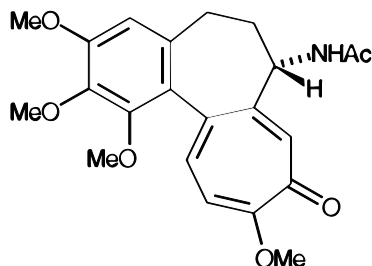


COLGOUT

NAME OF THE DRUG

Colchicine

Structural Formula



CAS No. 64-86-8

DESCRIPTION:

A phenanthrene derivative, Colchicine is an alkaloid obtained from various species of *Colchicum*. The chemical name for colchicine is (S)-N-(5,6,7,9-Tetrahydro-1,2,3,10-tetramethoxy-9-oxobenzo [α] heptalen-7-yl) acetamide (molecular weight 399.4).

Colchicine occurs as pale yellow, amorphous scales or powder and darkens on exposure to light. Colchicine is soluble in water, freely soluble in alcohol and chloroform, and slightly soluble in ether.

Each tablet contains 500 micrograms of colchicine and the following inactive ingredients: magnesium stearate, lactose, maize starch and povidone.

PHARMACOLOGY:

The exact mechanism of action of colchicine in gout is not completely understood. Colchicine decreases leucocyte chemotaxis and phagocytosis and thereby inhibits the formation and release of a chemotactic glycoprotein that is produced during the phagocytosis of urate crystals. Colchicine also inhibits urate crystal deposition, which is enhanced by a low pH in the tissues, probably by inhibiting oxidation of glucose and subsequent, lactic acid production in leucocytes.

Colchicine is not an analgesic, though it relieves pain in acute attacks of gout. It is not a uricosuric agent and will not prevent progression of gout to chronic gouty arthritis. It does have a prophylactic, suppressive effect that helps to reduce the incidence of acute attacks and to relieve the residual pain and mild discomfort that patients with gout occasionally feel.

Colchicine inhibits cell division in the metaphase by interfering with the mitotic spindle. Colchicine has other pharmacological actions in animals; it alters neuromuscular function, intensifies gastrointestinal activity by neurogenic stimulation, increases sensitivity to central depressants, heightens response to sympathomimetic compounds, depresses the

respiratory centre, constricts blood vessels, causes hypertension by central vasomotor stimulation, and lowers body temperature.

Pharmacokinetics

Absorption

Following oral administration of colchicine given as 1.8 mg colchicine over 1 hour to healthy, young adults under fasting conditions, colchicine appears to be readily absorbed, reaching mean maximum plasma concentrations of 6.2 ng/mL at a median 1.81 hours (range 1.0 to 2.5 hours). Following administration of 4.8 mg over 6 hours, mean maximal plasma concentrations were 6.8 ng/mL, at a median 4.47 hours (range: 3.1 to 7.5 hours).

In some subjects, secondary colchicine peaks are seen, occurring between 3 and 36 hours post-dose and ranging from 39% to 155% of the height of the initial peak. These observations are attributed to intestinal secretions and reabsorption and/or biliary recirculation.

Administration of colchicine with food has no effect on the rate of colchicine absorption, but did decrease the extent of colchicine by approximately 15%. This is without clinical significance.

Distribution

The mean apparent volume of distribution in healthy young volunteers was approximately 5 to 8 L/kg. In plasma, colchicine possesses a low to moderate protein binding (30 to 50%) and after reabsorption, is rapidly removed from the plasma and distributed to various tissues. The oral bioavailability of colchicine is between 25 to 50%. Colchicine is found in high concentrations in leucocytes, kidneys, the liver and spleen and as a consequence, accumulation in these tissues may lead to toxicity. Colchicine is rapidly distributed to peripheral leucocytes and concentrations in these cells may exceed those in plasma.

Colchicine crosses the placenta (plasma levels in the foetus are reported to be approximately 15% of the maternal concentration). Colchicine also distributes into breast milk at concentrations similar to those found in the maternal serum.

Metabolism and Excretion

Colchicine is demethylated to two primary metabolites, 2-O-demethylcolchicine and 3-O-demethylcolchicine (2- and 3-DMC, respectively), and one minor metabolite, 10-O-demethylcolchicine (also known as colchiceine). In vitro studies using human liver microsomes have shown that CYP3A4 is involved in the metabolism of colchicine to 2- and 3-DMC. Plasma levels of these metabolites are minimal (less than 5% of parent drug).

