
b) Information and recommendations for patients with follow-up instructions are provided verbally and in writing. Patients are advised to seek medical care promptly if symptoms develop or recur.
b) The physician is comfortable that the patient understands the health effects of aminonitrile and the provided follow-up instructions.
c) Site medical is notified, so that the patient may be contacted at regular intervals in the 24-hour period following release.
e) Heavy physical work should be precluded for 24 hours.
f) Exposure to cigarette smoke should be avoided for 72 hours; smoke may worsen the condition of the irritated respiratory tract.

In this document BASF has made a diligent effort to ensure the accuracy and currency of the information presented but makes no claim that the document comprehensively addresses all possible situations related to this topic. This document is intended as an additional resource for doctors in assessing the condition and managing the treatment of patients exposed to aminonitrile. It is not, however, a substitute for the professional judgement of a doctor and must be interpreted in the light of specific information regarding the patient available to such a doctor and in conjunction with other sources of authority.

BASF SE
Occupational Medicine &
Health Protection
Carl-Bosch-Straße 38
67056 Ludwigshafen
Germany

BASF Corporation
Medical Department
100 Campus Drive, M/S F 221
Florham Park, NJ 07932
USA

Reviewed: 2019
Code: E024-005