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.

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Colchicine 250 micrograms/ml oral solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1ml of solution contains 250 micrograms of colchicine
Excipient with known effect:
Each 1 ml of oral solution contains 2 mg of sodium methyl parahydroxybenzoate.
For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Oral solution.

A clear, colourless solution to nearly colourless liquid, free from visible foreign particles.

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.
- Colchicine is indicated for the treatment of acute and recurrent Pericarditis, as an adjunct to aspirin/NSAID 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

500 micrograms (2 ml) two to four (2-4) times daily until symptoms are relieved.

The course of treatment should end when symptoms are relieved or when a total of 6,000 micrograms (24 ml) have been taken. No more than 6,000 micrograms (24 ml) 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 should be discontinued immediately as these may be the first signs of an intoxication.

Prophylaxis of gout attack

500 micrograms – 1,000 micrograms per day (2 – 4 ml/day) to be taken in the evening.

Paediatric population
Colchicine should not be used in children and adolescents.

Acute and Recurrent Pericarditis

Adults
The recommended dose is 500 micrograms/day (2 ml/day) for patients weighing ≤70 kg or in patients with intolerance to higher doses.
The recommended dose is 500 micrograms (2 ml) twice daily for patients with a body weight of >70 kg.

Treatment duration is 6 months in recurrent pericarditis and 3 months in acute pericarditis.

Paediatric population
Colchicine should not be used in children and adolescents.

Familial Mediterranean Fever
The dose may be given as a single dose or doses higher than 1,000 micrograms/day (4 ml/day) may be divided and given twice daily.
Colchicine dosage should be increased in a stepwise fashion up to a maximum of 3,000 micrograms/day (12 ml/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. ≤ 1,000 micrograms/day, 4 ml).

Adults
1,000 to 3,000 micrograms per day (4 to 12 ml 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:
- 500 micrograms/day (2 ml/day) in children less than 5 years of age
- 1,000 micrograms/day (4 ml/day) in children from 5 to 10 years of age
- 1,500 micrograms/day (6 ml/day) in children over 10 years of age

In children with amyloid nephropathy, higher daily doses up to 2,000 micrograms/day (8 ml/day) might be needed.
Colchicine dosage should be increased in a stepwise fashion (e.g. 250 micrograms/step) up to a maximum of 2,000 micrograms/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.

Concomitant treatment with other medicinal products
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 500 micrograms (2 mL oral solution) per day in gout, acute and recurrent pericarditis and the starting dose should be reduced by 50% (e.g. ≤ 1,000 micrograms/day) in Familial Mediterranean Fever.
The dose should be carefully monitored for adverse effects of colchicine.
Patients with any degree of renal impairment should not be given colchicine in conjunction with strong P-glycoprotein inhibitors or strong CYP3A4 inhibitors (see section 4.4).
For severe renal impairment, see section 4.3 contraindications.

Patients with hepatic impairment
In patients with mild and moderate hepatic impairment, the dose is 500 micrograms (2 mL oral solution) per day in gout, acute and recurrent pericarditis and the starting dose should be reduced by 50% (e.g. ≤ 1,000 micrograms/day) in Familial Mediterranean Fever.
The dose should be carefully monitored for adverse effects of colchicine.

Patients with any degree of hepatic impairment should not be given colchicine in conjunction with strong P-glycoprotein inhibitors or strong CYP3A4 inhibitors (see section 4.4).
For severe hepatic impairment, see section 4.3 contraindications.

