Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Colchicine Indoco 500 microgram tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 0.5 mg of colchicine
Excipient with known effect:. Each tablet contains 79 mg lactose (as monohydrate)

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablet

White to pale yellow, round (6.0 mm in diameter) tablet, marked with 'C 75' on one side.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Colchicine Indoco is indicated in adults:

- For the treatment of acute gout.
- For the prophylaxis of a gout attack during initiation of uric acid lowering therapy.

4.2 Posology and method of administration

Posology

Adults
In acute gout attack
0.5 mg taken two to three times a day, possibly preceded by an initial dose of 1 mg.
The treatment should be discontinued if gastrointestinal complaints occur, if there is no symptom improvement after two to three days, or if the acute attack resolves.
No more than 6 mg should be taken as a course of treatment. After completion of a course, another course should not be started for at least 3 days (72 hours).

Prophylaxis of gout attack
0.5 - 1 mg per day (to be taken in the evening).

Patients with renal impairment
In patients with mild to moderate renal impairment, the dose is 0.5 mg per day. Such patients should be carefully monitored for adverse effects of colchicine.
The medicinal product is contraindicated in patients with severe renal impairment, (see section 4.3).

Patients with hepatic impairment
In patients with mild to moderate hepatic impairment, the dose is 0.5 mg per day. Such patients should be carefully monitored for adverse effects of colchicine.

The medicinal product is contraindicated in patients with severe hepatic impairment, (see section 4.3).

Specific groups

Concomitant treatment of colchicine with several drugs, mostly inhibitors of cytochrome P450 3A4 (CYP3A4)/P-glycoprotein have been shown to increase the risk for colchicine toxicity. If a patient has received concomitant therapy with a moderate or potent CYP3A4 inhibitor or with a P-glycoprotein inhibitor, the maximum recommended dosage of oral colchicine should be reduced and should be carefully monitored for adverse effects of colchicine

Method of administration

Oral.
The tablet should be taken with a glass of water.

4.3 Contraindications

- Hypersensitivity to the active substance, or to any of the excipients listed in section 6.1.
- Patients with blood dyscrasias.
- Women of childbearing potential unless effective contraceptive measures are taken.
- Patients with severe renal impairment.
- Patients with severe hepatic impairment.

4.4 Special warnings and precautions for use

Colchicine is potentially toxic, so it is important to not exceed the dose as prescribed by a medical professional specialist with the necessary knowledge and experience.
Colchicine has a narrow therapeutic window. Administration should be discontinued if toxic symptoms such as nausea, vomiting, abdominal pain, diarrhoea occur.

If patients develop signs or symptoms that could indicate blood cell dyscrasias, such as fever, stomatitis, sore throat or prolonged bleeding, treatment with colchicine should be discontinued immediately and a complete haematological examination should be performed.

Caution is advised in case of:

- hepatic and renal impairment
- cardiovascular disorders
- gastrointestinal disorders
- elderly and debilitated patients
- patients with blood count abnormalities

Colchicine can cause severe bone marrow depression (agranulocytosis, aplastic anaemia, thrombocytopenia). The change in the blood picture can be gradual, or very sudden. Aplastic anaemia in particular has a high mortality rate. Periodic checks of the blood count are necessary. In the event of skin abnormalities, the blood picture must be checked immediately.

Macrolides, CYP3A4 inhibitors, cyclosporine, HIV protease inhibitors, calcium channel antagonists and statins may cause clinically important interactions with colchicine which may lead to colchicine-induced lead to toxicity (see section 4.5)

Co-administration with P-gp inhibitors and/or strong CYP3A4 inhibitors will increase the exposure to colchicine, which may lead to colchicine-induced toxicity including fatalities. If treatment with a P-gp inhibitor or a strong CYP3A4 inhibitor is required in patients with normal renal and or hepatic function, a reduction in colchicine dosage is recommended (see sections 4.2 and 4.5) and patients should be carefully monitored for adverse effects of colchicine. For patients with an impaired renal or hepatic function, the combined use of colchicine and P-gp inhibitors and/or strong CYP3A4 inhibitors should be avoided whenever possible, as it may be difficult to forecast and control systemic exposure to colchicine. In those exceptional cases where continuation of colchicine when starting P-gp inhibitors and/or strong CYP3A4 inhibitors is considered a benefit, despite the potential risk of overdose, significant dose reductions of colchicine dose and careful clinical monitoring should be applied."

