# Nicorandil (Ikorel®)

**Ikorel Tablets 10mg PA540/102/1 and Ikorel Tablets 20mg PA540/102/2**

- **Do not use as first-line treatment for angina**
- **Risk of ulcerations and progression to complications – stop nicorandil treatment if ulceration occurs**

4th November 2015

Dear Healthcare professional,

In accordance with European Medicines Agency and the Health Products Regulatory Authority, Sanofi Ireland Ltd. would like to inform you of important restrictions to the licensed indication, the modification of posology and additional contraindications and warnings for nicorandil (Ikorel Tablets 10mg and Ikorel Tablets 20mg).

The most important advice is summarised below:

**Summary**

- Nicorandil is now indicated for treatment of stable angina only in patients whose angina is inadequately controlled by first line anti-anginal therapies, or who have a contraindication or intolerance to first line anti-anginal therapies such as beta-blockers and/or calcium antagonists.

- Nicorandil is now contraindicated in hypovolaemia, acute pulmonary oedema and for use with soluble guanylate cyclase stimulators such as riociguat.

- Use nicorandil with caution in combination with medicines which increase potassium levels, especially in patients with moderate to severe renal impairment.

As you are aware the SmPC and product labelling for Ikorel was updated in August 2014 with regard to the risk of ulcerations and progression to complications. The updated information is summarised below as a reminder:

- Nicorandil can cause serious skin, mucosal, and eye ulceration, which persists unless treatment is discontinued.

- Stop nicorandil treatment if ulceration develops on any part of the body. If stopping nicorandil treatment worsens angina symptoms, consult a cardiologist.

- Gastrointestinal ulcers may progress to perforation, haemorrhage, fistula, or abscess.

- Patients with diverticular disease may be at particular risk of fistula formation or bowel perforation compared with patients without diverticular disease.

- Taking aspirin, non-steroid anti-inflammatory drugs (NSAIDs) or corticosteroids concomitantly with nicorandil increases the risk of gastrointestinal ulceration, perforations, and haemorrhage compared with taking either medicine alone.

This letter follows reviews by European drug regulatory agencies of the risk of skin and mucosal ulceration with nicorandil and the indications for nicorandil use. The key recommendations from these reviews are outlined above and in the further information below.

Dose

Nicorandil should normally be used in the dose range 10 to 20mg twice daily (in the morning and in the evening preferably), starting at 10mg twice daily and titrating if necessary, in accordance with patient need, response and tolerance up to a maximum of 40mg twice daily. A lower starting dose of 5mg twice daily may be used in patients particularly prone to headache (a very common adverse reaction to nicorandil as a result of cerebral vasodilation).

Ulcers

There have been reports from clinical practice of ulceration and related complications following nicorandil use. Almost two-thirds of the reported gastrointestinal ulcerations were serious[a], the remaining events were non-serious. Almost all cases of perforations, fistula, abscess and haemorrhage were serious and hospitalisation was required for most of these cases.

The data showed that nicorandil-induced gastrointestinal ulcerations and related events are rare and conjunctivitis, conjunctival ulceration, and corneal ulceration are very rare.[b] It is still not known how nicorandil causes ulceration.

Ulcer location and time to onset

Ulcers may develop on different parts of the body in the same patient. The ulcers may develop at the same time or one after another. Ulceration can occur at any time during nicorandil treatment (including years after starting treatment).

Ulcer treatment

Ulcers caused by nicorandil do not respond to conventional ulcer treatment, including surgery. The only way to cure these ulcers is to stop nicorandil treatment. It may take weeks or months for the ulcers to heal, depending on their severity.

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a A serious adverse reaction is an adverse reaction which results in death, is life-threatening, requires in-patient hospitalisation or prolongation of existing hospitalisation, results in persistent or significant disability or incapacity, or is a congenital anomaly/birth defect

b Rare = ≥1/10,000 to <1/1,000; very rare= <1/10,000

Other advice

Use nicorandil with caution in the following situations:

- In patients with heart failure NYHA III or IV
- In patients with glucose 6 phosphate dehydrogenase (G6PD) deficiency (consider the risk of methemoglobinurea)
- In patients taking dapoxetine (consider the risk of reduced orthostatic tolerance)

The Summary of Product Characteristics (SmPC) and Patient Information Leaflet have been updated to reflect the new indications and contraindications as well as the new safety data and recommendations (see attached).

**Reporting of suspected adverse reactions**

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product.

Healthcare professionals are asked to report any suspected adverse reactions with the use of Ikorel to the Pharmacovigilance Section of the HPRA using the on-line reporting function on the HPRA website (www.hpra.ie) or alternatively by contacting the HPRA at 01 676 4971 or medsafety@hpra.ie

Adverse reactions should also be reported to Sanofi by telephone on 01 4035 600 or via e-mail to IEPharmacovigilance@Sanofi.com

**Company contact point**

For further medical information on Ikorel please contact:

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We remain at your disposal for any further information you may need.

Yours sincerely

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**Medical Director, Sanofi Ireland**