Table 1 – Colchicine dosage instructions

Indication	**Patient Group**	**Dose (µg)**	**Frequency**	**Special Notes**
Acute Gout Attack	Adults	500 micrograms (2 mL)	2–4 times daily	Maximum dose: 6,000 micrograms (24 mL) per course. Stop when symptoms resolve or max dose reached. Wait ≥72 hrs before the next course. Discontinue if diarrhoea or vomiting occurs.
	Renal impairment	500 micrograms (2 mL)	Once daily	Avoid with strong CYP3A4/P-gp inhibitors
	Hepatic impairment	500 micrograms (2 mL)	Once daily	Avoid with strong CYP3A4/P-gp inhibitors
	Children	Not suitable for paediatric use		
Prophylaxis of gout attack	Adults	500–1,000 micrograms (2–4 mL)	Once daily (evening)	—
	Renal impairment	500 micrograms (2 mL)	Once daily	Avoid with strong CYP3A4/P-gp inhibitors
	Hepatic impairment	500 micrograms (2 mL)	Once daily	Avoid with strong CYP3A4/P-gp inhibitors
	Children	Not suitable for paediatric use		
Acute Pericarditis	Adults ≤70 kg or intolerant to high doses	500 micrograms (2 mL)	Once daily	Duration: 3 months
	Adults >70 kg	500 micrograms (2 mL)	Twice daily	Duration: 3 months
	Renal impairment	500 micrograms (2 mL)	Once daily	Avoid with strong CYP3A4/P-gp inhibitors
	Hepatic impairment	500 micrograms (2 mL)	Once daily	Avoid with strong CYP3A4/P-gp inhibitors
	Children	Not suitable for paediatric use		
Recurrent Pericarditis	Adults ≤70 kg or intolerant to high doses	500 micrograms (2 mL)	Once daily	Duration: 6 months
	Adults >70 kg	500 micrograms (2 mL)	Twice daily	Duration: 6 months
	Renal	500	Once daily	Avoid with strong CYP3A4/P-gp

	impairment	micrograms (2 mL)		inhibitors
	Hepatic impairment	500 micrograms (2 mL)	Once daily	Avoid with strong CYP3A4/P-gp inhibitors
	Children	Not suitable for paediatric use		
Familial Mediterranean Fever (FMF)	Adults	1,000–3,000 micrograms (4–12 mL)	Once daily or doses higher than 1,000 µg can be divided twice daily	Maximum dose: 3,000 micrograms /day (12 ml/day). Increase dose in stepwise fashion (e.g. 250 micrograms steps). Monitor for adverse effects.
	Renal Impairment	Reduce FMF starting dose by 50% (e.g. ≤ 1,000 micrograms /day)	Once daily	Avoid with strong CYP3A4/P-gp inhibitors.
	Hepatic Impairment	Reduce FMF starting dose by 50% (e.g. ≤ 1,000 micrograms /day).	Once daily	Avoid with strong CYP3A4/P-gp inhibitors.
	Children <5 yrs	Starting does: 500 micrograms (2 mL)	Once daily	Specialist supervision required Maximum dose: Up to (8 mL). In children with amyloid nephropathy, higher daily doses up to 2,000 micrograms /day (8 ml/day) might be needed. Increase in stepwise fashion (e.g. 250 micrograms steps).
	Children 5–10 yrs	Starting dose: 1,000 micrograms (4 mL)	Once daily	
	Children >10 yrs	Starting dose: 1,500 micrograms (6 mL)	Once daily	

Method of Administration

Colchicine is for oral use only. The oral solution should be considered especially for children younger than 1 year.

A 5 ml graduated oral syringe with intermediate graduations of 0.1 ml and a “Press-In” Bottle Adapter (PIBA) are provided with the product.

1. Open the bottle and at first use, insert the “Press-In” Bottle Adapter (PIBA).

2. Insert the syringe into the PIBA and draw out the required volume from the inverted bottle.

3. Remove the filled syringe from the bottle in the upright position

4. Discharge the syringe contents into the mouth.

5. Rinse the syringe and replace the cap on the bottle (PIBA remains in place).

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, diarrhoea occur.

Colchicine in patients with pre-existing blood dyscrasias, gastrointestinal disease, elevated aminotransferase, creatinine or troponin levels, severe liver disease, myopathy, bacterial or neoplastic pericarditis should not be used due to the risk of developing neuromuscular toxicity is increased.

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
- Pregnant or lactating women

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.

P-gp inhibitors and/or strong CYP3A4 inhibitors

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.

P-gp inhibitors and/or strong CYP3A4 inhibitors and renal/hepatic function

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 are 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. Safety and effectiveness in paediatric patients have not been established in indications acute gout, prophylaxis of a gout attack and acute/recurrent pericarditis.