The majority of the drug and its metabolites are excreted primarily in the faeces while 10 to 20% is excreted in urine. Renal elimination may increase in patients with hepatic impairment. Due to the high levels of tissue uptake of colchicine, only 10% of a single dose is eliminated in the first 24 hours. Consequently, the elimination of colchicine from the body may continue for 10 days or more after the cessation of treatment.

Enterohepatic recirculation and biliary excretion are also postulated to play a role in colchicine elimination. Following multiple oral doses (0.6 mg twice daily), the mean elimination half-lives in young healthy volunteers (mean age 25 to 28 years of age) is 26.6 to 31.2 hours. Colchicine is a substrate of P-gp.

Following a single 1mg oral dose, the mean half-life of colchicine was determined to be 4.4 hours in patients with normal renal function while the mean half-life in patients with renal dysfunction was 18.8 hours. Similarly, a single oral dose of 1mg produces peak serum concentrations of between 3.9 to 11ng/mL within 2 hours.

The initial response to oral colchicine occurs between 12 to 24 hours and the peak response is expected within 48 to 72 hours.

Extracorporeal Elimination: Colchicine is not removed by haemodialysis.

INDICATIONS:

Treatment of acute gout. Colchicine should not be used unless NSAIDS are contraindicated, or have been used and found to lack efficacy or to have unacceptable side effects in the individual patient.

CONTRAINDICATIONS:

- Patients with combined hepatic and renal disease.
- Severe renal or hepatic impairment.
- Patients with mild or moderate renal or hepatic impairment taking a P-gp or strong CYP3A4 inhibitor (see interactions section).
- Patients with serious cardiac or gastrointestinal disorders.
- Patients with blood dyscrasias.
- Hypersensitivity to colchicine.
- Children.
- Lactation

PRECAUTIONS:

Colchicine has a low toxic threshold and extreme care should be taken when using this medicine.

Fatal overdose

Colchicine can be fatal in overdose. There have been cases of fatality when colchicine was taken for a therapeutic purpose with doses as small as 6 or 7mg.

Treatment with therapeutic doses should be discontinued immediately when gastrointestinal symptoms (abdominal pain, diarrhoea, nausea or vomiting) occur.

Patients with recurrent conditions

Colchicine should be given with care in geriatric or debilitated patients and to those with cardiac, renal or gastrointestinal disease. The drug should be used with caution in patients who may have early manifestations of these disorders.

Blood dyscrasias

The leukopenic and thrombocytopenic effects of colchicine may result in an increased incidence of microbial infection, delayed healing and gingival bleeding. If leukopenia or thrombocytopenia occur, dental work should be deferred until blood counts have returned to normal (see contraindications).

Use in patients with renal disease

A reduction in the size of individual doses, an increase in the interval between doses or a reduction in the daily dosage is recommended in patients with renal impairment (see contraindications).

Use in patients with hepatic disease

Colchicine should be given with care in patients with hepatic disease (see contraindications).

Use in Children

Safety and effectiveness in this age group have not been established, therefore use in children is not recommended. (*see contraindications*).

Use in the Elderly

The elderly, even those with normal renal and hepatic function, may be more susceptible to cumulative toxicity with colchicine. As the elderly are more likely to have age related renal function impairment, the risk of myopathy and other toxic effects increases in patients receiving colchicine. Caution and careful attention to dosage is recommended.

In those elderly patients who are small and slight (less than 50kg) and those with renal or hepatic impairment, other treatments should be considered. If colchicine is used in these patients a maximum cumulative dose of 3mg over four days should be observed.

Carcinogenicity and Mutagenicity

Mutagenicity studies of colchicine have not been evaluated. Colchicine is a known genotoxin, causing gene mutations, DNA damage and chromosomal damage in several in vitro and in vivo assays. Animal studies have not been performed to assess the potential carcinogenic effect of colchicine. Since colchicine is an established mutagen, its ability to act as a carcinogen must be suspected and treatment with Colgout should involve a weighing of the benefit vs risk when long term administration is being considered.

Impairment of Fertility

Animal studies of the effects of colchicine on fertility have not been evaluated. Colchicine arrests cell division in animals and plants and has adversely affected spermatogenesis in humans and in some animal species under certain conditions.

Use in Pregnancy: (Category D)

Cell division in animals can be arrested by colchicine. Colchicine should be avoided in pregnancy. Women of child-bearing age should be advised to use effective contraception whilst taking colchicine. If there is an absolute need to use colchicine during pregnancy, or if the patient becomes pregnant while taking it, the woman should be told of the potential hazard to the foetus.

