SUMMARY OF PRODUCT CHARACTERISTICS

Important warning!
Because of the narrow therapeutic range of colchicine, the recommended maximum dose must not be exceeded. Overdosing, including by ignoring interactions, can lead to a fatal, very painful and irreversible poisoning with a fatal outcome. Please refer to sections 4.4, 4.5., 4.8 and 4.9 of this SmPC.
The medicinal product must be kept out of reach of others before and after use.

1 NAME OF THE MEDICINAL PRODUCT

Colchicine Ascend 500 microgram Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 500 micrograms of colchicine.

Excipient with known effect

Each tablet contains 37.700 mg lactose (as monohydrate equivalent to 35.82 mg of lactose anhydrous.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablet

Round, off white coloured biconvex, uncoated tablets embossed "C5" on one upper side and plain on the bottom face. The tablet diameter is approximately “6 mm” and thickness is approximately “2.5 mm”.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Adults

- Colchicine is indicated for the treatment of acute gout.
- Colchicine is indicated for the prophylaxis of a gout attack during initiation of urate-lowering therapy.

Adults and paediatric patients

- Colchicine is indicated in Familial Mediterranean Fever for prophylaxis of attacks and prevention of amyloidosis.

4.2 Posology and method of administration

Posology

Gout

Acute gout attack

2 to 3 times daily 0.5 mg, possibly preceded by an initial dose of 1 mg. Treatment should end until the acute attack resolves, or earlier in the event of gastrointestinal symptoms and no improvement after 2 to 3 days.

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).

If diarrhoea or vomiting occurs, Colchicine Ascend should be discontinued immediately as these may be the first signs of an intoxication.

Prophylaxis of gout attack

0.5 – 1 mg per day (to be taken in the evening).

Paediatric population

Colchicine Ascend should not be used in children and adolescents.

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.

Patients with renal impairment

In patients with mild and moderate renal impairment, the dose is 0.5 mg per day and should be carefully monitored for adverse effects of colchicine. For severe renal impairment, see section 4.3 contraindications.

Patients with hepatic impairment

In patients with mild and moderate hepatic impairment, the dose is 0.5 mg per day and should be carefully monitored for adverse effects of colchicine. For severe hepatic impairment, see section 4.3 contraindications.

Familial Mediterranean Fever

The dose may be given as a single dose or doses higher than 1 mg/day may be divided and given twice daily.

Colchicine dosage should be increased in a stepwise fashion up to a maximum of 3 mg/day to control disease in patients who do not clinically respond to the standard dosage. Any increase of the daily dose should be monitored closely for adverse effects. Careful monitoring is needed in the presence of impaired renal or liver function. For these patients, the starting dose should be reduced by 50% (e.g. ≤ 1mg/day).

Adults

1 to 3 mg per day.

Paediatric population

For paediatric use, colchicine should only be prescribed under the supervision of a medical specialist with the necessary knowledge and experience.

A starting dose should be administered orally based on age:

- 0.5 mg/day in children less than 5 years of age
- 1 mg/day in children from 5 to 10 years of age
- 1.5 mg/day in children over 10 years of age

In children with amyloid nephropathy, higher daily doses up to 2 mg/day might be needed.

When 0.25mg doses are required, e.g. to control disease in patients who do not clinically respond to the standard dosage, the 0.5 mg and 1 mg tablet are not appropriate.

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.

Patients with renal impairment

In patients with mild and moderate renal impairment, the starting dose should be reduced by 50% (e.g. ≤ 1mg/day) and should be carefully monitored for adverse effects of colchicine. For severe renal impairment, see section 4.3 contraindications.

Patients with hepatic impairment

In patients with mild and moderate hepatic impairment the starting dose should be reduced by 50% (e.g. ≤ 1mg/day) and should be carefully monitored for adverse effects of colchicine. For severe hepatic impairment, see section 4.3 contraindications.

Method of Administration

Oral route.

Tablet should be swallowed with a glass of water.

For children younger than 1 year a colchicine oral solution can be considered.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Patients with blood dyscrasias
- 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 not to exceed the dose prescribed by a medical specialist with the necessary knowledge and experience. Colchicine has a narrow therapeutic window. The administration should be discontinued if toxic symptoms such as nausea, vomiting, abdominal pain, diarrhea occur.

If patients develop signs or symptoms that could indicate a blood cell dyscrasia, such as fever, stomatitis, sore throat, or prolonged bleeding, treatment with colchicine should be immediately discontinued and a full haematological investigation should be conducted.

Caution is advised in case of:

- Liver or renal impairment
- Cardiovascular disease
- Gastrointestinal disorders
- Elderly and debilitated patients
- Patients with abnormalities in blood counts

Colchicine may cause severe bone marrow depression (agranulocytosis, aplastic anaemia, thrombocytopenia). The change in blood counts may be gradual or very sudden. Aplastic anaemia in particular has a high mortality rate. Periodic checks of the blood count are essential. If skin abnormalities (petechiae) occur, blood counts should be checked immediately.

