This English version is intended to be a reference material to provide convenience for users. In the event of inconsistency between the Japanese original and this English translation, the former shall prevail.

Appendix

Summary of Disproportionality Analysis Using VigiBase

July 20, 2023

Scope of investigation	Target drugs • Drugs categorized as “C10AA (HMG CoA reductase inhibitors)” under the ATC classification Target events • MedDRA v26.0 PT “Myasthenia gravis” or “Ocular myasthenia”
Outline of method	A disproportionality analysis for reports of myasthenia gravis associated with statins was performed using the dataset of the World Health Organization (WHO) Individual Case Safety Reports (ICSRs) Global Database (VigiBase) Note 1 as of May 23, 2023. Information components (ICs) were calculated as signal indices, and when the lower limit of the 95% confidence interval of IC (IC_{025}) was greater than 0, it was considered that a signal was detected. (Eur J Clin Pharmacol. 1998; 54: 315–21, Pharmacoepidemiol Drug Saf. 2009; 18: 427-36) VigiLyze, a signal detection/management tool of the WHO, was used for the data analysis.
Outline of results	Results The results of the disproportionality analysis for reports of myasthenia gravis and ocular myasthenia associated with statins using VigiBase are shown in Table 1 and 2. The number of adverse reactions of myasthenia gravis or ocular myasthenia reported for statins overall or for some individual statins (pravastatin, simvastatin, rosuvastatin, atorvastatin) was shown to be statistically higher than would be expected from the entire database.

Table 1: IC values for myasthenia gravis in the VigiBase dataset

Active ingredient	Number of adverse drug reaction reports	Number of reports of myasthenia gravis (observed)	Number of reports of myasthenia gravis (expected)	IC	IC_{025}

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	(observed)				
Statins	348 968	96	42	1.2	0.9
Pravastatin	22 341	16	3	2.4	1.6
Simvastatin	77 962	30	9	1.6	1.1
Rosuvastatin	68 032	22	8	1.4	0.7
Atorvastatin	143 314	37	17	1.1	0.6
Fluvastatin	8 366	3	1	1.2	−0.8
Lovastatin†	18 830	4	2	0.7	−1.0

* The number of cases of myasthenia gravis reported for all drugs was 4 142.
† Not marketed in Japan

Table 2: IC values for ocular myasthenia in the VigiBase dataset

Active ingredient	Number of reports of adverse drug reactions (observed)	Number of reports of ocular myasthenia (observed)	Number of reports of ocular myasthenia (expected)	IC	IC_{025}
Statins	348 968	18	3	2.4	1.7
Pravastatin	22 341	0	−	−	−
Simvastatin	77 962	4	1	2.0	0.2
Rosuvastatin	68 032	5	1	2.4	0.8
Atorvastatin	143 314	11	1	2.7	1.8
Fluvastatin	8 366	2	0	2.1	−0.5
Lovastatin†	18 830	0	−	−	−

*The number of cases of ocular myasthenia gravis reported for all drugs was 294.
† Not marketed in Japan

Discussion based on the results

The results of the disproportionality analysis using VigiBase suggested a relationship between statins and myasthenia gravis or ocular myasthenia. Note 2

Note 1: VigiBase is the WHO global database of reported potential adverse reactions of medicinal products, developed and maintained by Uppsala Monitoring Center (UMC). The information comes from a variety of sources, and the probability that the suspected adverse reaction is drug-related is not the same in all cases.

Note 2: The information does not represent the opinion of the WHO or UMC.