FOI 22/1143 - Dolobid

REQUEST
25 November 2022

It has been noted from the Merck US Label 2007 for DOLOBID® (the active ingredient is diflunisal and the product was also marketed by Merck under the brand name DONOBID) that some nonclinical toxicity studies were performed after the original marketing authorisation submission in the late 1970's.

Freedom of information (FOI) request for the study reports (including summary, methods, results, tables, individual animal data, and appendices for each study) for the following studies that were performed after the original marketing authorisation submission (for reference, these study reports are marked in yellow in the enclosed US Label from 2007 for Dolobid on pages 8-9):

- A second long-term carcinogenicity study in mouse with a highest dose level of 80 mg/kg/day.
- Ames microbial mutagen test.
- V-79 Chinese hamster lung cell assay (genotoxicity/mutagenicity assay).
- Rat reproduction/fertility studies with highest dose levels of 50 mg/kg/day.
- Teratogenicity (embryo-fetal toxicity/ developmental toxicity) studies in rabbits with highest dose levels of 50 mg/kg/day and 60 mg/kg/day, respectively.
- Teratogenicity (embryo-fetal toxicity/ developmental toxicity) study in rats with a highest dose level of 100 mg/kg/day.
- Neonatal beagle dog toxicity study, including beagle dogs assessed at 4-5 days and 25 days after birth, with a highest dose level of 80 mg/kg/day.
- Neonatal rat toxicity study with a highest dose level of 140 mg/kg/day.
- If possible, any other nonclinical pharmacology, pharmacokinetics (ADME) and toxicity studies that have been submitted after the original NDA submission.

MHRA RESPONSE
19 January 2023

Dear

Thank you for your email and we apologise for the delay in responding.

Regarding your request, we have searched our records (including our archived paper records), for the non-clinical studies you refer to. However, we have been unable to obtain any information regarding these studies. Therefore, having exhausted all the usual avenues, we must conclude that we do not hold this

information. Further to this, we have been unable to locate any non-clinical pharmacology, pharmacokinetics or toxicity studies that have been submitted after the original marketing authorisation applications for Dolobid/Diflunisal 125, 250 & 375mg Tablets (PL 00025/0127-9) were made.

If you disagree with how we have interpreted the Freedom of Information Act 2000 with regards to your request, you can ask for the decision to be reviewed. The review will be carried out by a senior member of the Agency who was not involved with the original decision.

If you have a query about the information provided, please reply to this email.

Please remember to quote the reference number above in any future communications.

If you were to remain dissatisfied with the outcome of the internal review, you would have the right to apply directly to the Information Commissioner for a decision. Please bear in mind that the Information Commissioner will not normally review our handling of your request unless you have first contacted us to conduct an internal review. The Information Commissioner can be contacted at:

Information Commissioner's Office
Wycliffe House
Water Lane
Wilmslow
Cheshire
SK9 5AF

Yours sincerely

MHRA Customer Service Centre
Medicines and Healthcare products Regulatory Agency
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