Reproductive toxicity studies of colchicine have not been evaluated. In published studies, colchicine has been shown to be teratogenic in mice given doses of 0.5mg/kg and has produced foetotoxic and teratogenic effects in hamsters given 10mg/kg. In other studies, colchicine was embryotoxic in rabbits and cattle but not in monkeys. The possibility of such effects in humans has been reported. However, there are no adequate and well-controlled studies in pregnant women or in men conceiving children while taking colchicine.

Colchicine crosses the placental barrier and was present in a sample of umbilical cord blood taken from a newborn child.

Use in lactation

Breast-feeding should be avoided while the patient is taking colchicine.

Colchicine has been shown to be highly excreted into human breast milk and the concentration in the breast milk is similar to that found in the corresponding serum.

Peak concentrations of 1.2 to 2.5 nanograms per mL (< 0.001 micromole per litre) have been measured 40 to 50 minutes after administration of a 0.6mg dose to a patient receiving long term therapy with 0.6mg twice a day. No adverse effects were apparent in the breastfed infant during the first 6 months of life.

Animal studies have not been performed to assess whether treatment of the mother with colchicine during lactation affects the newborn infant.

Interactions with other drugs

Pharmacokinetic interactions

In vitro studies in human liver microsomes have shown that colchicine is not an inhibitor or inducer of CYP1A2, CYP2A6, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6, CYP2E1 or CYP3A4 activity.

CYP3A4 AND P-gp inhibitors

Colchicine is a substrate of the efflux transporter P-glycoprotein (P-gp).

Of the cytochrome P450 enzymes tested, CYP3A4 was mainly involved in the metabolism of colchicine. If colchicine is administered with drugs that inhibit P-gp, most of which also inhibit CYP3A4, increased concentrations of colchicine are likely. Fatal drug interactions have been reported.

Physicians should ensure that patients are suitable candidates for treatment with colchicine and remain alert for signs and symptoms of toxicities related to increased colchicine exposure as a result of a drug interaction. Signs and symptoms of colchicine toxicity should be evaluated promptly and, if toxicity is suspected, colchicine should be discontinued immediately.

Medicines inhibiting CYP3A4 and P-gp and known to cause significant increase in colchicine concentrations include:

Cyclosporin

Clinical evidence suggests that the concurrent use of colchicine and cyclosporin may result in the patient developing pronounced side effects ranging from diarrhoea, elevation in liver enzymes, hyperbilirubinemia and elevations in serum creatinine levels. In addition myopathies and rhabdomyolysis have been reported especially in patients with renal impairment. The concentration of cyclosporine may also rise, increasing the risk of nephrotoxicity.

Clarithromycin. There have been postmarketing reports of colchicine toxicity with concomitant use of clarithromycin and colchicine, especially in the elderly, some of which occurred in patients with renal insufficiency. Deaths have been reported in some such patients.

Erythromycin

Life threatening colchicine toxicity has been described after 2 weeks of concomitant erythromycin administration in a patient with hepatic and renal impairment.

Ketoconazole, Protease Inhibitors such as ritonavir, Verapamil, Diltiazem, Digoxin, HMG-Co A Reductase Inhibitors such as atorvastatin, fluvastatin, pravastatin and simvastatin and other lipid lowering drugs such as fibrates and gemfibrozil.

Acidifying and Alkalinising agents

Colchicine is inhibited by acidifying agents such as ammonium chloride, ascorbic acid and acid phosphates and the action of colchicine is potentiated by alkalinising agents (eg. sodium bicarbonate and potassium citrate).

Pharmacodynamic Interactions

Dosage reductions may be required when 2 or more bone marrow depressants, including radiation, are used concurrently or consecutively.

CNS Depressants

Colchicine may increase the sensitivity to the CNS depressants such as the opiates, sedative hypnotics, benzodiazepines and ethanol. The response to sympathomimetic agents such as adrenaline, dopamine, dobutamine, isoprenaline and ephedrine may be enhanced when used concurrently with colchicine.

Alcohol

The concurrent use of alcohol and orally administered colchicine increases the risk of gastrointestinal toxicity, especially in alcoholics. Furthermore, the alcohol increases blood uric acid concentrations that may decrease the efficacy of prophylactic gout therapy.

