

Lareb originates from the idea that attention to adverse drug reactions contributes to preventing injury and thus to a better use of medicines.

Attention to adverse drug
reactions contributes to preventing
injury

Netherlands Pharmacovigilance Centre Lareb Annual report 2009

Background information about Lareb and the expected developments the coming years, can be found in the policy plan.

Additional information with this annual report can be found on the Lareb website: www.lareb.nl.

If this annual report raises questions, please do not hesitate to ask. You can contact us at info@lareb.nl.



Lareb in 2009

Index numbers:

9989	reports in total
1566	reports directly from patients
21	messages to the Dutch Medicines Evaluation Board
37	publications, national and international
1253	participants LIM
312.000	Lareb website visitors

Extra, due to the influenza pandemic:

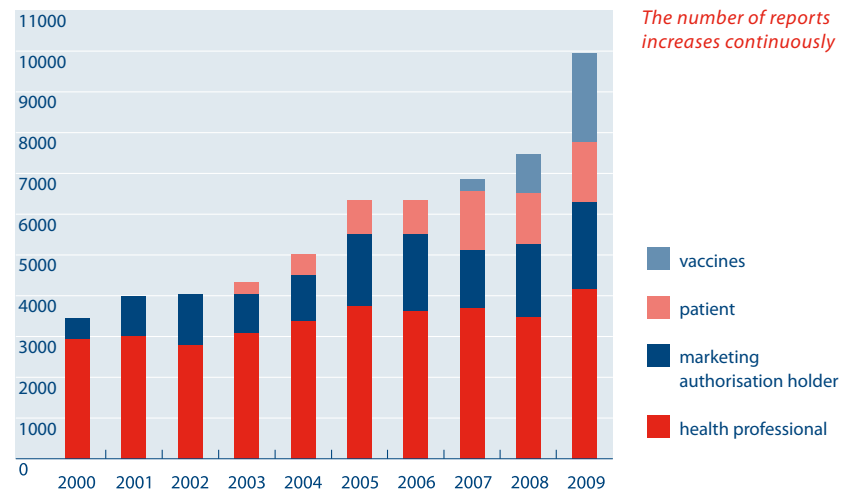
7138	reports in total on the swine flu vaccine
5981	swine flu vaccine reports directly from patients

The year 2009 has been a busy year with more reports than ever, including more reports directly from patients. It has been hard work for the people working for Lareb.

On top of that came the swine flu pandemic. Lareb had to make a huge effort to quickly assess all these reports and thus contribute to the confidence in the used vaccines.

While maintaining their own independency and autonomy, Lareb is willing to cooperate with all stakeholders in the Netherlands and abroad in the field of pharmacovigilance and safety of medicines.

Number of reports in 2009



The number of reports in 2009 was nearly 10,000. This is exclusive the reports which were received as part of the H1N1 campaign. The reports from marketing authorisation holders are serious reports reported to the pharmaceutical companies themselves and are also assessed by Lareb and filed into the database.

The reports are shared internationally to the *European Medicines Agency* and the *WHO Uppsala Monitoring Centre*.

Innovations at Lareb

2001 Quantitative signal detection

2003 Patient reports

2004 Transparency

2006 Lareb Intensive Monitoring

2010 Online signal confirmation

Where do the reports come from?



Most of the reports come directly from physicians, pharmacists or the medicine users, who were responsible for 5890 reports in 2009. This number makes the Netherlands belonging to the top five countries participating in the WHO Drug Monitoring Programme.

The reports Lareb received from marketing authorisation holders and the vaccine reports are not included in this figure.

Striking is the increase in the number of reports coming from patients ('consumers') and the increase in reports from specialist doctors.