Macrolides, CYP3A4 inhibitors, ciclosporin, HIV protease inhibitors, calcium channel blockers, and statins may cause clinically significant interactions with colchicine which may lead to colchicine-induced 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.

Long-term use of colchicine may be associated with vitamin B12 deficiency.

In case colchicine is used for treatment of acute gout or for prophylaxis of a gout attack during initiation of urate-lowering therapy

Patients should be carefully informed about the potential risk of a possible pregnancy and about effective contraception measures to be followed. Female patients should use effective contraception during and for at least three months following termination of colchicine therapy (see section 4.6). Based on concerns about a potential damage to sperm cells (see section 5.3), male patients should not father a child during and for at least 6 months following termination of colchicine therapy (see section 4.6).

Paediatric population

No long-term safety data are available in paediatric patients. The use of colchicine in children is primarily indicated for the indication FMF.

Colchicine Ascend 500 microgram Tablets contains lactose

Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Colchicine Ascend 500 microgram Tablets contains sodium

This medicine contains less than 1 mmol sodium (23 mg) per tablet, 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 scarcely documented. Given the nature of the side effects, caution is advised with concomitant administration of drugs that can affect the blood count or have a negative effect on hepatic and/or renal function.

In addition, substances such as cimetidine and tolbutamide may reduce metabolism of colchicine and thus increase plasma levels of colchicine.

Colchicine is a substrate for both CYP3A4 and the transport protein P-gp. In the presence of CYP3A4 or P-gp inhibitors, the concentrations of colchicine in the blood may increase. Toxicity, including fatal cases, have been reported during concurrent use of inhibitors such as macrolides (clarithromycin and erythromycin), ciclosporin, 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 discontinuation, clinical follow-up, and potentially follow-up of serum levels of colchicine, is required (see section 4.4).

Grapefruit juice may increase plasma levels of colchicine. Grapefruit juice should therefore not be taken together with colchicine.

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

Reversible malabsorption of cyanocobalamine (Vitamin B12) may be induced by an altered function of the intestinal mucosa.

The risk of myopathy and rhabdomyolysis is increased by a combination of colchicine with statins, fibrates, ciclosporin or digoxin.

4.6 Fertility, pregnancy and lactation

Fertility

Animal research has shown that administration of colchicine may negatively influence spermatogenesis (see section 5.3). Rare cases of reversible oligospermia and azoospermia in men are known from literature.

In case Colchicine is used for treatment of FMF

Since the course of FMF without treatment may also lead to infertility, the use of colchicine should be weighed against the potential risks and may be considered, if clinically needed.

In case colchicine is used for treatment of acute gout or for prophylaxis of a gout attack during initiation of urate-lowering therapy

Male patients should not father a child during and for at least 6 months following termination of colchicine therapy (see section 4.4). If, nevertheless, pregnancy occurs during this time period, genetic counselling should be tasked.

Pregnancy

Animal studies denote reproductive toxicity (see section 5.3).

In case colchicine is used for treatment of FMF

A moderate amount of data on pregnant women with FMF indicate no malformative or feto/ neonatal toxicity of colchicine. Since the course of FMF without treatment may also negatively influence pregnancy, the use of colchicine during pregnancy should be weighed against the potential risks and may be considered, if clinically needed.

In case colchicine is used for treatment of acute gout or for prophylaxis of a gout attack during initiation of urate-lowering therapy

There is a limited amount of data from the use of colchicine in pregnant women with gout. As a precautionary measure, use of colchicine in this patient population and in women of childbearing potential not using effective contraception, should be avoided and may only be considered if other treatment options, including NSAIDs and glucocorticoids, are not applicable.

Female patients have to use effective contraception during and for at least three months following termination of colchicine therapy (see section 4.4). If, nevertheless, pregnancy occurs during this time period, genetic counselling should be tasked.

Breast-feeding

Colchicine/metabolites is /are found in breastfed newborns/infants of treated women. There is insufficient information on the effects of colchicine in newborns/infants. Colchicine should not be used in breast-feeding women with gout. In lactating mothers with FMF, a decision must be made whether to discontinue breast-feeding or to discontinue/abstain from Colchicine Ascend therapy taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman.

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 adverse reactions have been observed.

The frequencies are unknown, unless listed under one of the following classifications:

Very common (≥ 1/10)

Common (≥ 1/100, < 1/10)

Uncommon (≥ 1/1,000, < 1/100)

Rare (≥ 1/10,000, < 1/1,000)

Very rare (< 1/10,000)

Blood and lymphatic system disorders

Bone marrow depression with agranulocytosis and aplastic anemia.

