

VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

Folic acid deficiency

Folic acid deficiency may lead to anemia a deficiency of red blood cells. If you do not have enough red blood cells or if they are not functioning, you get symptoms of mild hypoxia and become tired and lethargic. Anemia is caused by reduced production of red blood cells, or an increased loss of red blood cells.

The red blood cells are made in the bone marrow and have a life of about four months. In order to produce new blood cells iron, vitamin B12 and folic acid must be available otherwise the production of red blood cells will be affected resulting in anemia.

Lack of folic acid may have different causes.

Lack of folic acid in the diet is especially seen in patient groups that do not eat much food or eat food low in nutrients

Lack of folic acid can be seen in patients on chronic dialysis, where folic acid is dialyzed away and in patients with reduced uptake by the small intestinal such as in patients with gluten intolerance.

Increased need of folic acid can be relevant in conditions with large production of red blood cells because of hereditary anemia, before and during pregnancy and growth sprints in childhood.

Reduction of side effects and prevention of folate deficiency during low-dose methotrexate therapy

Low dose methotrexate use is limited by side effects in certain patients resulting in interruptions or discontinuation of therapy.

The major limiting factor for methotrexate use is its toxicity. 30-90% of patients develop side effects including nausea, loss of appetite, stomatitis, diarrhea gastrointestinal intolerance, gastroduodenal atrophy, headache, fatigue, rash, malaise, alopecia, hematologic abnormalities (anaemia, cytopenias, macrocytosis), hepatotoxicity, flu-like syndrome, tremors, visual loss/toxic optic neuropathy, and pulmonary toxicity.

Liver toxicity may be the most common limitation of treatment in psoriasis patients, and although the exact mechanism is unclear, MTX-induced hepatotoxicity is believed to be caused by methotrexate accumulation in hepatocytes. The side effects mentioned above are related to folate deficiency.

VI.2.2 Summary of treatment benefits

Treatment with folic acid improves the availability of folic acid and reduces the symptoms of anemia caused by folic acid deficiency.

VI.2.3 Unknowns relating to treatment benefits

None

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Allergic reactions (hypersensitivity)	Folic acid may cause allergic reactions in susceptible individuals	Doctors and patients should be aware of this and the product should not be prescribed to patients with known allergies to folic acid or any of the excipients in the product.
Vitamin B12 deficiency	Vitamin B12 deficiency can be masked during long-term treatment with folic acid. Untreated Vitamin B12 deficiency can cause damage in the body.	It is important to monitor if symptoms of anemia are due to lack of folic acid or vitamin B12.
Concomitant use of chloramphenicol	Use of folic acid and chloramphenicol concomitantly may delay the response to folic acid.	It is important to monitor the patient's response to folic acid if chloramphenicol is used concomitantly.

VI.2.5 Summary of risk minimisation measures by safety concern

All medicines have a Summary of Product Characteristics (SmPC) which provides physicians, pharmacists and other health care professionals with details on how to use the medicine, the risks and recommendations for minimising them. An abbreviated version of this in lay language is provided in the form of the package leaflet (PL). The measures in these documents are known as routine risk minimisation measures.

The Summary of Product Characteristics and the Package leaflet for Folsyre Orifarm can be found on the homepage of the Danish Medicines Agency.

This medicine has no additional risk minimisation measures.

VI.2.6 Planned post authorisation development plan

None.

VI.2.7 Summary of changes to the Risk Management Plan over time

Not applicable as this is the initial risk management plan.