

VI.2 Elements for a public summary

VI.2.1 Overview of disease epidemiology

Essential thrombocythaemia also known as ET, is a rare chronic blood disorder characterised by the overproduction of blood platelets. Platelets are the smallest of the three types of blood cells and are needed for successful blood clotting after an injury.

The most common symptoms are bleeding, blood clots, headache, nausea, vomiting, abdominal pain, visual disturbances, dizziness, fainting, and numbness in the extremities (Fu R, et al, 2013).

The incidence of ET is 0.6-2.5/100,000 per year, the median age at onset is 65–70 years and it is more frequent in females than in males. The incidence in children is 0.09/100,000 per year, and typically is an inherited genetic disorder (Fabris F, et al, 2009).

Patients with essential thrombocytosis have a 10-year survival rate of 64-80%, which may not be significantly different from that of the age-matched general population. Death occurs from thrombotic complications (formation of a blood clot inside a blood vessel, obstructing the flow of blood through the circulatory system) (Mesa RA et al, 1999).

VI.2.2 Summary of treatment benefits

Based on the available data from clinical studies and clinical experience of several years, anagrelide represents an effective drug in the treatment of essential thrombocythaemia.

If administered as indicated in the Summary of Product Characteristics and taking into account the contraindications, the warnings and precautions, anagrelide can be considered effective in the approved indications.

VI.2.3 Unknowns relating to treatment benefits

According to the SmPC, there is limited information regarding anagrelide use in pregnancy, breast-feeding and children. However, based on current knowledge, there is no indication to suggest that treatment results would be different in any subgroup of the target population.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Incidents that may cause damage to the heart muscle in young patients (aged 50 years and under) (Cardiac events in young patients (aged 50 years and under))	Heart problems can manifest as heart failure (which signs include shortness of breath, chest pain, swelling of the legs due to fluid build-up). Cardiovascular disease generally refers to conditions that involve narrowed or blocked blood vessels that can lead to a heart attack, chest pain (angina) or stroke. Severe chest pain	Patients should talk to their doctor before taking anagrelide: - if they have or think they might have a problem with their heart; If patient notices any of these side effects, doctor should be contacted immediately.

Risk	What is known	Preventability
	(angina pectoris), heart muscle disease (signs include fatigue, chest pain and palpitations), enlarged heart, accumulation of fluid around the heart may affect up to 1 in 1,000 people treated with anagrelide.	
Heart rhythm disorder that can cause serious irregular heart rhythms (Cardiac events related to Corrected QT Interval (QTc) prolongation and Torsade de Pointes (TdP))	Rapid heart beat, irregular or strong heartbeat (palpitations) may affect up to 1 in 10 people treated with anagrelide. Potentially life-threatening, irregular heart beat (torsade de pointes) has been reported but it is not known exactly how often it occurs.	Patients should talk to their doctor before taking anagrelide: - if they were born with or have family history of prolonged QT interval (seen on ECG, electrical, recording of the heart), or they are taking other medicines that result in abnormal ECG changes or if they have low levels of electrolytes e.g. potassium, magnesium or calcium.

Important potential risks

Risk	What is known
Non-cancerous and cancerous tumours including bone marrow disorder that disrupts the body's normal production of blood cells (with cells acquiring the properties of cancer or cancer that does not begin in the blood or bone marrow) (Benign or malignant neoplasms (including MF) o Malignant transformation o Non-hematologic malignancies)	Myelofibrosis is an uncommon type of chronic leukemia — a cancer that affects the blood-forming tissues in the body. Myelofibrosis belongs to a group of diseases called myeloproliferative disorders. Many people with myelofibrosis get progressively worse, and some may eventually develop a more serious form of leukemia. Essential thrombocythaemia is a condition which occurs when the bone marrow produces too many of the blood cells known as platelets and it may lead to leukaemia and myelofibrosis, especially in children.
(Lack of efficacy/Thrombo-hemorrhagic events o Thrombotic events o Haemorrhagic events)	Reduction in blood platelets, which increases the risk of bleeding or bruising (thrombocytopenia) may affect up to 1 in 100 patients. In combination with acetylsalicylic acid (a substance present in many medicines used to relieve pain and lower fever, as well as to prevent blood clotting, also known as aspirin), there is an increased risk of major haemorrhages (bleeding)
Pulmonary disorders that affect the absorption of oxygen into the lungs (Interstitial Lung Disease (ILD))	Interstitial lung disease describes a large group of disorders characterized by progressive scarring of the lung tissue supporting the air sacs. The scarring associated with interstitial lung disease may cause progressive lung stiffness, eventually affecting your ability to breathe and get enough oxygen into the

	bloodstream. The following side effects have been reported but it is not known exactly how often they occur: lung inflammation (signs include fever, coughing, difficulty breathing, wheezing; which causes scarring of the lungs) (allergic alveolitis, including interstitial lung disease, pneumonitis)
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Missing information

Risk	What is known
Use in women who are pregnant (Exposure during pregnancy)	Patients should tell their doctor if they are pregnant or are planning to become pregnant. Anagrelide should not be taken by pregnant women. Women who are at risk of becoming pregnant should make sure that they are using effective contraception when taking anagrelide.

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 Patient Information Leaflet (PIL). The measures in these documents are known as routine risk minimisation measures.

VI.2.6 Planned post-authorisation development plan

Not applicable.

Studies which are a condition of the marketing authorisation (if applicable)

Not applicable.

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

Not applicable for pre-approval versions.