Nicorandil "DOUBLE-E PHARMA" tablets

VI.2 Elements for a public summary

VI.2.1 Overview of disease epidemiology

From a review and analysis of data from 31 countries, it is estimated that 4.6 million women and 3.3 million men have angina pectoris. The higher number in women was found across countries. It was noted that women had a higher rate of mortality from myocardial infarction (heart attack) as did non-white ethnic groups.[*] Conversely, in one country, the UK, the rate of cases was 80% higher in men than women. It was also associated with an increase in age, with the highest frequency being in the 65-74 age group for both men and women.

A recent study looked at first-time myocardial infarction patients in Denmark from 2004 to 2012.[†] Among all myocardial infarction patients, 18.4% had prior angina. It was found that there was a lower rate of mortality (death) in patients experiencing preinfarction angina (angina before the heart attack), in particular when the angina occurred within 14 days before the heart attack.

VI.2.2 Summary of treatment benefits

Nicorandil may be used to prevent and treat long-term chest pain (angina pectoris). Nicorandil works by increasing the blood flow and oxygen supply through the blood vessels of the heart.

The effectiveness of nicorandil has been demonstrated in the Impact of Nicorandil in Angina (IONA) study.[3] This clinical trial (randomised, double-blind, placebo controlled) was performed in 5,126 high risk patients who received nicorandil at a dose of 20 mg twice daily. The patients were followed up for an average of 19 months. The results showed a reduction of coronary heart disease complications in patients treated with nicorandil compared with those who received placebo.

VI.2.3 Unknowns relating to treatment benefits

Nicorandil is not recommended for use in children and adolescents under the age of 18 years because it has not been studied in this age group.

There is no information on use of nicroandil during pregnancy or lactation.

[*] Hemingway H, Langenberg C, Damant J et al. Prevalence of angina in women versus men: a systematic review and meta-analysis of international variations across 31 countries. Circulation 2008;117(12):1526-36.

[†] Schmidt M, Horvath-Puho E, Pedersen L et al. Time-dependent effect of preinfarction angina pectoris and intermittent claudication on mortality following myocardial infarction: A Danish nationwide cohort study. **Int J Cardiol** 2015 May 6;187:462-9.

[3] Public Assessment Report**.** Decentralised Procedure. Nicorandil 10 mg and 20 mg Tablets. Procedure Nos: UK/H/3858/001-2/DC. UK Licence. Accessed on 24-May-2013. Available at http://www.mhra.gov.uk/home/groups/par/documents/websiteresources/con126155.pdf

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Ulcers at different locations of the body, such as in the mouth, stomach, gut, genitals, skin, or eyes. (Ulceration at different locations of the body (including gastrointestinal, skin, genital, mucosal, conjunctival and corneal ulcerations) and related events (including perforations, fistula, abscess and gastrointestinal haemorrhage))	Rare cases of ulcers in mouth, stomach, gut, on skin or in the eyes have been reported. These ulcers usually respond only to stopping of the nicorandil treatment. This condition may be serious since it may result in localised inflammation or even perforation (a hole in) of the affected organ. Patients taking NSAIDs (anti-inflammatory medications, including aspirin) have an increased risk of severe complications such as gut ulcers.	Stopping nicorandil will stop worsening of the symptoms and lead to recovery.
High blood potassium level (Hyperkalaemia)	Severe high blood potassium levels have been very rarely reported with nicorandil. Nicorandil should be used with care in combination with other products that may increase potassium levels, especially in patients with moderate to severe renal (kidney) damage.	This risk can be minimised by patients with kidney damage (moderate to severe) avoiding use of nicorandil and particularly by patients minimising use of nicorandil with other medicines that increase potassium levels.
Low blood pressure, in particular when taking medicine for erectile dysfunction (Hypotension [particularly with concomitant use of phosphodiesterase type 5 inhibitors])	Nicorandil and products used to treat erectile disorder should not be used together, as this may seriously affect blood pressure.	This risk can be minimised by patients avoiding the use of nicorandil with some erectile disorder products.
Desiccant taken accidentally instead of nicorandil (medication error)	Nicorandil tablets are sensitive to moisture so patients should be advised to keep the tablets in their blister until intake. In each blister, each nicorandil tablet is linked to a desiccant (which keeps nicorandil dry) in a separate blister part which is marked. The patients should be advised not to take the desiccant. Any accidental intake of this desiccant is usually harmless; but it may change the planned intake of the nicorandil tablets.	This risk can be minimised by doctors and pharmacists explaining to patients and by patients reading the product information which warns to not take the desiccant by mistake.

Important potential risks

None

Important missing information

Risk	What is known
Use in pregnancy and breastfeeding (Use during pregnancy and lactation)	There is limited data on the use of nicorandil in pregnant women. Animal studies do not show direct or indirect damaging results with regard to reproductive harmfulness. As a safety measure**,** it is better to avoid the use of nicorandil during pregnancy unless the benefits of use outweigh the risks. Animal studies have shown that nicorandil is found in small amounts in the breast milk. It is not known whether nicorandil is found in human milk, therefore nicorandil is not recommended during breastfeeding.
Use in children (Paediatric use)	Nicorandil is not recommended for use in children since its safety and efficacy have not been shown in this patient group.

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 this product can be found on the competent authority's webpage.

This medicine has no additional risk minimisation measures.

VI.2.6 Planned post authorisation development plan

No post authorisation development plan was proposed.