Nervous system disorders

Peripheral neuritis, neuropathy

Gastrointestinal disorders

Common: abdominal pain, nausea, vomiting and diarrhea

Hepatobiliary disorders

Hepatotoxicity

Skin and subcutaneous tissue disorders

Alopecia, rash

Musculoskeletal and connective tissue disorders

Myopathy and rhabdomyolysis

Reproductive system and breast disorders

Amenorrhoea, dysmenorrhoea, oligospermia, azoospermia

Respiratory, thoracic en mediastinal disorders

Pharyngolaryngeal pain

Metabolism and nutrition disorders

Vitamin B12 deficiency

Paediatric population

No long-term safety data are available in paediatric patients.

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 the Yellow Card Scheme website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Colchicine has a narrow therapeutic window and is extremely toxic in overdose. Patients at particular risk of toxicity are those with renal or hepatic impairment,

gastro-intestinal or cardiac disease and patients at extremes of age. Following colchicine overdose, all patients, even in the absence of early symptoms should be referred for immediate medical assessment.

Clinical:

Symptoms of acute overdosage may be delayed (3 hours on average): nausea, vomiting, abdominal pain, hemorrhagic gastroenteritis, volume depletion, electrolyte abnormalities, leukocytosis, hypotension in severe cases. The second phase with life threatening complications develops 24 to 72 hours after drug administration: multisystem organ dysfunction, acute renal failure, confusion, coma, ascending peripheral motor and sensory neuropathy, myocardial depression, pancytopenia, dysrhythmias, 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 initial ingestion.

Treatment:

No antidote is available.

Elimination of toxins by gastric lavage within one hour of acute poisoning.

Consider oral activate charcoals in adults who have ingested more than 0.1 mg/kg bodyweight within 1 hour of presentation and in children who have ingested any amount within 1 hour of presentation.

Haemodialysis has no efficacy (high apparent distribution volume).

Close clinical and biological monitoring in hospital environment.

Symptomatic and supportive treatment: control of respiration, maintenance of blood pressure and circulation, correction of fluid and electrolytes imbalance.

The lethal dose varies strongly (7 – 65 mg in one dose), but for adults it is generally about 20 mg.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: drugs for gout, 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 completely known. Urate crystals are phagocytosed by leukocytes. Hereby inflammatory factors

are released. Colchicine inhibits these processes. Other properties of colchicine, such as interaction with microtubules, could also contribute to its action.

Onset of actions is approximately 12 hours after oral administration and is maximal after 1 to 2 days.

5.2 Pharmacokinetic properties

Absorption

Colchicine is rapidly and almost completely absorbed after oral administration. Maximum plasma concentrations are met usually after 30 to 120 minutes.

Distribution

Plasma protein binding of colchicine is approximately 30%. It accumulates in leucocytes.

Elimination

Colchicine is partially metabolized in the liver and then then in part via the bile. It is largely excreted (80%) in unchanged form and as metabolites in the faeces. 10-20% is excreted in urine. The plasma half-life is 30-60 minutes and approximately 60 hours in leukocytes.

Paediatric population

No pharmacokinetics data are available in children.

5.3 Preclinical safety data

Colchicine causes DNA damage in vitro and chromosomal aberrations were observed in vivo. No toxicity data are available from own preclinical research.

Studies in animals have shown that colchicine-induced disruption of microtubule formation has an effect on meiosis and mitosis. After colchicine exposure a reduced sperm count and sperm cells with abnormal morphology have been demonstrated in male animals. The doses used in these studies were substantially higher than the dose prescribed for use in patients. High doses of colchicine can cause teratogenicity and embryo toxicity in mice, rats and rabbits.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Starch, Pregelatinized

Lactose monohydrate

Cellulose, Microcrystalline

Sodium Starch Glycolate (Type A)

Magnesium Stearate

6.2 Incompatibilities

Not applicable

6.3 Shelf life

36 months

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

Blisters:

- 10 tablets in OPA/Alu/PVC//Alu blister, with 10, 30 & 100 tablets in a carton box
- 12 tablets in OPA/Alu/PVC//Alu blister, with 12 tablets in a carton box
- 10 tablets in OPA/Alu/PVC//Alu perforated unit dose blister, with 10, 30 & 100 tablets in a carton box
- 12 tablets in OPA/Alu/PVC//Alu perforated unit dose blister, with 12 tablets in a carton box

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements

7 MARKETING AUTHORISATION HOLDER

Ascend Laboratories (UK) Limited
Elsley Court,
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W1W 8BE
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8 MARKETING AUTHORISATION NUMBER(S)

PL 43805/0164

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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10 DATE OF REVISION OF THE TEXT

09/04/2026