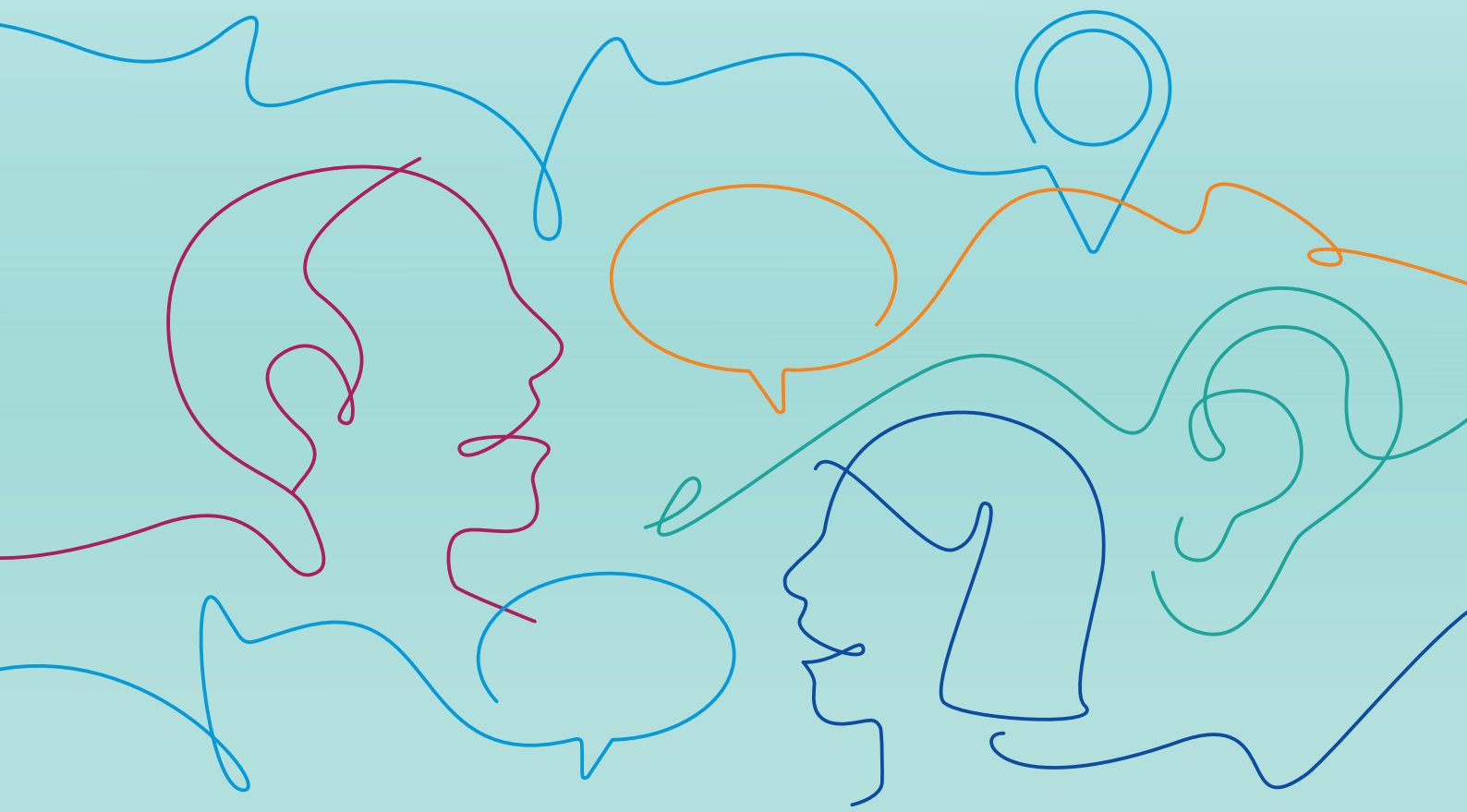




EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Summary of the EMA public hearing on quinolone and fluoroquinolone antibiotics

Public hearing held on 13 June 2018



Background

On 13 June 2018, the European Medicines Agency (EMA) held a public hearing on quinolone and fluoroquinolone antibiotics to hear the views of patients and the general public on the persistence of side effects reported with this group of medicines.

Quinolones and fluoroquinolones are synthetic antibiotics used for a wide range of bacterial infections. Available in the EU since 1962, they have been used to treat millions of patients with bacterial infections, including serious or life-threatening infections and those resistant to other treatments.

