

Elisabeth Perlman

Sent via email: request-264200-3fd7a7f0@whatdotheyknow.com

MHRA

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Ref No: 15/186

15th May 2015

Dear Ms Perlman,

Thank you for your email of 16th April where you requested:

- 1. According to the data, how many people are living in the UK are currently taking Roaccutane? And how many people in total have taken Roaccutane in the past 20 years?*
- 2. What is the average revenue generated in pound sterling of Roaccutane sales in the UK each year? How much would a private patient pay for a six month supply of 20mg pills?*
- 3. Why did Roche withdraw Roaccutane in the United States in 2009?*
- 4. What has the MHRA done to combat the illegal sale of Roaccutane on the web?*
- 5. Please take me through the changes that have taken place in terms of how Roaccutane has been regulated since it first came on the market in the 1980s.*
- 6. How regularly must patients on Roaccutane have blood tests and pregnancy tests? If private consultant dermatologists do not require this, how are they held to account? And how are NHS dermatologists monitored with reference to prescribing roaccutane?*
- 7. How many individuals became pregnant whilst taking Roaccutane in 2014/2015?*
- 8. What is the most common dosage given to people with severe acne and over what period? How is the right dosage determined?*

We informed you in our initial response that we cannot answer Q 1-3 as they fall outside the agency's remit. In an effort to be helpful to you, we have given further explanation of why we cannot answer these questions, and provided background information which you may find helpful. Our responses to your remaining questions are also below.

1. According to the data, how many people are living in the UK are currently taking Roaccutane? And how many people in total have taken Roaccutane in the past 20 years?

The MHRA and other regulators worldwide use data from sales figures and prescription numbers to estimate the number of patients receiving each medicine. We have concluded that disclosing the specific usage figures for the 20 year period requested would not be appropriate because providing this information subject to section 43 of the Freedom of Information Act would be prejudicial to commercial interests. Furthermore, we do not believe that there is an overriding public interest in disclosing this information in this instance.

Information on the estimated usage of Roaccutane and other brands of isotretinoin in the UK for the last 5 years is available in a Public Assessment Report available on the MHRA website at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/391670/isotretinoin_and_psychiatric_disorders_PAR_Final_web.pdf

Within the UK, the exact number of patients taking a medicine is not known for any medicine. There are databases which use patient records and prescribing information such as the Clinical Practice Research Datalink in the UK. However, these databases only collect information from a proportion of GP practices and the figures are projected to provide estimates for the UK. Unfortunately, as GP's do not prescribe isotretinoin CPRD does not contain sufficient data to estimate usage of isotretinoin in the UK.

2. What is the average revenue generated in pound sterling of Roaccutane sales in the UK each year? How much would a private patient pay for a six month supply of 20mg pills?

The MHRA does not hold information on the revenue of pharmaceutical companies, or the prices charged by medical practitioners for private prescriptions, therefore we are unfortunately unable to provide this requested information.

3. Why did Roche withdraw Roaccutane in the United States in 2009?

The MHRA is the medicines regulator for the UK, and is not required to hold information on the activity of pharmaceutical companies in other countries such as the United States.

The US regulator is the Federal Drug Administration (FDA); they issued a notice on their Federal Register in 2010 confirming that the withdrawal of Accutane was not due to reasons of safety or efficacy.

<https://www.federalregister.gov/articles/2010/07/07/2010-16439/determination-that-accutane-isotretinoin-capsules-10-milligrams-20-milligrams-and-40-milligrams-were>

4. What has the MHRA done to combat the illegal sale of Roaccutane on the web?

The MHRA take all reports of illegal sales of prescription medicines seriously. In the UK, there are robust regulatory requirements around the sale and supply of medicines and these legal requirements apply without distinction to medicines for human use sold or supplied via the internet or e-mail transactions. Prescription-only medicines can only be supplied in response to a prescription and must comply with other all other specific requirements.

We routinely monitor medicines being offered for sale on the Internet. Enforcement action is taken against suppliers who operate outside the legal requirements in the UK, we have closed down thousands of websites and brought into compliance hundreds more. Although websites based overseas are not caught by the scope of UK medicines legislation, with the assistance of the regulatory authorities and law enforcement agencies in countries where the website is hosted, wherever possible, offending websites have been amended to reflect the law.

We have investigated cases where POMs have been supplied to members of the public from websites without a prescription and / or the involvement of a qualified healthcare professional. A number of individuals have been successfully prosecuted by the MHRA for selling medicines illegally over the internet.

Information on buying medicines online is available on the MHRA website:

<http://www.mhra.gov.uk/Safetyinformation/Generalsafetyinformationandadvice/Adviceandinformationforconsumers/Buyingmedicinesonline/index.htm>

An annual initiative to tackle the illegal online trade in medicines, named Operation Pangea, coordinated by Interpol illustrates the benefits of international collaboration to address the global nature of the problem. During last year's operation, UK seizures of 3.6 million doses of counterfeit, falsified and illegally traded medicines with a value of £9.5 million. 1,862 websites were closed down across the world and illegal adverts on Social Media Websites were removed.

5. Please take me through the changes that have taken place in terms of how Roaccutane has been regulated since it first came on the market in the 1980s.

The marketing authorisation for Roaccutane has been regulated in the same way since it was first authorised in 1982. Roaccutane has always been a prescription only medicine (POM) which must be prescribed by or under the supervision of a Consultant Dermatologist.