Other warnings

Clinical trial data showed a trend for an increased risk of non-cardiovascular death in patients treated with colchicine. There is no clear association between colchicine therapy and non-cardiovascular death, nevertheless caution should be exercised in colchicine-treated patients with chronic coronary disease and with comorbidities that may underlie potential causes of mortality. The potential benefits and risks should always be weighed, and the patients should be carefully monitored for any signs or symptoms of toxicity.

This medicine contains sodium methyl parahydroxybenzoate.

This medicine contains Sodium methyl parahydroxybenzoate as an excipient. May cause allergic reactions (possibly delayed).

This medicine Solution contains sodium

This medicine contains less than 1 mmol sodium (23 mg) per 1ml of solution, 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 ketoconazole) 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 cyanocobalamin (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 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

Adverse reactions are listed below by system organ class and in decreasing frequency. Frequencies are defined as:

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)

Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug.

Table 2 - Frequency of adverse reactions

Frequency System Organ Class	**Very common**	**Common**	**Uncommon**	**Rare**	**Very rare**	**Not known**
Blood and lymphatic system disorders						Bone marrow depression with agranulocytosis, aplastic anaemia, pancytopenia, neutropenia, thrombocytopenia, leukopenia
Nervous system disorders						Peripheral neuritis, neuropathy.
Gastrointestinal disorders		Abdominal pain, nausea, vomiting and diarrhoea				
Hepatobiliary disorders						Hepatotoxicity, transaminases increased
Renal and urinary disorders						Renal impairment
Skin and subcutaneous tissue disorders				Urticaria, maculopapular rash, erythema, edema		Alopecia, rash
Musculoskeletal and connective tissue disorders						Myopathy, rhabdomyolysis, muscle weakness
Reproductive system and breast disorders				Amenorrhoea, dysmenorrhoea, oligospermia, azoospermia		

Respiratory, thoracic and 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 Yellow Card Scheme at: 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.

Pharmacodynamic effects

Colchicine has found to exert a selective effect in suppressing MSU (monosodium urate) crystal-induced superoxide anion production in human neutrophils in vitro. Moreover, colchicine inhibits deformability and motility of human neutrophils in confined spaces, which is crucial for neutrophil extravasation during inflammation.

The correlation of the inhibition of microtubule polymerization with the effects on these aforementioned pathways support colchicine's inhibition of microtubule polymerization and its effects on downstream pathways as a primary target in the mechanism of action of this molecule in the treatment of gout.

The pharmacodynamics of colchicine in the prevention of cardiovascular events have not been clearly elucidated. Previous mechanistic and preclinical studies revealed anti-inflammatory and immunomodulatory effects of colchicine exerted through its principal mechanism of microtubule polymerization inhibition, however, other pleiotropic effects beneficial to the cardiovascular system were observed such as inhibition of platelet aggregation and suppression of endothelial proliferation.

Clinical efficacy and safety

Acute and recurrent pericarditis
A prospective, randomized, open-label design trial [COPE] was performed to verify the safety and efficacy of colchicine as an adjunct to conventional therapy for the treatment of the first episode of acute pericarditis. A total of 120 patients with a first episode of acute pericarditis were randomly assigned to conventional treatment with

aspirin or conventional treatment plus colchicine 1.0 to 2.0 mg for the first day and then 0.5 to 1.0 mg/d for 3 months. Colchicine plus conventional therapy significantly reduced the recurrence rate (recurrence rates at 18 months were, respectively, 10.7 % vs 32.3 %; P=0.004) and symptom persistence at 72 h (respectively, 11.7 % vs 36.7 %; P=0.003).