NSAIDS

The concurrent use of phenylbutazone with colchicine may increase the risk of leukopenia, thrombocytopenia or bone marrow depression while the concurrent use of other NSAIDs with colchicine may increase the risk of gastrointestinal ulceration or haemorrhage. NSAID-induced inhibition of platelet aggregation may increase the risk of bleeding in areas other than the gastrointestinal tract should colchicine-induced thrombocytopenia or clotting defects (with overdose) occur.

Antineoplastic agents

The use of rapidly cytolytic antineoplastic agents with colchicine may increase serum uric acid concentrations and decrease the efficacy of prophylactic gout therapy.

Medicines with the potential to cause blood dyscrasias

The leukopenic effects and/or thrombocytopenic effects of colchicine may be intensified with the concurrent or recent therapy with blood-dyscrasia causing medications and bone marrow depressants. These medications are defined as those drugs causing unpredictable myelotoxicity that usually occurs in a minority of patients and is not dose-dependent, or as bone marrow depressants which produce a predictable dose-related myelotoxicity. Such medications include aldesleukin, amphotericin B lipid complex, anastrozole, angiotensin-converting enzyme (ACE) inhibitors, anti-inflammatory drugs, antithyroid agents, azathioprine, busulfan, carbamazepine, carboplatin, carmustine, chlorambucil, chloramphenicol, cisplatin, cladribine, clozapine, cyclophosphamide, cytarabine, dacarbazine, dactinomycin, dapsone, daunorubicin, didanosine, docetaxel, doxorubicin, etoposide, flecainide, flucytosine, fludarabine, fluorouracil, foscarnet, gamma and alpha interferon, ganciclovir, gemcitabine, gold compounds, hydroxyurea, idarubicin, ifosfamide, irinotecan, levamisole, lomustine, mechlorethamine, melphalan, mercaptopurine, methotrexate, mitomycin, mitoxantrone, paclitaxel, pegasparagase, penicillamine,

pentamidine, phenothiazines, pimozide, primaquine, primidone, procainamide, procarbazine, pyrimethamine, rifampicin, sodium iodide I 131, strontium 89 chloride, sulfasalazine, sulfamethoxazole and trimethoprim, sulfonylurea antidiabetic agents, sulphonamides, thioguanine, thiotepa, thioxanthenes, ticlopidine, topotecan, tricyclic antidepressants, trimethoprim, valproic acid, vinblastine, vincristine, vinorelbine and zidovudine.

Medicines with the potential to cause haemorrhage

Furthermore, the possibility should be considered that colchicine, due to its potential to cause gastrointestinal haemorrhage, thrombocytopenia (with chronic use) and coagulation defects such as disseminated intravascular coagulation (with overdose), may cause an increased risk to patients receiving other medications that may impair blood clotting or cause haemorrhage. Such medications may include anticoagulants such as coumarin or indandione derivatives or other hypoprothrombinemia inducing medicines, heparin, thrombolytic agents, platelet aggregation inhibitors, other thrombocytopenic inducing medications and other medicines with the significant potential for causing gastrointestinal ulceration or haemorrhage.

Vitamin B12

Colchicine has been shown to induce reversible malabsorption of Vitamin B₁₂, apparently by altering the function of ileal mucosa.

Effect on laboratory tests

Colchicine treatment has been shown to produce alterations to laboratory test results. The effects of potentially clinical significance include false positive test results for Red Blood Cells (RBC) and haemoglobin levels in diagnostic urine tests and interference of the Reddy, Jenkins and Thorn procedure when determining 17-Hydroxycorticosteroid levels in urine. Furthermore, physiology/laboratory test values for serum alkaline phosphatase and aspartate aminotransferase (AST [SGOT]) values may be increased while the platelet count may be decreased.

ADVERSE REACTIONS:

The most common adverse reactions reported in the clinical trial with colchicine for treatment of gout flares were diarrhoea (23%) and pharyngolaryngeal pain (3%).

Postmarketing experience

Blood disorders

Anaemia, leukopenia, neutropenia, thrombocytopenia, nonthrombocytopenia purpura, agranulocytosis, pancytopenia and aplastic anaemia.

Body as a whole

Hypothyroidism, prostration and reversible muscular weakness. Losses of body and scalp hair, loss of appetite and myopathy have been reported with prolonged administration of colchicine.