Top ten reporting hospitals

1	University Medical Centre Utrecht	63
2	Medical Centre Leeuwarden	46
3	University Medical Centre, Groningen	34
4	University Medical Centre St. Radboud, Nijmegen	33
5	Academic Medical Centre, Amsterdam	32
5	Haga Hospital, Den Haag	32
7	Meander Medical Centre, Amersfoort	27
7	Delfzicht Hospital, Delfzijl	27
9	Elkerliek Hospital, Helmond	26
10	Amphia Hospital, Breda	24
10	Leiden University Medical Centre, Leiden	24

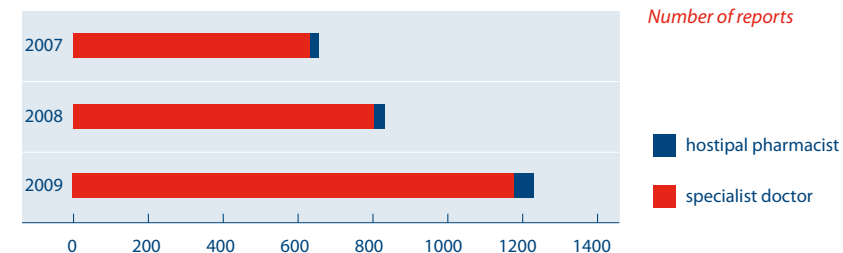
The top ten of reporting hospitals with the highest number of reported adverse drug reactions. The complete list can be found at www.lareb.nl.

Together dealing with adverse drug reactions

The campaign 'Together dealing with adverse drug reactions', with the goal of increasing the number of reports from hospitals, was ended in 2009. The aim of the campaign was to receive at least 50% more reports from hospitals in 2009 in comparison to the year before the campaign, which started in 2008. The figure underneath shows a 70% increase has been achieved!

Attention to adverse drug reactions in hospitals is very important. After all: that is where the most serious adverse drug reactions are seen. The number of reports from a hospital is an indication for the quality of pharmacotherapy in that hospital. Therefore, Lareb publishes the number of reports reported by each hospital. See: www.lareb.nl.

Number of reports





Thanks to an extra grant from the Ministry of Health, Welfare and Sport the practical guide above was sent to all physicians and pharmacists. It is used regularly in education of medical and pharmacy students. The Pharmacovigilance Centre of Suriname has released the practical guide in a Suriname edition.

Reports to the MEB

Each quarter Lareb informs the Dutch Medicines Evaluation Board. These messages are public and can be found on the website: www.lareb.nl. These signals of adverse drug reactions are an important outcome of the work of Lareb. There is considerable interest from other countries for these messages.

First quarter 2009

1. Alpha-1 blocking agents and liver disorders
2. SSRIs and hypoglycemia
3. Atomoxetine and tics
4. Tamsulosin and hyperglycemia in patients with type 2 diabetes
5. Bupropion and cardiac ischaemia
6. Angioedema and allergic reactions in metoclopramide containing products

Third quarter 2009

12. Fexofenadine and bradycardia
13. SSRIs and aggression
14. Topical imidazole derivatives and drug interactions
15. Omeprazole and coumarin interactions
16. Adalimumab and pustular psoriasis

Second quarter 2009

7. Omeprazole, esomeprazole and hypomagnesaemia
8. Phosphodiesterase 5 inhibitors and pulmonary embolism
9. Angiotensin II AT1 receptor antagonists and nightmares or abnormal dreaming
10. Valproic acid and hair texture changes
11. Bisphosphonates and stomatitis

Fourth quarter 2009

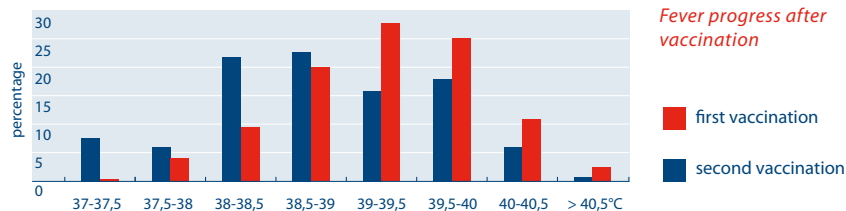
17. Proton pump inhibitors and tongue discoloration
18. Doxycycline and smell and taste disorders
19. Tamsulosin and epistaxis
20. Oseltamivir and coumarin potentiation
21. ACE-inhibitors and nightmares or abnormal dreaming

