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Stakeholders and Communication Division

Rapid response to BMJ

Re: Pandemrix vaccine: why was the public not told of early warning signs?

By Peter Arlett, Head of Pharmacovigilance and Epidemiology at EMA

We consider that this article misrepresents the work of the European Medicines Agency (EMA) on Pandemrix, including EMA's drive for transparency in its communication to the public during the 2009/2010 pandemic influenza. The article also draws incorrect conclusions based on scientifically invalid comparisons of data.

Authorisation and safety monitoring of Pandemrix

Pandemrix was developed for use specifically in a flu pandemic. It was authorised in the European Union (EU) on 29 September 2009 to immunise citizens against the H1N1 pandemic influenza strain. Information from clinical trials in more than 6,000 subjects was assessed as part of an extensive review of the vaccine's safety profile before its authorisation, and the outcome of the assessment is available on the EMA website (1,2).

Pandemrix was subject to the EU's robust system of safety monitoring. In this system, EMA regularly assesses data on suspected adverse reactions provided by patients and healthcare professionals, national authorities and companies. Whenever a new safety signal emerges, EMA takes rapid action and discloses information to the public.

During the 2009/10 pandemic, EMA further intensified its safety monitoring of pandemic vaccines (3). All the available data were collected by EMA and assessed in real-time by a team of experts from EMA and the national authorities of the member states. Potential signals of possible new safety issues were promptly reviewed using all the available information. At the time, these evaluations indicated that the overall benefit-risk profile of Pandemrix remained favourable.

In August 2010, EMA learnt of cases of narcolepsy in a small number of patients who had been vaccinated with Pandemrix, and promptly started a safety signal review into this potential association. Since that time, EMA remained vigilant on this issue and examined new scientific data as soon as they became available, in coordination with experts from around the world. This evaluation included data from well-designed, large-scale epidemiological studies.

While the biological mechanism for the association between Pandemrix and narcolepsy remains unknown, the data available led EMA to restrict its authorised use to cases where alternative seasonal

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tri-and quadrivalent influenza vaccines are not available (EMA concluding that there is a positive benefit-risk balance in this population). Since that restriction by EMA, the marketing authorisation for Pandemrix has expired and it is currently not available in the EU.

Transparency

The intense and rigorous scientific monitoring of the safety of pandemic vaccines was matched by equal attention to transparency. Between December 2009 and August 2010, in its effort to provide comprehensive and timely information to the public, EMA published on its website weekly to bi-weekly updates on estimates of exposure, a summary of the pharmacovigilance data collected in the EudraVigilance database and conclusions of safety reviews (4).

The safety monitoring work carried out during the pandemic and afterwards is still available on EMA's website for all to see and scrutinise. Researchers wanting to further analyse the data can also request access to detailed technical documents. In addition, since 2012, data on suspected adverse drug reactions for medicines authorised in the European Economic Area (EEA), including influenza pandemic vaccines, are published on the EU website of suspected adverse drug reaction reports (5).

Scientifically invalid comparisons

The BMJ article suggests that Pandemrix was less safe than another pandemic flu vaccine based on a comparison of the number of suspected adverse reactions reports received. EMA's view is that this comparison is not scientifically valid and the BMJ article's consequent conclusions are flawed and misleading to its readers and the wider public. The number of suspected adverse reactions reports spontaneously submitted by healthcare professionals and patients depends on the number of people receiving a vaccine, the organisation of the local reporting system where the vaccine is administered, different target populations in different geographical regions, as well as any differences in the nature and frequency of adverse reactions to the vaccine itself. Therefore to conclude that one product is safer than the other, based on numbers of spontaneous suspected adverse reaction reports alone, without consideration of all other relevant data, including clinical trials and epidemiological studies, is in our view ostensibly simplistic, invalid and misleading.

As an EU agency whose role is to serve EU citizens, EMA welcomes public scrutiny of its work. However, as a science organisation, we consider it essential that any issue raised is based on valid analysis of objective evidence. In this case, the comparison is from our perspective not scientifically valid and the author's consequent conclusions are flawed and misleading to its readers and the wider public.

References.

1. EMA webpage on Pandemrix
http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/000832/human_med_000965.jsp&mid=WC0b01ac058001d124

2. Pandemrix Assessment report http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Public_assessment_report/human/000832/WC500038124.pdf

3. Report summarising the key activities that took place at the Agency before and during the H1N1 pandemic:
http://www.ema.europa.eu/docs/en_GB/document_library/Report/2011/04/WC500105820.pdf

4. Pandemic influenza pharmacovigilance updates
http://www.ema.europa.eu/ema/index.jsp?curl=pages/special_topics/general/general_content_000246.jsp&mid=WC0b01ac058004bf57

5. European database of suspected adverse drug reaction reports
http://www.adrreports.eu/en/index.html