A phenanthrene derivative, colchicine, is the active alkaloidal principle derived from various species of *Colchicum*; it appears as pale-yellow amorphous scales or powder that darkens on exposure to light. One g dissolves in 25 mL of water and in 20 mL of alcohol. Colchicine is freely soluble in alcohol and chloroform.

Chemically, it is Acetamide, N-(5,6,7,9-tetrahydro-1,2,3,10-tetramethoxy-9-oxobenzo[a]heptalen-7-yl)-, (S)-. The molecular weight is 399.44, the molecular formula is C_{22}H_{25}NO_{6}, and the structure is as follows:

![Colchicine Structure](image)

Colchicine, an acetyltrimethylcolchicinic acid, is hydrolyzed in the presence of dilute acids or alkalies, with cleavage of a methyl group as methanol and formation of colchiceine, which has very little therapeutic activity. On hydrolysis with strong acids, colchicine is converted to trimethylcolchicinic acid.

Colchicine Injection, USP, provides a sterile aqueous solution of colchicine for intravenous use. Each vial contains 1 mg (2.5 µmol) of colchicine in 2 mL of solution. Sodium hydroxide may have been added during manufacture to adjust the pH.

**CLINICAL PHARMACOLOGY**

The mechanism of the relief afforded by colchicine in acute attacks of gouty arthritis is not completely known, but studies on the processes involved in precipitation of an acute attack have helped elucidate how this drug may exert its effects.

The drug is not an analgesic, does not relieve other types of pain or inflammation, and is of no value in other types of arthritis. It is not antirheumatic and does not influence the renal excretion of uric acid or its level in the blood or the magnitude of the "mislabeled" pool of uric acid. It also does not alter the solubility of urate in the plasma.

Colchicine is not a uricosuric agent. An acute attack of gout apparently occurs as a result of an inflammatory reaction to crystals of monosodium urate that are deposited in the joint tissue from hyperuric body fluids; the reaction is aggravated as more urate granulocytes that phagocytize the urate crystals. Interference with these processes will prevent the development of an acute attack. Colchicine apparently exerts its effect by reducing the inflammatory response to the deposited crystals and also by diminishing phagocytosis. The deposition of uric acid is favored by an acid pH. In synovial tissues and in leukocytes associated with inflammatory processes, lactic acid production is high; this favors a local decrease in pH that enhances uric acid deposition. Colchicine diminishes lactic acid production by leukocytes both directly and by diminishing phagocytosis, thereby interrupting the cycle of urate crystal deposition and inflammatory response that sustains the acute attack. The oxidation of glucose in phagocytizing as well as in nonphagocytizing leukocytes in vitro is suppressed by colchicine; this suppression may explain the diminution of lactic acid production. The precise biochemical step that is affected by colchicine is not yet known. The antimitotic activity of colchicine is unrelated to its effectiveness in the treatment of acute gout, as indicated by the fact that trimethylcolchicinic acid, an analog of colchicine, has no antimitotic activity except in extremely high doses.

**INDICATIONS AND USAGE**

Colchicine is indicated for the treatment of gout. It is effective in relieving the pain of acute attacks, especially if therapy is begun early in the attack and in adequate dosage. Many therapists use colchicine as interval therapy to prevent acute attacks of gout. It has no effect on nongouty arthritis or on uric acid metabolism.

The intravenous use of colchicine is advantageous when a rapid response is desired or when gastrointestinal side effects interfere with oral administration of the medication. Occasionally, intravenous colchicine is effective when the oral preparation is not. After the acute attack has subsided, the patient can usually be given colchicine tablets by mouth.

**CONTRAINDICATIONS**

Colchicine is contraindicated in patients with gout who also have serious gastrointestinal, renal, hepatic, or cardiac disorders. Colchicine should not be given in the presence of combined renal and hepatic disease.

**WARNINGS**

Colchicine can cause fetal harm when administered to a pregnant woman. If this drug is used during pregnancy, or if the patient becomes pregnant while taking it, the woman should be apprised of the potential hazard to the fetus.

Mortality Related to Overdosage - Cumulative intravenous doses of colchicine above 4 mg have resulted in irreversible multiple organ failure and death (see DOSAGE AND USAGE).
ADVERSE REACTIONS

These are usually gastrointestinal in nature and consist of abdominal pain, nausea, vomiting, and diarrhea. The diarrhea may be severe. The gastrointestinal symptoms may occur even though the drug is given intravenously; however, such symptoms are unusual unless the recommended dose is exceeded. Prolonged administration may cause bone marrow depression, with agranulocytosis, thrombocytopenia, and aplastic anemia. Peripheral neuritis and depilation have also been reported. Myopathy may occur in patients on usual maintenance doses, especially in the presence of renal impairment.