Innovative research provides quick insight

Lareb received over 3,000 reports of pyrexia in children who were vaccinated against swine flu. Additional research was done to quickly get more insight in the course of the fever and be able to inform parents about this during the vaccination campaign. We sent almost 900 parents a questionnaire by email. Within 24 hours more than half of the parents completed the questionnaire. The occurred adverse reaction was for only 111 parents reason to not get the second vaccination. In children who received the second vaccination, the height of the fever was significantly lower than after the first administration.

A group of 3,000 vaccinees is being followed over a longer period of time through internet questionnaires, which gives us insight in the occurrence and course of adverse reactions in a longer time period in a randomly selected group of people.

Fever progress after vaccination

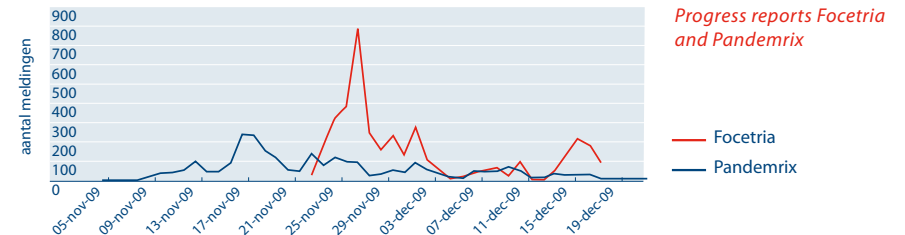


Flu pandemic

Lareb got the assignment from the Ministry of Health, Welfare and Sport to collect and assess the adverse events of the vaccines used for the prevention of influenza A/H1N1. This assignment meant a lot of extra work: the reports were assessed on the same day to be able to take immediate measures if necessary! Lareb has made maximum use of automation: the reports came through the internet and were automatically classified where possible. Each report has been assessed separately. Often, consultation of the reporter or treating physicians was needed to get more information about particular reports. There was much deliberation with the Ministry of Health, Welfare and Sport, the Dutch Centre for Disease Control and other stakeholders.

A summary of the findings was published on the website on a weekly basis. All the received reports were also publicly assessable on the website. Careful reporting was an important aspect in this period.

Progress reports Focetria and Pandemrix





Lareb Intensive Monitoring

Besides the spontaneous reports, since 2006 Lareb actively asks for adverse drug reactions by using Lareb Intensive Monitoring (LIM). The patient is central herein. When someone comes in the pharmacy and starts using a medicine that is being followed with LIM for the first time, the patient gets an information leaflet with a login code. This can be used to subscribe for the study via www.larebmonitor.nl. Then, the patient receives a number of questionnaires during a certain period of time, in which is asked for adverse drug reactions.

Every year about 1,200 patients subscribe. Over 58% of the Dutch pharmacies participate in LIM. Currently, LIM follows the smoking cessation drug Champix® (varenicline) and all antidiabetic drugs, excluding insulins. Of the participations in the antidiabetics, approximately 60% uses metformin. A minority of the participants uses the newer antidiabetic drugs, such as vildagliptin.

Lareb hopes to develop the LIM-methodology further to be able to give quick insight in the adverse drug reaction pattern of (new) drugs.

www.lareb.nl

Source of information about adverse drug reactions for everyone!

Information accessible to everyone

The Lareb website contains much information and is becoming richer. The website is not only for the reporting of adverse drug reactions, but also for the dissemination of information about adverse drug reactions.

The website has separate sections for users/patients and professionals. The information is mostly similar, but on the patients section specific medical terms are avoided. In the adverse drug reaction database on the website can both be searched on brand and generic drug name to previously reported adverse drug reactions to Lareb. The opposite is also possible: searching on adverse drug reactions. The database consists of more than 100,000 individually assessed reports!

If your answer to your question about adverse drug reactions can not be found on our website, please contact Lareb via info@lareb.nl or 073-6469700.

