Summary –

Drug utilization study of dexamfetamine in European countries

A drug utilisation study (DUS) to follow the use of prescribed dexamfetamine in the European countries had been proposed during the marketing authorisation application as part of the risk management plan. The study provides drug utilisation data on an annual basis for up to 5 years for European countries, where dexamfetamine was marketed. The objectives are to describe how dexamfetamine is prescribed by physicians including the evaluation of off-label use (in terms of indication, age, prescribed overdose) and to collect data on abuse, misuse, overdose, diversion and dependence related to individual dexamfetamine use.

This study uses data from cross-sectional prescription databases, longitudinal EMR databases and national registries for the evaluation of the prescription behaviour of physicians. The data collection on abuse, misuse, overdose, diversion and dependence related to dexamfetamine use was performed by active examination of different kind of information sources like poison control centres/drug monitoring centres and supplemented by searches in the literature and the internet.

Due to the different methodological approaches, the results are presented in two separate reports. For the final report, the database report provides findings on the dexamfetamine prescription behaviour of physicians in Germany, the UK, the Netherlands, Finland, Denmark, Sweden and Norway up to 2015-2019. The literature review report provides updated findings on abuse, misuse, overdose, diversion and dependence related to individual dexamfetamine use in Denmark, Germany, the Netherlands, Norway and UK from 2011 to 2020.

Compared to last year's report of the database part, 1,704 prescriptions (IMS Medical Index) and 209 patients with 990 prescriptions (IMS Disease Analyzer) were added in Germany, 91 prescriptions (IMS Medical Index) in the Netherlands, 247 prescriptions (IMS Medical Index) in Finland, 1,105 patients with 12,900 prescriptions (Danish National Prescription Registry) in Denmark, 9,594 patients with 55,581 prescriptions (Swedish Prescription Database) in Sweden and 3,219 patients with 28,930 prescriptions (Norwegian Prescription Database) in Norway. In the UK, data was not received in time to be updated and therefore remained as in the previous year's report with 574 prescriptions (IMS Medical Index) and 149 patients with 1,340 prescriptions (CPRD). The updated results of the database part indicate that dexamfetamine prescriptions in children below 6 years continue to be issued very rarely. Off-label use of dexamfetamine due to prescriptions for adults were considerably high in all countries studied. Prescription of doses over 40 mg/day were observed rarely in the majority of countries, but more often in Finland and Sweden. Predominant use of dexamfetamine in adults might have contributed to these frequent doses over 40 mg/day. In contrast, prescriptions for non-licensed indications were low in all countries. When comparing off-label use over the years, no major change or trend outside normal annual fluctuations could be observed in any country. With the exception of one case in Germany, no evidence was found regarding the development of dependence to dexamfetamine. However, these findings were based on a relatively small number of patients and prescriptions especially in the Netherlands and Finland. In addition, in various countries, pharmacy produced dexamfetamine was on the market until recently or further indications were currently licensed. Therefore, the results of the database analyses should be evaluated carefully and the generalisability is limited.

According to the findings of the literature review, none of the searches revealed any substantial reports on abuse, misuse, overdose, diversion and dependence related to the use of dexamfetamine in Denmark, the Netherlands, Norway and the UK. In Germany, a representative study from 2018 reported that the lifetime prevalence of the use of prescription drugs containing amphetamines to

improve cognitive performance or mood without a medical indication was 1.7%, the last year prevalence was 0.8% and last month prevalence was 0.3%. The exact product names that fell into the category "prescription drugs containing amphetamines" as well as the exact proportion of dexamfetamine in the total number remained unclear. The sources used collecting spontaneous reporting contained only very few individual case reports but no evidence of a abuse, misuse, overdose, diversion and dependence related to dexamfetamine on a larger scale. Feedback from contacted poison control centres and drug monitoring centres in Denmark, Germany, the Netherlands, Norway and the United Kingdom did not lead to any additional reports, thus confirming that no substantive reports were missed. Based on search findings until September 2020, no evidence of potential abuse, misuse, overdose, diversion or dependence of dexamfetamine on a larger scale was found in the countries studied.

This is the final out of 5 consecutive reports and provides insights on the dexamfetamine prescription behaviour of physicians based on a broader patient and prescription basis. Overall, all findings were very consistent over the years. With regard to the study objectives, apart from frequent prescriptions to adults, general off-label use was low and no evidence of potential abuse, misuse, overdose, diversion or dependence of dexamfetamine on a larger scale was found.