VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

Indication Gout

Gout is caused by a build-up of uric acid in the blood. Uric acid is a waste product made in the body every day and excreted mainly via the kidneys. It forms when the body breaks down chemicals in the cells known as purines. If you produce too much uric acid or excrete too little when you urinate, the uric acid builds up and may cause tiny crystals to form in and around joints. These hard, needle-shaped crystals build up slowly over several years. You will not know this is happening.

Gout affects 1-2% of adults in Western countries. Most of the adults are elderly men. The majority of the patients recover from acute gout within 7 days. However, treatment is necessary due to the severe pain that is experienced by the patients.

Indication Familial Mediterranean Fever (FMF)

Familial Mediterranean fever is an inherited inflammatory disorder that causes recurrent fevers and painful inflammation of your abdomen, lungs and joints. It affects approximately 100,000 people worldwide and is almost always restricted to non-Ashkenazi Jews and people of Arabic, Turkish or Armenian descent . In these populations, the disease occurs in 1 in 200 to 1,000 people. The disease is quite rare in other populations.

Familial Mediterranean fever is typically diagnosed during childhood. Typical symptoms are episodes of fever accompanied by chest pain, achy, swollen joints, constipation followed by diarrhea. The episodes can last around 1 – 3 days.

Some complications that are known when the disease stays untreated are: 1. Kidney damage. Amyloidosis (condition wherein normally soluble proteins become insoluble and are deposited in the kidney, disrupting normal function) can damage the kidneys, causing nephrotic syndrome. People with this

condition may lose large amounts of protein in their urine. Nephrotic syndrome can lead to blood clots in your kidneys (renal vein thrombosis) or kidney failure. 2. Infertility in women due to inflammation. 3. Joint pain. The most commonly affected joints are the knees, ankles and hips.

VI.2.2 Summary of treatment benefits

- Indication gout

  Most of the evidence for the efficacy of colchicine and the treatment of acute gout or prevention of gout flares comes from literature.
  For acute gout colchicine dosing (low- and high-dose, 74 and 52 patients, respectively) was shown to be more effective than placebo for the treatment of acute gout. There were 28 responders in the low-dose group (37.8%, 17 responders (32.7%) in the high-dose group and 9 responders (15.5%) in the placebo group. In another study pain improvement was scored, showing major improvement in patients treated with colchicine within 48 hours after treatment with respect to the clinical and pain score. This was 64% and 73%, respectively for the colchicine group (n=22) compared to 23% and 36% for the placebo group (n=21).
  For prevention of gout effectiveness was studied looking at the number of gout flares per month. Patients in the colchicine / probenecid group (n=20) had a significant lower rate of gout flares per month compared to the placebo group (n=18; 0.19 vs 0.48; $p<0.05$). Another study showed fewer total flares for the colchicine (n=22) treated group compared to placebo (n=22; 0.52 vs 2.91; $p=0.008$).
- Indication FMF
  Colchicine is the standard care for patients with FMF and most of the evidence comes from its use in clinical practice.
  The efficacy of colchicine for the treatment of FMF is measured by studying the frequency of acute attacks. A double-blind trial showed that during 60 courses of placebo or colchicine the occurrence of attacks was enormously decreased in the colchicine group (38 attacks in the placebo group compared to 7 attacks in the colchicine treated group; $p<0.001$). A double-blind cross over study confirmed this as the patients receiving colchicine (n=10) experienced significantly fewer attacks than the placebo group (n=10; 1.15 compared to 5.25 per patient; $p<0.001$).

VI.2.3 Unknowns relating to treatment benefits

Indication gout

Clinical effectiveness was investigated in patients with diagnosis of gout. All studies were performed in adults. The mean age of the patients in all studies was above 50 years. The majority of the patients were male. Gout in children is very rare. No studies were performed in children. There is no evidence to suggest that results would be any different for female patients or patients younger than 50 years.

Indication FMF
Clinical effectiveness was investigated in patients of various ethnicities commonly affected by FMF. The majority of the patients were male. No randomized controlled studies were performed in children and adolescents. There is no evidence to suggest that results would be any different for female patients or for children and adolescents.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Decrease in cells responsible for providing immunity, carrying oxygen, and those responsible for normal blood clotting (Bone marrow depression with agranulocytosis and aplastic anaemia)	This risk was identified during use in clinical practice. After an acute overdose it can occur within 24-48 hours.	Yes, by monitoring for early symptoms.
A muscular disease in which the muscle fibres do not function for any one of many reasons, resulting in muscular weakness / breakdown of muscle fibres (Myopathy, Rhabdomyolysis)	This risk was identified during use in clinical practice. Prognosis depends on the recognition of the syndrome and development of additional complications like renal failure. The effects are reversible within weeks to months after discontinuation of colchicine.	Treatment with colchicine for a longer period and concomitant use with statins should be monitored.

Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)

Risk	What is known (Including reason why it is considered a potential risk)
Potential for medication errors	Administration of the incorrect tablet(s) if a patient receives two different strengths or the wrong strength. This can lead to an error in the administered dose.
Potential for harm of overdose	Incorrect dosing of renal and/or hepatic impaired patients can lead to a potential overdose.

Missing information

Risk	What is known
Use in pregnancy	Limited data are available in the published scientific literature. Up till now the published data do not give rise to concern.
Use in lactation	Limited data are available in the published scientific literature. Up till now the published data do not give rise to concern.
Use in men with child wish	Limited data are available in the published scientific literature. Up till now the published data do not give rise to concern.

VI.2.5 Summary of risk minimisation measures by safety concern

This medicine has no additional risk minimisation measures.

VI.2.6 Planned post authorisation development plan

There is no planned post authorisation development plan for colchicine.