FAVOREX

Colcitex
(Colchicine)

Each tablet of Colcitex contains 0.6 mg colchicine. 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 220 ml of ether. Colchicine is freely soluble in alcohol and chloroform.

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.

Clinical Pharmacology :
The mechanism of the relief afforded by Colcitex 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 valve in other types of arthritis. It is not a diuretic and does not influence the renal excretion of uric acid or its level in the blood or the magnitude of the "miscible pool" of uric acid. It also does not alter the solubility of urate in the plasma.

Colcitex 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 fluid; the reaction is aggravated as more urate crystals accumulate. The initial inflammatory response involves local infiltration of granulocytes that phagocytize the urate crystals. Interference with these processes will prevent the development of an acute attack. Colcitex 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. Colcitex 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 diminished lactic acid production. The precise biochemical step that is affected by Colcitex is not yet known. The antimitotic activity of Colcitex 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 :
Colcitex 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 Colcitex as interval therapy to prevent acute attacks of gout. It has no effect on nongouty arthritis or on uric acid metabolism.

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

Warnings :
Colcitex 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.

Precautions :
General : Colcitex should be administered with great caution to aged and debilitated patients, especially those with renal, hepatic, gastrointestinal, or heart disease. Reduction in dosage is indicated if weakness, anorexia, nausea, vomiting, or diarrhea occurs.

Drug Interactions :
Colcitex has been shown to induce reversible malabsorption of vitamin B12, apparently by altering the function of ileal mucosa. The possibility that Colcitex may increase response to central-nervous-system depressants and to sympathomimetic agents is suggested by the results of experiments on animals.

Cyclosporin : Colchicine may increase the plasma cyclosporin concentration, which enhace the risk of nephrotoxicity and muscular toxicity when two drugs are used together.

Usage in Pregnancy :
Pregnancy Category D--See Warnings.

Nursing Mothers :
It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Colcitex is administered to a nursing woman.

Usage in Children :
Safety and effectiveness in children have not been established.

Adverse reactions :
In full dosage, Colcitex produces nausea, vomiting, and/or diarrhea. However, it is generally necessary to reach such dose levels for an adequate therapeutic effect. Paregoric may be given either concurrently or when diarrhea develops.
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 : Symptoms, 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 occur and, by the fifth day after the overdose, leukopenia, thrombocytopenia, and coagulopathy may also occur. If the patient survives, alopecia and stomatitis may be experienced. There is no clear separation of non toxic, toxic, and lethal doses of colchicine. The lethal dose of colchicine has been estimated to be 65 mg; however, death has resulted from acute doses as small as 7 mg. 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. Telepone numbers of certified poison control centers are listed in the Physicians'Desk Reference (PDR). In managing overdosage, consider the possibility of multiple drug overdoses, interaction among drug, 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. Absorption of drugs from the gastrointestinal tract may be decreased by giving activated charcoal which, in many 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 perfusion have not been established as beneficial for an overdose of colchicine.

Dosage and administration :
Colcitex should be started at the first warning of an acute attack; a delay of a few hours impairs its effectiveness. The usual adult dose is 1 or 2 tablets initially, followed by 1 tablet every 1 to 2 hours until pain is relieved or nausea, vomiting, or diarrhea develops. Some physicians prescribe 2 tablets every 2 hours. Since the number of doses required may range from 6 to 16, the total dosage is variable. As interval treatment, 1 tablet may be taken 1 to 4 times a week for the mild or moderate case, once or twice daily for the severe case. If an acute attack of gout occurs while the patient is taking Colcitex as maintenance therapy, an alternative drug should be instituted in preference to increasing the dose of Colcitex.

Store below 30°C

Keep medicines out of reach of children.

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