Health and Youth Care Inspectorate
Ministry of Health, Welfare and Sport

The main topics of the results of the risk-based pharmacovigilance survey 2017

On 1 May 2017, a survey was sent to 811 marketing authorization holders (MAHs) with a marketing authorization of human medicinal products in the Netherlands.

Before the survey was sent to all MAHs, it was tested during two pilot phases in 2016 where 33 MAHs voluntarily participated and completed the survey. The results of the pilot were used to improve the survey. The survey was also discussed with and reviewed by the board members of the Pharmacovigilance Platform Nederland (PPN). A presentation was given in November 2016 to announce the use of the survey by the Health and Youth Care Inspectorate (IGJ). A post meeting with representatives of several MAHs was held to further discuss the questions raised by the field. We received valuable feedback from the MAHs and the board members of the PPN and used this information to further improve the survey.

All MAHs were asked to complete the survey within 3 months. Reminders were sent (letters and e-mails) to MAHs which did not complete the survey before the deadline and a number of MAHs were contacted by telephone.

Altogether, 802 MAHs (98.9%) responded to the request and completed the survey (if applicable) and **9 MAHs did not complete the survey when requested**. From the 802 MAHs, 131 MAHs were not required to complete the survey for several reasons:

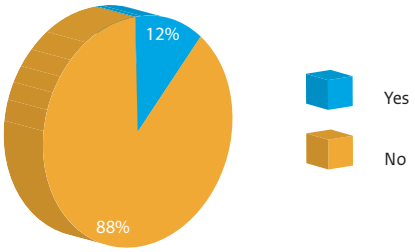
- They did not have any marketing authorizations (anymore) for products in the Netherlands. The information in the eXtended Eudravigilance Medicinal Product Dictionary (XEVMPD or article 57) database was not up to date.
- They were merged with another company. The information in the XEVMPD database was not up to date.
- They were registered in the XEVMPD database multiple times and therefore received more than one survey for the same MAH. The information in the XEVMPD database was not correct.
- They only had parallel marketing authorizations and no other marketing authorizations (CAPs, NAPs, MRPs or DCPs). MAHs with parallel import marketing authorizations only are required to follow the "MEB 14: Parallel import: marketing authorization and maintenance" guidelines with regard to the pharmaco-vigilance requirements. These organizations were not within the scope of the survey.

Pharmacovigilance system in the Netherlands

All MAHs were requested to complete the survey, but information from MAHs were collected on a pharmacovigilance (PV) system level. This means that only one MAH (the 'PSMF owner') was asked to complete all sections of the survey if the PV system was shared with other MAHs who received the survey. The other MAHs (non-PSMF owners) were asked to complete the shorter version of the survey.

Of the 671 MAHs which completed the survey, **5 MAHs answered 'no'** to the question about whether a PSMF was available. The information in the XEVMPD database was compared to the answers that were provided in the survey. The PSMF information of 2 MAHs could not be found in the XEVMPD database. Of the 666 MAHs with a PSMF, 71.8% completed all sections of the survey and 28.2% completed the shorter version of the survey. The number of MAHs covered by one PV system ranged from 1 to 25 MAHs with an average of 2 MAHs per PV system. Altogether,12.0% of the MAHs have their PSMF located in the Netherlands.

Figure 1. PSMF location in the Netherlands (n=666)



Marketing authorizations in the Netherlands

MAHs that did not actively market ("release into the distribution chain") their medicinal products on the Dutch market and will not market until the year 2020, were not required to complete all sections of the survey. In total, MAHs have marketing authorizations that are actively placed on the Dutch market. Altogether 138 (27.3 %) MAHs have marketing authorizations that are subject to additional monitoring.

Of the 498 MAHs that actively place their product on the Dutch market, 56 % have only nationally authorized products (NAP) (including the mutual recognition (MRP) and decentralized procedure (DCP)) and no centrally authorized products.

Figure 2. MAHs with marketing authorizations in the Netherlands (n=498)

In figure 2, the number of MAHs with different types of authorization applications are shown. The number of MAHs with CAPs and other marketing authorizations (MRPs and/or NAPs) are shown in blue. The yellow bar represents the number of MAHs without CAPs and only NAPs (including MRPs and DCPs).

Figure 3. MAHs with or without marketing authorisations (MAs) that are subject to additional monitoring (n=498)

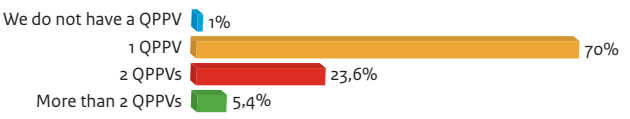
The number (in %) of MAHs with marketing authorizations that are subject to additional monitoring is shown in figure 3. The majority of MAHs do not have marketing authorizations that are subject to additional monitoring (72.7%).

These MAHs fall within the scope of the risk-based national inspection program, as MAHs with centrally authorized products will be inspected by designated supervisory authorities according to the EMA risk-based inspection program.

Qualified Person for Pharmacovigilance (QPPV)

As part of the pharmacovigilance system, MAHs are required to appoint an appropriately qualified person responsible for pharmacovigilance in the EU. MAHs were asked to provide the number of different QPPVs that they had between January 2015 and end of December 2016 (see figure 4). This question was filled in by 483 MAHs, including those which stated that they do not have a PSMF (n=5). According to the answers provided in the survey, 5 MAHs did not have a QPPV during that time period. The information in the XEVMPD (article 57) database was compared to the answers that were provided. The QPPV information of 2 MAHs could not be found in the XEVMPD database. The majority of the MAHs had one QPPV (70.0%), 114 MAHs (23.6%) had 2 QPPVs and 26 MAHS (5.4%) had more than 2 QPPVs in the 2-year period.

Figure 4. MAHs with the number of different QPPVs between January 2015 and December 2016 (n=483)



XEVMPD database

We observed that the product information in the XEVMPD database was not up to date for a large number of marketing authorization holders. Marketing authorization holders are obliged to submit and maintain the information as described in the EMA (European Medicines Agency) Guidance documents, in the XEVMPD database (article 57(2) of Regulation (EC) No 726/2004).

MAHs are required to submit notifications on any changes that impact the data such as transfers, renewals or withdrawal of the marketing authorisation as soon as possible and no later than within 30 calendar days. This also includes change of QPPV or PSMF location. Furthermore, they should notify the EMA of any new marketing authorisations within 15 calendar days from the date of notification of the granting of the marketing authorisation by the competent authority. These changes also include updates of general information such as the QPPV contact details or address of the MAH. This information should be updated for each product.

Risk-based inspections in 2018

The information in the survey that was collected will be used to make a risk profile for each MAH. These risk profiles are used as a tool to set up a risk-based national inspection program where also other information sources will be used. In order to use this tool for our inspection program in the future, the survey needs to be evaluated. In the inspection program of 2018, we will be focusing on the MAHs with a high risk profile, based on the results of the survey. The inspection outcomes will be used to verify the answers and to test the risk-based tool that has been developed.
In the inspection planning of 2018, MAHs with a high risk profile will be selected, but priority will be given to the following MAHs:

- MAHs which did not complete the survey
- MAHs where no PSMF information was available
- MAHs where no QPPV information was available

The supervisory authority inspections are not within the scope of the risk-based national inspection program and will therefore be conducted as planned according to the inspection program of the EMA.

Reference:
GVP module III, III.B.2. Inspection planning