Today, quinolones and fluoroquinolones are used for over 120 indications in the EU, including different types of urinary tract, respiratory, genital, gastrointestinal tract, skin, bone, and joint infections. The most commonly used medicines in this class are ciprofloxacin, levofloxacin, moxifloxacin, norfloxacin and ofloxacin.

EMA's Pharmacovigilance Risk Assessment Committee (PRAC) started a review of this class of medicines following reports of serious, long-lasting side effects mainly affecting muscles, tendons, joints and the nervous system. The reports have included life-changing disabilities and long-term pain. Although the side effects themselves have been known, this review is looking at the persistence and long-lasting nature of the side effects and their impact on patients' lives.

Given the seriousness of the side effects, Melanie Carr, Head of EMA's Stakeholders and Communication Division remarked in her welcome address that this public hearing was "particularly important because it allows us to consider your views on the risk associated with these medicines and consider options for regulatory action in a wider public health context".

Sixty-nine participants attended in person at EMA offices in London (or called in by telephone), including 40 patients and patient representatives, 14 healthcare professionals and academics, 13 representatives from pharmaceutical industry as well as members of the media. Many other members of the public who could not attend sent [submissions in writing](#), which will all be taken into account during the review.

The hearing was chaired by June Raine, the Chair of the PRAC, with an introduction of the topic from by Eva Jirsová, the PRAC Rapporteur (lead assessor) and additional guidance from Juan Garcia-Burgos, EMA's Head of Public Engagement.

The hearing was broadcast live and a recording is available on [EMA's website](#).

Questions addressed to participants

- What is your view on the role of quinolones and fluoroquinolones in the treatment of infections?
- What is your view of the risks associated with quinolone and fluoroquinolone use?
- In your opinion, what further measures could be taken to optimise the safe use of quinolones and fluoroquinolones?

Summary of issues raised

Patients described life-changing symptoms following treatment with quinolone and fluoroquinolone antibiotics, including pain and disability lasting several years, with some patients only experiencing limited improvement over time. Furthermore, some patients can no longer work or engage in exercise

and active pursuits or even carry out daily tasks such as tying a shoe lace or buttoning a shirt; some are in constant pain, with symptoms affecting a wide range of muscles and tendons. The tendon problems generally affected multiple tendons, in contrast to many other tendon disorders which usually affect one. Other symptoms include mood disturbances and other mental health effects as well as effects on the heart. These side effects were reported by patients who took medicines by mouth or injection and medicines given as ear and eye drops were also considered to cause them.

In many cases, quinolones and fluoroquinolones had been prescribed for minor infections or were used to prevent infections. Many patients continued taking these medicines while they had symptoms, unaware of a possible link to their treatments. Some patients also reported a worsening of symptoms when they were subsequently given NSAID painkillers or steroids.

A recurring theme was the lack of knowledge of the possible side effects among doctors. Many patients were not informed of the risks and said that they did not feel they were listened to when they reported a possible link to their treatments. While some doctors were aware of symptoms affecting the Achilles tendon, many did not know of, recognise or report other side effects that could possibly have been linked to quinolones and fluoroquinolones.

In the absence of answers from healthcare professionals, patients have had to rely on information on the Internet to understand the symptoms they were experiencing.

Main points raised

- Symptoms were life-changing and wide ranging.
- Patients were not given information about risks.
- Healthcare professionals were generally unaware of the range and severity of possible symptoms, with the exception of Achilles tendon disorders.

The consensus among patients was that the use of quinolone and fluoroquinolone antibiotics should be greatly restricted. Patients said that these medicines should be used only in life-and-death situations, when nothing else works, or for very serious infections that have been confirmed by laboratory tests. Patients should also have to give informed consent before treatment. There was minority support for an outright ban of these medicines, and some patients supported restricting use to hospitals.

Patients called for better recognition of patterns of toxicity with quinolones and fluoroquinolones (sometimes referred to as 'fluoroquinolone-associated disability syndrome'). Patients also called for better education of healthcare professionals, including during medical training when they first learn about this class of medicines. Almost all patients said they would not have taken their treatments if they had known of the extent of the potential risks and if such risks were described properly in the package leaflets.

Other participants including healthcare professionals and academics called for more research, including genetic research, to establish the precise mechanisms through which the medicines cause these side effects, determine how they affect different populations and quantify the overall magnitude of the risk.

Patients and healthcare professionals noted the need to improve management of patients with side effects and bring together expertise from different fields to deal with the wide-ranging symptoms. Furthermore, the prescribing of these medicines should be better monitored and 'red flags' should be raised so that patients who have had these side effects are advised to stop treatment immediately and

are never prescribed these medicines again. They also stressed the importance of microbial testing to make sure the medicines are only used when necessary.