Musculoskeletal

Myopathy is more likely to occur in patients with impaired renal or hepatic function who are receiving long term treatment with prophylactic doses of colchicine. This condition is characterised by proximal muscle weakness, spontaneous activity in an electromyogram and elevated creatinine kinase levels.

Rhabdomyolysis has also been reported.

Cardiovascular

Prolonged or toxic levels of colchicine may cause generalised vascular damage.

Eye disorders

Colchicine may delay or prevent corneal wound healing. Cases of corneal ulcers refractory to conventional treatment and delayed corneal wound healing following strabismus surgery have been reported while the patients were receiving oral colchicine therapy. Discontinuation of colchicine therapy resulted in satisfactory wound healing within several days.

Gastrointestinal

Nausea, vomiting, abdominal pain and diarrhoea present approximately 8 to 12 hours after oral administration in 80% of patients, especially when maximal doses are used. Therapy should be discontinued at the onset of gastrointestinal intolerance in order to avoid serious toxicity, regardless of whether joint pain has been relieved. Further treatment should be postponed for at least 3 days when gastrointestinal symptoms are encountered.

Steatorrhoea has been reported.

Colchicine produces a reversible malabsorption syndrome by disrupting the intestinal mucosal function and in particular, the absorption of Vitamin B12 may be impaired by long term therapy.

At toxic doses, colchicine may cause severe diarrhoea that may be haemorrhagic and can lead to metabolic acidosis, dehydration, hypotension and shock. Antidiarrhoeal agents may be required for the treatment of diarrhoea resulting from colchicine therapy. Paralytic ileus and stomatitis have also been reported.

Genitourinary

Reversible azoospermia and oligospermia, reduction in sperm motility and abnormal sperm penetration assay results.

Renal effects

Bladder spasm has been reported while anuria, haematuria and oliguria have been associated with prolonged colchicine therapy. At toxic doses, colchicine may cause renal damage which results in haematuria and oliguria.

Hepatobiliary effects

Increased serum concentrations of alkaline phosphatase.

Hypersensitivity and Skin

Nonthrombocytopenic purpura, rashes, urticaria, dermatoses and dermatitis have been reported and very rarely, hypersensitivity including angioedema.

Neurological

Myoneuropathy, although both skeletal muscles and peripheral nerves are affected, myopathy is most prominent and associated axonal neuropathy is mild. In most cases of myoneuropathy, symptoms have manifested after several years of therapy. Colchicine may also cause peripheral neuropathy (numbness of fingers and toes) with prolonged administration.

Respiratory

Adult Respiratory Distress Syndrome which may be fatal.

DOSAGE and ADMINISTRATION:

The total amount of oral colchicine needed to control an acute attack of gout in otherwise healthy adults usually ranges from 4 to 6mg over 4 days. A cumulative oral dose of 6mg over four days should not be exceeded. Additional colchicine should not be administered for at least 3 days after a course of oral treatment.

Adults:

Initial dosage: 2 tablets (1mg) followed every six hours by 1 tablet (500 micrograms) until relief is obtained, up to a maximum daily dose of 5 tablets (2.5mg) in the first 24 hours. The total dose given in an acute attack should not exceed 6mg over four days. If gastrointestinal adverse effects occur, discontinue immediately.

Colchicine may be taken with or without food.

Children:

Colchicine is not recommended for use in children.

Elderly:

The elderly, even those with normal renal and hepatic function, may be more susceptible to cumulative toxicity with colchicine. As the elderly are more likely to have age related renal function impairment, caution and careful attention to dosage is recommended.

In those elderly patients who are small and slight (less than 50kg) and those with renal or hepatic impairment, other treatments should be considered. If colchicine is used in these patients a maximum cumulative dose of 3mg over four days should be observed.

Reduced hepatic and renal function:

A reduction in the size of individual doses, an increase in the interval between doses or a reduction in the total daily dosage may be necessary in patients with renal or hepatic impairment. Specifically, it is recommended that dosage be reduced by half if the patient's creatinine clearance is 50mL per minute (0.83 mL per second) or less and that colchicine not be used at all if the patient's creatinine clearance is 10mL per minute (0.17mL per second) or less. (*See Contraindications*)

Furthermore, as renal dysfunction significantly reduces the clearance and prolongs the half-life of colchicine, close monitoring of the renally impaired patient is advised.

Duration of treatment:

Treatment with therapeutic doses of colchicine should be discontinued immediately, even if symptoms of the acute attack of gout have not been relieved, when gastrointestinal symptoms (abdominal pain, diarrhoea, nausea or vomiting) occur. The patient should be told to note the total dose taken prior to the appearance of these symptoms and during subsequent attacks of gout to use smaller doses.