OVERDOSAGE

Signs and Symptoms - Signs, the onset of which may be delayed, include nausea, vomiting, diarrhea, abdominal pain, hemorrhagic gastroenteritis, and burning pain in the throat, stomach, and skin. Fluid extravasation may lead to shock. Myocardial injury may be accompanied by ST-segment elevation, decreased contractility, and profound shock. Muscle weakness or paralysis may occur and progress to respiratory failure. Hepatocellular damage, renal failure, and lung parenchymal infiltrates may also occur, and, by the fifth day after overdose, leukopenia, thrombocytopenia, and coagulopathy may also occur. If the patient survives, alopecia and stomatitis may be experienced. There is no clear separation of nontoxic, toxic, and lethal doses of colchicine. The lethal oral dose of colchicine has been estimated to be 65 mg; however, death has resulted from intravenous doses as small as 7 mg acutely (see WARNINGS AND DOSAGE AND ADMINISTRATION). Serum concentrations that may be toxic or lethal are not defined. The intravenous median lethal dose in rats is 1.7 mg/kg. Treatment - To obtain up-to-date information about the treatment of overdose, a good resource is your certified Regional Poison Control Center. Telephone numbers of certified poison control centers are listed in the Physicians' Desk Reference (PDR). In managing overdosage, consider the possibility of multiple drug overdoses, interactions among drugs, and unusual drug kinetics in your patient.

Protect the patient's airway and support ventilation and perfusion. Meticulously monitor and maintain, within acceptable limits, the patient's vital signs, blood gases, serum electrolytes, etc. If colchicine was recently ingested, an activated charcoal should be administered. If leakage has not occurred, perform gastric lavage once the patient is stabilized. Absorption of drugs from the gastrointestinal tract may be decreased by giving activated charcoal, which, in some cases, is more effective than emesis or lavage; consider charcoal instead of or in addition to gastric emptying. Repeated doses of charcoal over time may hasten elimination of some drugs that have been absorbed. Safeguard the patient's airway when employing gastric emptying or charcoal.

Forced diuresis, peritoneal dialysis, hemodialysis, or charcoal hemoperfusion have not been established as beneficial for an overdose of colchicine.

DOSAGE AND ADMINISTRATION

Colchicine injection is for intravenous use only. Severe local irritation occurs if it is administered subcutaneously or intramuscularly. It is extremely important that the needle be properly positioned in the vein before the drug is injected. If leakage is suspected prior to注射, normal saline as the intravenous fluid. Colchicine Injection should not be diluted with 5% Dextrose in Water. If a decrease in concentration of colchicine in solution is required, 0.9% Sodium Chloride Injection, which does not contain a bacteriostatic agent, should be used. Solutions that become turbid should not be used.

In the treatment of acute gouty arthritis, the average initial dose of Colchicine Injection is 2 mg (4 mL). This may be followed by 0.5 mg (1 mL) every 6 hours until a satisfactory response is achieved. In general, the total dosage for the first 24-hour period should not exceed 4 mg (8 mL). Cumulative doses of colchicine above 4 mg have resulted in irreversible multiple organ failure and death. The total dosage for a single course of treatment should not exceed 4 mg. Some clinicians recommend a single intravenous dose of 3 mg, whereas others recommend an initial dose of not more than 1 mg of colchicine intravenously, followed by 0.5 mg once or twice daily if needed. If a recurrence occurs, it may be necessary to administer a daily dose of 1 to 2 mg (2 to 4 mL) for several days; however, no more colchicine should be given by any route for at least 7 days after a full course of IV therapy (4 mg). Many patients can be transferred to oral colchicine at a dosage similar to that being given intravenously.

In the prophylactic or maintenance therapy of recurrent or chronic gouty arthritises, a dosage of 0.5 to 1 mg (1 to 2 mL) once or twice daily may be used. However, in these cases, oral administration of colchicine is preferable, usually taken in conjunction with a uricosuric agent. If an acute attack of gout occurs while the patient is taking colchicine as maintenance therapy, an alternative drug should be instituted in preference to increasing the dose of colchicine. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

REFERENCES


HOW SUPPLIED

Colchicine Injection, USP 0.5 mg per 1 mL is supplied in cartons of 10 x 2 mL vials NDC 55390-605-02. Store at controlled room temperature, 59° to 86°F (15° to 30°C).

Manufactured by: Ben Venue Laboratories, Inc., Bedford, OH 44146
Manufactured for: Bedford Laboratories™, Bedford, OH 44146

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