Publications

Lareb publishes in both Dutch and international medical and pharmaceutical journals. These publications have the aim to spread the knowledge Lareb disseminates from the reports, so that it can be applied in clinical practice. All 37 publications and 7 abstracts published in 2009 can be found at www.lareb.nl.

Finance

Most of the work Lareb does, is performed due to the Medicines Act. The Medicines Evaluation Board coordinates these tasks to support pharmacovigilance and provides Lareb funding to be able to do this job.

In 2009, Lareb received € 1,932,000 for the execution of these tasks. Lareb received € 250,000 from other sources. The year was ended with a small deficit.

The people at Lareb (per 1 april 2010)

Department & staff and secretariat

- Prof. A.C. van Grootheest (Kees), MD PhD, doctor, director
- C. van Wijnen (Clara), director's secretary
- M.C.F.P. Hendriksen-Roelofs (Sandra), secretary
- A.M. Vallenga (Astrid), receptionist, secretary

Research & analysis

- E.P. van Puijenbroek (Eugène), MD PhD, general practitioner, department manager
- N. Broos (Nancy), PharmD, pharmacist, scientist
- J.L.M. Passier (Anneke), PhD, scientist
- F.P.A.M. van Hunsel (Florence), PharmD, pharmacist, scientist
- R.P.H. Jager (Rob), IT-coordinator
- P.G.M.A. Zweers (Petra), MD, doctor, scientist

Reporting department

- L.V.D. Härmark (Linda), PharmD, pharmacist, department manager
- P.C.M. de Beer (Paulien), dataprocessing
- R.F. Gerritsen (Roald), MD, doctor, assessor, scientist
- P.T.M. van der Horst (Petra), junior assessor
- I. Oosterhuis (Ingrid), PharmD, pharmacist, assessor, coordinator Lareb Intensive Monitoring
- A.O.A. Plouvier (Annette), MD, nursing home physician, regional coordinator
- P.C. Scheltinga (Paula), PharmD, pharmacist, regional coordinator
- G.M. Steenvoorden (Gisela), project worker
- F.F.J. van Toly (Flip), PharmD, pharmacist, junior assessor
- W. aan den Toorn (Wilma), dataprocessing

Advisor

- J.F.M. Bergen, MD, HR advisor



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general practitioner
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gynaecologist, OMS
- J.G.W. Kosterink, PharmD PhD, hospital
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- E. Visser, NPCF
- A. van der Zeijden, Dutch Council of
the chronically ill and the disabled

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- E.N. van Roon, PharmD PhD, clinical
pharmacist-clinical pharmacologist
Medical Centre Leeuwarden
- H.C. Rümke, PhD, medical director
Vaxinostics
- R.J. Verkes, MD PhD, psychiatrist, UMC
Sint Radboud Nijmegen

Preview 2010

The year 2010 is the first year of the new policy period. Over 2009 it became clear that in 2010 a number of tasks, which are now executed by the Dutch Centre for Disease Control, will be taken over by Lareb:

Monitoring vaccine safety

It was decided that collecting and assessing reports of adverse events following immunization such as following the administered vaccines under the National Vaccination Programme will be carried out by Lareb.

Lareb already did the safety monitoring of travel and influenza vaccines, such as recently the vaccines against Influenza A/H1N1. Now, the 'children's vaccines' will be added.

Teratology Information Service

The use of drugs around and during pregnancy is sometimes necessary, but should be well monitored. It is important doctors, midwives and pharmacists discuss the most up-to-date information about potential risks to pregnant women and their partners. The tasks of the Teratology Information Center will be executed by Lareb.

Dilemmas and choices

The growth of the organization, but even more the growth in the number of reports leads to adjustments, especially if the funding stays behind the rising number of reports. As a consequence, the regional work should be restructured, with less regional offices and reports will be assessed more efficiently. The challenge is to remain creative under these circumstances, in which not the process but the contents remain leading. After all, it concerns the optimal monitoring of the safety of drugs used in clinical practice.

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