Excipients

Patients with rare hereditary problems of galactose intolerance, the total lactase deficiency or glucose-galactose malabsorption should not take this medicinal product.
This medicinal product contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

Interactions with other drugs are not or hardly documented. Given the nature of the side effects, caution should be exercised with concomitant administration of medicinal products that the can affect blood counts or negatively affect liver and/or kidney function.

Colchicine is a substrate for both CYP3A4 and the P-glycoprotein transporter. Inhibitors of CYP3A4 and P-glycoprotein can increase the concentrations of colchicine in the blood.
Toxicity, including fatalities, has been reported during concomitant use of inhibitors such as macrolides (clarithromycin and erythromycin), cyclosporine, ketoconazole, itraconazole, voriconazole, HIV protease inhibitors, calcium channel antagonists such as verapamil and diltiazem. It has been reported that co-administration of azithromycin with colchicine leads to increased serum levels of colchicine. During treatment with azithromycin and after its discontinuation, clinical follow-up, and monitoring of serum colchicine levels may be required

If treatment with a P-glycoprotein inhibitor (e.g. ciclosporin, verapamil or quinidine) or a strong CYP3A4 inhibitor (e.g. ritonavir, atazanavir, indinavir, clarithromycin, telithromycin, itraconazole or ketaconazole) is necessary in patients with normal renal and hepatic function, colchicine dose adjustment may be necessary. Concomitant use of these inhibitors with colchicine should be avoided in patients with a renal or hepatic damage (see section 4.4).

In addition, substances such as cimetidine, and tolbutamide may affect the metabolism of colchicine thereby increasing colchicine plasma levels.

Grapefruit juice may increase the plasma level of colchicine. Grapefruit juice should therefore not to be taken together with colchicine.

Reversible malabsorption of cyanocobalamin (vitamin B12) can be induced by altered functioning of the intestinal mucosa.

The risk of myopathy and rhabdomyolysis is increased when colchicine is combined with statins, fibrates, cycloporin or digoxin.

4.6 Fertility, pregnancy and lactation

Fertility
Colchicine administration in animals induces significant reductions in fertility

Pregnancy
Animal studies have shown that colchicine is teratogenic (see section 5.3).
Colchicine should not be used during pregnancy.
Women of childbearing potential should not use this product unless effective contraceptive measures are taken (see section 4.3).

Breastfeeding
Colchicine is extensively excreted in breast milk. Colchicine should not be used during breast-feeding.

4.7 Effects on ability to drive and use machines

No data are available regarding the influence of colchicine on the ability to drive and use machines. However, the possibility of drowsiness and dizziness should be taken into account.

4.8 Undesirable effects

The following side effects have been observed.
The frequencies are unknown, unless listed under one of the following classifications:

Very common (≥1/10)
Common (≥1/100 to <1/10)
Uncommon (≥1/1 000 to <1/100)
Rare (≥1/10 000 to <1/1 000)
Very rare (<1/10 000)
Not known (cannot be estimated from the available data)

A class of organ systems	**Frequency**	**Adverse event**
Blood and lymphatic system disorders	Not known	Bone marrow depression with agranulocytosis and aplastic anemia
Nervous system disorders	Not known	Peripheral neuritis, neuropathy
Gastrointestinal disorders	Common	abdominal pain, nausea, vomiting and diarrhoea
Hepatobiliary disorders	Not known	Hepatotoxicity
Skin and subcutaneous tissue disorders	Not known	Baldness, skin rashes (rashes)
Musculoskeletal and Connective Tissue Disorders	Not known	Myopathy and Rhabdomyolysis
Reproductive system and breast disorders	Not known	Amenorrhoea, dysmenorrhoea, oligospermia, azoospermia

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via www.hpra.ie.

