Safety Alert **April 2025**

Azathioprine –Risks of Non-cirrhotic portal hypertension, porto-sinusoidal vascular disease and hepatic Damage

EDA performs label update to include the following:

Special warnings and precautions for use

Monitoring
Cases of non-cirrhotic portal hypertension/porto-sinusoidal vascular disease have been reported. Early clinical signs include liver enzyme abnormalities, mild jaundice, thrombocytopenia, and splenomegaly. The patient should be informed about the symptoms of liver injury and advised to contact their doctor immediately if these occur

Undesirable effects

Hepatobiliary disorders :

- Frequency "Not known": Non-cirrhotic portal hypertension, porto-sinusoidal vascular disease
- Rare, but life-threatening hepatic damage associated with chronic administration of azathioprine has been described primarily in transplant patients. Histological findings include sinusoidal dilatation, peliosis hepatis, veno-occlusive disease and nodular regenerative hyperplasia. In some cases, withdrawal of azathioprine has resulted in either temporary or permanent improvement in liver histology and the symptoms.

Background:

Theraputic Indication

Azathioprone is indicated as immunosuppressant antimetabolite either alone or, more commonly, in combination with other agents (usually corticosteroids).

Background on safety concern:

- Non-cirrhotic portal hypertension (NCPH) is a rare disease characterized by portal hypertension, splenomegaly, hypersplenism, and pancytopenia.
- Porto-sinusoidal vascular disease is defined as vascular liver disease characterized by the absence of cirrhosis on liver biopsy and the presence of histological lesions suggestive of this disease (such as obliterative portal venopathy, nodular regenerative hyperplasia, incomplete septal fibrosis)

References:

EMA (Click here)