Although the way Roaccutane is regulated has not changed, the information provided to prescribers and patients has changed.

The Roaccutane Summary of Product Characteristics (SmPC) reflects the terms of the licence and provides guidance on prescribing isotretinoin as well as warnings about potential side effects. The SmPC is updated as required to reflect emerging data.

The risk of possible birth defects was known before it was approved and therefore the SmPC has always contained warnings and the recommendation not to use isotretinoin during pregnancy. Over the years these warnings have been updated, particularly in 2004 with the introduction of the Pregnancy Prevention Program across Europe.

Information on side effects may be updated to include new side effects or strengthening the warnings for existing side effects. Data regarding the possible risk of depression and other psychiatric disorders started to emerge in the late 1990's and the first warnings were added in 1997, with updates in 1998 and 2004. The risks of psychiatric adverse reactions have been reviewed within the UK and across Europe in 2005 and 2014 but no further amendments to the SmPC have been made.

6. How regularly must patients on Roaccutane have blood tests and pregnancy tests? If private consultant dermatologists do not require this, how are they held to account?

The Roaccutane Summary of Product Characteristics (SmPC) provides guidance to healthcare professionals on blood tests and pregnancy testing.

The recommendations for blood tests are as follows:

Regarding blood tests, the recommendation is that liver enzymes and blood lipids (fats) should be checked before treatment, 1 month after the start of treatment, and subsequently at 3 monthly intervals unless results suggest more frequent monitoring is needed.

Patients with diabetes, obesity, alcoholism or a problem with the way their body processes lipids might need more frequent tests, including blood glucose.

The recommendations for pregnancy testing are as follows.

- Female patients should have a pregnancy test before starting contraception.
- After at least 1 month of contraceptive use and before Roaccutane is prescribed they should have a second pregnancy test to exclude pregnancy before starting treatment.

- The recommendation is that follow up visits for female patients should be at 28 day intervals. The need for a pregnancy test at each visit should be decided according to the patient's sexual activity and menstrual history.
- A final pregnancy test should be made 5 weeks after stopping treatment.

More detailed information can be found in the Roaccutane SmPC at <http://www.mhra.gov.uk/spc-pil/>.

The MHRA regulates licenced medicines, and regulation of clinical practice is outside the Agency's remit. However, the MHRA liaised with the British Association of Dermatologists (BAD) who have produced clinical guidelines for the use of Roaccutane and other isotretinoin-containing medicines. www.bad.org.uk/library-media/documents/Isotretinoin_2010.pdf

This guideline is accredited by the National Institute for Health and Care Excellence (NICE). Any questions about how these guidelines are implemented in practice could be addressed to BAD via their website at <http://www.bad.org.uk>.

No differentiation is given to NHS and private prescribers in terms of the testing and monitoring of patients receiving Roaccutane.

How are NHS dermatologists monitored with reference to prescribing Roaccutane?

The MHRA does not regulate clinical practice and therefore does not hold any information about how NHS dermatologists are monitored. A decision to prescribe Roaccutane must be based on the advice provided within the SmPC and the clinical judgement of the prescribing dermatologist. Doctors are able to prescribe any medicine, if they consider it to be in the best interests of their patient. However, the prescriber then becomes personally responsible for the patient's treatment when they prescribe "off-label".

7. How many individuals became pregnant whilst taking Roaccutane in 2014/2015?

The MHRA has received 12 Adverse Drug Reaction reports for Roaccutane with pregnancy or related terms between 01/01/2014 and 12/05/2015:

ADR	Number of Reports
Pregnancy	8
No adverse event, Pregnancy	2
Exposure via father	2

Please note that this figure includes only cases in which the brand Roaccutane is specifically named. It does not include cases involving other brands of isotretinoin or cases where the brand has not been specified.

Of the 12 case reports received two involved male patients who took Roaccutane, one while his partner was pregnant and the other male patient had stopped Roaccutane more than a month before his partner became pregnant. The risk of birth defects does not apply when male patients take Roaccutane. The patient information contains the following information "Roaccutane does not appear to damage sperm. Very low levels of isotretinoin are present in the semen of men taking Roaccutane, but too little to harm the unborn baby of your partner."

Of the remaining 10 case reports, 5 became pregnant after stopping Roaccutane, 2 of which were within the 4 week at risk period. The remaining 5 cases were using contraception and 3 of these reports specifically mention that the women were aware of and had signed the PPP acknowledgement form, further information is awaited on the final 2 cases.

**8. What is the most common dosage given to people with severe acne and over what period?
How is the right dosage determined?**

Information on the recommended dosage for Roaccutane is presented in the SmPC which reflects the data obtained from clinical trials.

Dosing of Roaccutane is based on the patient's weight and how they respond to treatment. The starting dose should be 0.5 milligrams (mg) for every kilogram (kg) of body weight. The dose is then adjusted during treatment according to the patient response. The most common dose range is 0.5 – 1.0 mg per kg of body weight per day. The duration of treatment depends on the daily dose of the patient. No substantial additional benefit is expected beyond a total dose of 120 – 150 mg/kg over the full course of treatment, so a treatment course of 16 – 24 weeks is normally sufficient.

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 two months of the date of receipt of the response to your original request and should be addressed to: The Communications Division, 4-T, MHRA, 151 Buckingham Palace Road, London, SW1W 9SZ, or by response to this email.

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

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, Cheshire, SK9 5AF.

Yours Sincerely,

FOI Team,
Vigilance and Risk Management of Medicines Division

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