4.9 Overdose

Colchicine has a narrow therapeutic index and is highly toxic in overdose. Patients with a increased risk for toxicity are patients with renal or hepatic insufficiency, gastrointestinal or cardiac disease and patients in old age.
In the case of colchicine overdose, all patients, even in the absence of early symptoms, should be referred for immediate medical assessment.

Clinical:
Symptoms of acute overdose may be delayed (3 hours on average): nausea, vomiting, abdominal pain, haemorrhagic gastroenteritis, volume depletion, electrolyte abnormalities, leukocytosis, hypotension in severe cases. The second stage with life-threatening complications develops 24 to 72 hours after administration of the drug: multisystem organ failure, acute renal failure, confusion, coma, ascending peripheral motor and sensory neuropathy, myocardial depression, pancytopenia, arrhythmias, respiratory failure, consumption coagulopathy. Death is usually a result of respiratory depression and cardiovascular collapse. If the patient survives, recovery may be accompanied by rebound leukocytosis and reversible alopecia, starting about one week after the first ingestion.

Therapy:
There is no antidote available.
Toxins can be eliminated by gastric lavage within an hour of acute poisoning.
Consider oral activated charcoal in adults who have ingested more than 0.1 mg/kg body weight within 1 hour of presentation and in children regardless of the amount ingested within 1 hour of presentation..
Hemodialysis has no effect (high apparent volume of distribution).
Intensive clinical and biological monitoring in a hospital setting is indicated.
Symptomatic and supportive treatment: control of respiration, maintenance of the blood pressure and circulation, correction of fluid and electrolyte imbalance.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: *Antigout preparations. Preparations with no effect on uric acid metabolism.*
ATC code: M04AC01

Mechanism of action
The mechanism of action of colchicine in the treatment of gout is not fully understood. Urate crystals are phagocytosed by leukocytes. This releases inflammatory factors. Colchicine inhibits these processes. Other properties of colchicine, such as interaction with the microtubules, could also contribute to its action.
Onset of actions is approximately 12 hours after oral administration and is maximal after 1 - 2 days.

5.2 Pharmacokinetic properties

Absorption
Colchicine is rapidly and almost completely absorbed after oral administration. Maximum plasma levels are usually reached after 30-120 minutes.

Distribution
Plasma protein binding is approximately 30%. It accumulates in leukocytes.

Elimination
Colchicine is partly metabolized in the liver and then partly excreted via the bile. Colchicine is largely excreted (80%) in unchanged form and excreted as a metabolites in the faeces. 10-20% is excreted in urine. The terminal half-life is 3 to 10 hours.

Paediatric population
No pharmacokinetic data are available in children.

5.3 Preclinical safety data

Colchicine causes DNA damage in vitro and chromosome aberrations were observed *in vivo*. There are no toxicity data known from the preclinical research.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Cellulose, microcrystalline E460
Lactose monohydrate
Sodium starch glycolate (Type A)
Magnesium stearate E470B

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

6.4 Special precautions for storage

This medicinal product does not require any special temperature storage conditions. Store in the original package in order to protect from light.

6.5 Nature and contents of container

OPA/Alu/PVC//Alu blisters containing 10, 12, 20, 30, 50, 100, 150 or 200 tablets.
Not all pack sizes may be marketed

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Indoco Remedies Czech s.r.o.
Trtinova 260/1, Čakovice,
196 00 Praha 9, Czech Republic

8 MARKETING AUTHORISATION NUMBER

PA23337/001/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 6th December 2024

10 DATE OF REVISION OF THE TEXT