VI.2 Elements for a public summary

VI.2.1 Overview of disease epidemiology

Purimmun 50 mg tablets is indicated for the treatment of acute leukemia, particularly in children. It is also indicated for the treatment of chronic myeloid leukemia, in early and late stages.

ALL is the most common cancer diagnosed in children and represents approximately 25% of cancer diagnoses among children younger than 15 years. ALL occurs at an annual rate of 35 to 40 cases per 1 million people in the United States. There are approximately 2,900 children and adolescents younger than 20 years diagnosed with ALL each year in the United States. Over the past 25 years, there has been a gradual increase in the incidence of ALL.

A sharp peak in ALL incidence is observed among children aged 2 to 3 years (>90 cases per 1 million per year), with rates decreasing to fewer than 30 cases per 1 million by age 8 years. The incidence of ALL among children aged 2 to 3 years is approximately fourfold greater than that for infants and is likewise fourfold to fivefold greater than that for children aged 10 years and older.

The incidence of ALL appears to be highest in Hispanic children (43 cases per 1 million). The incidence is substantially higher in white children than in black children, with a nearly threefold higher incidence of ALL from age 2 to 3 years in white children than in black children. (DPQ)

VI.2.2 Summary of treatment benefits

This medicine contains the active ingredient 6-mercaptopurine. 6-mercaptopurine is an inactive pro-drug that acts as purine antagonist after cellular uptake and intracellular conversion into thioguanine-nucleotides for cytotoxicity.

6-mercaptopurine metabolites suppress the de novo synthesis of purine and purine-nucleotide formation. The thioguanine nucleotides are also incorporated into nucleic acids and this leads to the cytotoxic effect of the drug.

The cytotoxic effect of 6-mercaptopurine may be related to the levels of thioguanine nucleotides in red blood cells, but not to the plasma concentration of 6-mercaptopurine.

The efficacy of 6-mercaptopurine (6-MP) for the treatment of acute leukemia and chronic myeloid leukemias been established over many decades of clinical use and through a high number of clinical trials.des

The efficacy of 6-MP for the maintenance treatment of acute leukemia especially in children and of chronic myeloid leukemia in early and late stages is well established through more than 50 years of clinical use. Mercaptopurine serves as a critical agent in the post-induction and maintenance phases of ALL therapy. Adherence to prescribed dose intensity of mercaptopurine is positively associated with higher event-free survival in patients with acute leukemia and chronic myeloid leukemia.

VI.2.3 Unknowns relating to treatment benefits

There are no adequate data from the effects of 6-mercaptopurine on the ability to drive vehicles and use machines and such effects could not be attributed to the pharmacological properties of Mercaptopurine 50 mg tablets.

VI.2.4 Summary of safety concern

Important identified risks

Table 8. Important identified risks

Risk	What is known	Preventability
Carcinogenicity	Patients receiving immunosuppressive therapy, including mercaptopurine are at an increased risk of developing lymphoproliferative disorders and other malignancies, notably skin cancers (melanoma and nonmelanoma), sarcomas (Kaposi's and non-Kaposi's) and uterine cervical cancer in situ. The increased risk appears to be related to the degree and duration of immunosuppression.	Discontinuation of immunosuppression may provide partial regression of the lymphoproliferative disorder. Treatment with 6-mercaptopurine must be under the supervision of a physician or other healthcare professional experienced.

Important potential risks

Table 9. Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
Use in pregnancy and breast-feeding	If you are pregnant or breastfeeding, you think you may be pregnant, or plan to have children, consult a physician or pharmacist before taking this medication. Miscarriage and premature deliveries have been observed in pregnant women receiving treatment. Also, multiple malformations and congenital malformations have been observerd after the father or mother was treated with 6-mercaptopurine.
Use in patients with inflammatory bowel disease	Hepatosplenic T-cell lymphomas were reported in patients with inflammatory bowel disease (IBD), when 6-mercaptopurine was administered in combination with anti-TNF drugs. Also, secondary leukemia and myeldysplasia have been reported.

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 this documents as well as the prescription-only status are known as routine risk minimization measures which are considered sufficient for this medicinal product.

No additional risk minimization measures are proposed.

VI.2.6 Planned post authorisation development plan

Not applicable

VI.2.7 Summary of changes to risk management plan over time

Not applicable, first RMP or summary of changes