Additional colchicine should not be administered for at least 3 days after a course of oral treatment.

OVERDOSAGE:**Symptoms**

A latent period of 2 to 12 hours occurs between overdose and the onset of gastrointestinal symptoms.

The first signs of toxicity may be a feeling of burning and rawness in the mouth and throat and difficulty in swallowing. These symptoms are followed by severe nausea, vomiting, abdominal pain, haemorrhagic gastroenteritis, with resulting electrolyte abnormalities, volume depletion and hypotension.

The second phase consists of multisystem failure and generally occurs at 24 to 72 hours post ingestion. Effects include CNS toxicity, bone marrow depression, hepatocellular damage, muscle damage, respiratory distress, myocardial injury and renal damage. Multiple organ failure caused by tissue damage including bone marrow hypoplasia is likely to be followed by agranulocytosis, leukopenia, thrombocytopenia and disseminated intravascular coagulation. In some patients, disseminated intravascular coagulation may be the first haematological sign of toxicity, with the most severe coagulopathy occurring about 25 hours following the administration of a large overdose. Leucopenia may persist for several days followed by leucocytosis with numerous metamyelocytes and myelocytes. Other haematological manifestations of colchicine poisoning include granulocytopenia, immature leukocytes, pancytopenia, anaemia with anisocytosis, polychromasia and basophilic stippling.

Cerebral oedema and CNS toxicity are also associated with acute colchicine toxicity and may be characterised by marked muscular weakness and the development of ascending CNS paralysis with the patient remaining conscious. Mental confusion, delirium, seizures and convulsions may occur as a result of CNS toxicity. There may be a loss of deep tendon and Achilles tendon reflexes, and Babinski's reflex may be elicited.

A fever may develop; sepsis is a well recognised complication and should not be ruled out.

Death may occur as a result of respiratory depression, cardiovascular collapse, or sepsis.

In surviving patients, alopecia, rebound leucocytosis and stomatitis may occur about 10 days after the acute overdose.

Severe toxicity and death have been associated with oral doses exceeding 0.5mg/kg. The lethal dose varies. While it appears to be about 40 mg in adults with normal renal function, a fatal dose of 7mg has been recorded.

Treatment

When treating colchicine overdose or acute poisoning, patients should be carefully monitored for at least 12 hours to take into account the delayed onset of symptoms.

There is no specific antidote for colchicine poisoning. Activated charcoal should be administered, preferably within one hour of ingestion. Repeated oral charcoal dosing (every 2 to 6 hours), administered as a slurry, may enhance total body clearance and elimination, but has not been shown to affect outcome and is not routinely recommended. Consider administration of more than one dose of activated charcoal in patients with moderate to severe poisoning or very large ingestions, and those with clinical deterioration or rising levels despite initial decontamination.

Measures to prevent shock should be taken and diarrhoea should not be treated as this is the main route of elimination.

Other treatment is symptomatic and supportive with attention being given to the control of respiration, maintenance of blood pressure and the circulation, and correction of fluid and electrolyte imbalance.

Analgesics with or without atropine may relieve the abdominal pain, but monitor carefully for possible paralytic ileus.

A benzodiazepine such as diazepam may be given to control convulsions.

Both acute and chronic toxicity may lead to bone marrow depression. Isolate patient if there is evidence of bone marrow depression.

Due to the large apparent volume of distribution of colchicine, haemodialysis and peritoneal dialysis are not recommended.

Monitoring should include haemodynamic, cardiac, and respiratory status and blood electrolytes. In some circumstances, prolonged observation may be recommended as the most severe toxic effects may not appear until 24 hours after ingestion of an acute dose.

PHARMACEUTICAL PRECAUTIONS:

Shelf-life: 3 years
Store below 30°C and protect from light.
Contains lactose.

PRESENTATION:

Round, white, slightly biconvex tablets embossed "C" on the upper side, and plain on the bottom face; HDPE bottle containing 100 tablets, or 30 tablets*

* Not available in New Zealand.

MEDICINE CLASSIFICATION:

Prescription Only Medicine

SPONSOR:

Pharmacy Retailing (NZ) Limited
Trading as Healthcare Logistics
58 Richard Pearse Drive
Airport Oaks
Auckland
New Zealand

Date of preparation: 26 Jan 2016