FOI 23/076

23rd February 2023

Dear

Thank you for your email, dated 26 January 2023, in which you requested:

• A copy of the full clinical study report (CSR) of the IONA study first published on April 13th, 2002, in *The Lancet* under the title of "Effect of nicorandil on coronary events in patients with stable angina: the Impact Of Nicorandil in Angina (IONA) randomised trial" authored by The IONA Study Group with a corresponding author Prof H J Dargie (Dargie HJ *et al*. *Lancet.* 2002;359;1269-75.) including any and all protocol amendments that may have occurred during the preparation and during the conduct of the study.

• The detailed and complete safety data analysis set of the IONA study published – in part – on April 13th, 2002, in *The Lancet* under the title of "Effect of nicorandil on coronary events in patients with stable angina: the Impact Of Nicorandil in Angina (IONA) randomised trial" authored by The IONA Study Group with a corresponding author Prof H J Dargie (Dargie HJ *et al*. *Lancet.* 2002;359;1269-75.) – if not already contained *in toto* in the full clinical study report.

• Identification and manufacturing information of the version of the 10 mg and 20 mg tablets used in the IONA study (presumably Ikorel, Sanofi) and the UK Summary of Product Characteristics (SmPC) of the respective nicorandil product used in the study that was in effect at the time of the conduct of the IONA study.

MHRA response:

Marketing Authorisations for Ikorel/Nicorandil 10 mg and 20 mg Tablets (PL 04425/0327- 0328) were granted in the UK to Aventis Pharma Limited on 24 September 2009, following a change of authorisation holder (CoA). The original Marketing Authorisations, Ikorel/Nicorandil 10 mg and 20 mg Tablets (PL 00012/0229-0230), were authorised to May and Baker Limited on 06 June 1994.

In response to your request, please find attached:

(i) a copy of the redacted CSR, including the protocol and protocol amendments appendix to the CSR, and CSR addendum, which were submitted in support of the variation to amend sections 4.1 (Therapeutic Indications) and 5.1 (Pharmacodynamic Properties) of the Summary of Product Characteristics (SPC) and the Patient Information Leaflet (PIL) for Ikorel/ Nicorandil 10 mg and 20 mg Tablets (PL 00012/0229-0230_0034), to reflect the findings of the IONA clinical study.

The CSR documentation has been redacted under Section 40 (Personal information), Section 41 (Information given in confidence) and Section 43 (Commercial Iinterests) of the Freedom of Information (FOI) Act.

Disclosure of information subject to Section 40 (Personal information) would be an infringement of personal data. Section 40 (Personal information) is an absolute exemption and no consideration of the public interest is required.

Section 41 (Information given in confidence) is an absolute exemption, and no consideration of the public interest is necessary, except to state that the release of this information withheld under this section of the FOI Act would be considered an actionable breach by the MHRA.

We have redacted some parts of the attached documentation under Section 43 (Commercial interests) of the FOI Act because the release of all, or part of, the information would, or would be likely to, cause harm to the third party's commercial interests. The exemption is to safeguard the commercially sensitive information/commercial enterprise. This exemption is conditional on the public interest in releasing it not outweighing the company's/commercial enterprise's right to confidentiality and the probable damage that the company/commercial enterprise could suffer as a result of the information being released. We have considered the balance of the public interest when applying this exemption. In this case, we have not identified any issues which would benefit the public, as a whole, by being brought to their attention.

(ii) the 'clinical particulars' section of the SmPCs for Ikorel 10 mg and 20 mg Tablets (PL 00012/0229-0230) approved on 11 February 1998, 02 August 1999 and 04 April 2000 and the complete SmPCs for Ikorel 10 mg and 20 mg Tablets (PL 00012/0229-0230) approved on 26 October 1999 and 08 August 2000, which were in effect over the period that the IONA study was conducted (May 1998 and August 2001). The table below provides details of the variations to the clinical particular sections of the SmPCs, approved from February 1998 onwards, which determined the clinical particulars content of the SmPCs for Ikorel 10 mg and 20 mg Tablets (PL 00012/0229-0230) in effect at the time of the conduct of the IONA study.

Date of Approval of SmPC fragment /SmPC	**Reason for variation**
11/02/1998	To update the 'Other undesirable effects' and 'Other special warnings' and precaution' sections of the SmPC to include the occurrence of persistent aphtosis or mouth ulcers with use of Ikorel and their cessation once treatment is discontinued.
02/08/1999	To update the Summary of Product Characteristics in respect of a potential interaction with sildenafil.
26/10/1999	Renewal
04/04/2000	To update the clinical details of the SmPC to include reference to very rare reports of angioedema and hepatic function abnormalities

Please note that we have searched our records and have not found complete copies of the SmPCs approved on 11 February 1998, 02 August 1999 and 04 April 2000. Therefore having exhausted the usual avenues in our search for this information, we have concluded that, these are no longer on our systems in a retrievable form.

Identification and manufacturing information of the version of the 10 mg and 20 mg tablets used in the IONA study beyond the information provided in the clinical study report is being refused under Section 41 (Information given in confidence) and Section 43 (Commercial interests) of the Freedom of Information (FOI) Act.

Section 41 (Information given in confidence) is an absolute exemption, and no consideration of the public interest is necessary, except to state that the release of this information withheld under this section of the FOI Act would be considered an actionable breach by the MHRA.

Concerning Section 43 (Commercial interests), this exemption is conditional on the public interest in releasing it not outweighing the company's/commercial enterprise's right to confidentiality and the

probable damage that the company/commercial enterprise could suffer as a result of the information being released. We have considered the balance of the public interest when applying this exemption. In this case, we have not identified any issues which would benefit the public, as a whole, by being brought to their attention.

We now consider this FOI request closed. If you have a query about this letter, please contact the MHRA FOI Licensing mailbox using the email address listed below.

If you are dissatisfied with the handling of your request, you have the right to ask for an internal review. Internal review requests should be submitted within 2 months of the date you receive this response and addressed to: info@mhra.gov.uk, quoting reference FOI 23/076.

If you are not content with the outcome of the internal review, you have the right to apply directly to the Information Commissioner for a decision. The Information Commissioner can be contacted at: Information Commissioner's Office, Wycliffe House, Water Lane, Wilmslow, and Cheshire, SK9 5AF.

Yours sincerely,

The FOI Licensing Team