Another issue raised was the reaction to foods, which patients said should be further investigated. Some patients described worsening of symptoms after eating certain foods, including meat and fish, and patients were concerned that they could have been exposed to quinolones and fluoroquinolones used to treat farmed animals.

Finally, a representative of a pharmaceutical company that markets this class of antibiotics, acknowledged the need to improve information on the risk of these medicines in their product information, particularly the package leaflets.

Proposals

- Restrict quinolone and fluoroquinolone use to situations where there are no alternatives.
- Improve education for healthcare professionals (including during medical training).
- Improve management of patients with side effects (taking account of wide-ranging symptoms).
- Improve communication on quinolone and fluoroquinolone toxicity, including possible risk factors, and add more information in the product information, including the package leaflet.
- Encourage research on how the medicines cause side effects, including genetic research.
- Consider how certain foods affect patients' symptoms, particularly meat treated with quinolones and fluoroquinolones.

Next steps

In closing the discussions, Dr Raine praised the courageous testimonies from patients and other participants. "More than anything we need to restore the chain of trust," she noted, adding that one of the hardest things for patients with these debilitating symptoms was the lack of recognition of what they are experiencing.

The PRAC will now reflect on all the views expressed at the hearing, including written submissions, and will take them into account as it considers its recommendations on the use of these antibiotics. The recommendations will then be sent to the Committee for Medicinal Products for Human Use (CHMP), responsible for questions concerning medicines for human use, which will adopt the Agency's opinion. The final stage of the review procedure is the adoption by the European Commission of a legally binding decision applicable in all EU Member States.

EMA would like to express its warmest gratitude to all those who have contributed to this public hearing.

List of Speakers

General public (patient representatives, carers, families)

Speaker 1:

Elizabeth Carmouche, Belgium

Speaker 2:

Manex Bettan Arguinzoniz, Spain

Speaker 3:

Richard Cooknell, UK

Speaker 4:

Markus Hamedinger, Austria

Speaker 5:

Miriam Knight, Quinolone Toxicity Support UK

Raymond Miller, Quinolone Toxicity Support UK

Geoffrey Robinson, Fluoroquinolone Toxicity Victims in Europe

Speaker 6:

Julie Le Normand, France

Speaker 7:

Elsa Leitão, Germany

Speaker 8:

Jaroslawn Linka, Poland

Speaker 9:

Andrea Noya, Italy

Speaker 10:

Joshua Sutton, UK

Speaker 11:

Miriam van Staveren, The Netherlands

Speaker 12 (joining via telephone):

John Crowley, Luxembourg

Speaker 13 (joining via telephone):

Enikő Pongrácz, Hungary

Pharmaceutical companies

Speaker 14:

Leo Plouffe, Bayer AG

Healthcare professionals and academia

Speaker 15:

Jamie Wilkinson, Pharmaceutical Group of the European Union (PGEU)

Speaker 16:

Graham Bothamley, European Respiratory Society (ERS)

Speaker 17:

Mary McCarthy, European Union of General Practitioners (UEMO)

Speaker 18:

Neal L Millar, Institute of Infection, Immunity and Inflammation, University of Glasgow, UK

Speaker 19:

Ber Oomen, European Specialist Nurses Organisations (ESNO)

Speaker 20:

Paul Tulkens, Louvain Drug Research Institute, Belgium

Speaker 21:

Florian Wagenlehner, European Association of Urology (EAU)

Additional interventions

As time permitted, the Chair invited additional comments from the floor. Comments were provided by Stephanie Fowler, Elizabeth Pyne (attending on behalf of her son), Deborah Kinrade and David Morison.

Nigel Stacey provided comments after the video recording had been stopped. He spoke of the need for improvements in package leaflets to take account of those who may not be able to understand the text.

Notes

1. The legal basis for public hearings is Article 107j of Directive 2001/83/EC of the [pharmacovigilance legislation](#), which gives the PRAC the possibility to hold public hearings for safety reviews conducted by the Committee under Article 20 of Regulation (EC) No 726/2004, and Articles 31 or 107i of Directive 2001/83/EC.
2. Public hearings are held on a case-by-case basis, where the Committee determines that collecting the views of the public would bring added value to its review, in addition to the other channels of stakeholder engagement such as stakeholder submissions or through inclusion of patients and healthcare professionals in expert meetings.
3. Public hearings are conducted according to the [rules of procedure](#) for public hearings.
4. More information on the ongoing review of quinolone and fluoroquinolone antibiotics is available on a [dedicated webpage](#).
5. More information on the work of the European Medicines Agency can be found on its website: www.ema.europa.eu

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