Another prospective, randomized, open-label, parallel-group trial [CORE] was also used to investigate the safety and efficacy of colchicine therapy as adjunct to conventional therapy for the first episode of recurrent pericarditis. Eighty-four consecutive patients with a first episode of recurrent pericarditis were randomly assigned to receive conventional treatment with aspirin alone or conventional treatment plus colchicine (1.0-2.0 mg the first day and then 0.5-1.0 mg/d for 6 months). During a 20-months mean follow-up treatment with colchicine significantly decreased the recurrence rate (actuarial rates at 18 months were 24.0 % vs 50.6 %; P=0.02) and symptom persistence at 72 h (10 % vs 31 %; P=0.03)

In a third prospective, randomized, double-blind, placebo-controlled multicentre trial [CORP] the efficacy and safety of colchicine for the secondary prevention of recurrent pericarditis was also evaluated. In addition to conventional treatment, 120 patients with a first recurrence of pericarditis were randomly assigned to receive either placebo or colchicine, 1.0 to 2.0 mg on the first day followed by a maintenance dose of 0.5 to 1.0 mg/d, for 6 months. At the 18-month follow-up the recurrence rate was 24 % in the colchicine and 55 % in the placebo group (absolute risk reduction, 0.31; relative risk reduction, 0.56). Colchicine reduced the persistence of symptoms at 72 h (absolute risk reduction, 0.30; relative risk reduction, 0.56) and mean number of recurrences, increased the remission rate at 1 week, and prolonged the time-to subsequent recurrence.

A multicentre, double-blind, placebo-controlled randomised trial has been also performed in 240 adult patients with a first episode of acute pericarditis in order to assess the use of colchicine during a first attack of acute pericarditis and in the prevention of recurrent symptoms. In this study patients received conventional therapy with or without colchicine (0.5-1 mg/day for 3 months, 0.5 mg twice daily for patients weighing >70 kg or 0.5 mg once daily for patients weighing ≤ 70 kg). The primary study outcome of incessant or recurrent pericarditis occurred in 20 patients (16.7 %) in the colchicine and 45 patients (37.5 %) in the placebo group (relative risk reduction in the colchicine group: 0.56). Colchicine reduced the rate of symptom persistence at 72 h (19.2 % vs 40.0 %, P=0.001), the number of recurrences per patient (0.21 vs 0.52, P=0.001) and the hospitalization rate (5.0 % vs 14.2 %, P=0.02). Colchicine also improved the remission rate at 1 week (85.0 % vs 58.3 %, P<0.001).

In a subsequent multicentre, double-blind, placebo-controlled randomised trial [CORP-2] evaluating the efficacy and safety of colchicine (0.5 mg twice daily for patients weighing >70 kg or 0.5 mg once daily for patients weighing ≤ 70 kg for 6 months in addition to conventional therapy) for the treatment of multiple recurrences of pericarditis in 240 adults, the proportion of patients who had recurrent pericarditis was 26 (21.6%) of 120 in the colchicine and 51 (42.5 %) of 120 in the placebo group (relative risk: 0.49; P=0.0009).

Paediatric population

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

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

About 40% of colchicine is bound to albumin. 30% of available colchicine is distributed to the GI tract, muscles, heart, spleen and white blood cells. Colchicine accumulates in leucocytes.

Elimination

Colchicine is partially metabolized in the liver and 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.

Colchicine and/or its metabolites are found in breastfed newborns/infants of colchicine-treated women.

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

Sodium methyl parahydroxybenzoate (E 219)

Citric acid

Sodium citrate

Sucralose

Glycerol (E422)

Orange flavour [flavouring preparation, natural flavouring substance, 1,2-Propylene glycol (E 1520), alpha-Tocopherol (E 307)]

Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

After first opening: 75 days

6.4 Special precautions for storage

Store in the original packaging to protect from light.

6.5 Nature and contents of container

75 ml type III amber glass bottles with a white high-density polyethylene (HDPE) child-proof and tamper evident cap.

The product is supplied with a low-density polyethylene (LDPE) plastic plug that is able to fit on the bottles and a LDPE 5 ml oral syringe.
The oral syringe is graduated in 0.1 ml steps up to 5 ml.
Not all pack sizes may be marketed

6.6 Special precautions for disposal

No special requirements for disposal.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Aspire Pharma Limited
4 Rotherbrook Court
Bedford Road
Petersfield
Hampshire
GU32 3QG
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 35533/0239

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10/03/2026

10 DATE OF REVISION OF THE TEXT

10/03/2026