NON-INTERVENTIONAL (NI) FINAL STUDY REPORT

PASS information

Title	Effectiveness of the Additional Risk Minimization Measures in Conveying Safety Information to HCPs Dispensing, Administering or Prescribing Fosphenytoin
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Joint PASS	No
Research question and objectives	Research question: How effective are the additional risk minimization measures that have been implemented across the European Union (EU) to mitigate the risks of medication errors in patients using fosphenytoin and off-label use in children under 5 years of age? Objectives: To estimate, among healthcare professionals (HCPs) who are involved in the prescribing, dispensing and administration of fosphenytoin, the proportion who: • Received the fosphenytoin Direct Healthcare Professional Communication (DHPC); • Read the fosphenytoin DHPC; • Know the risks of medication error and off-label use in children under 5 years of age associated with the use of fosphenytoin as described in the DHPC; • Understand the appropriate method of fosphenytoin dose calculation/ prescription as described by the dosing aid and Summary of Product Characteristics (SmPC); • Utilized the dosing aid in fosphenytoin dose prescription/dispensing/ administration.
Country(-ies) of study	France, United Kingdom (UK), Sweden
Author	Kofi Asomaning, Ph.D. Director, Epidemiology Pfizer Inc. 500 Arcola Road,

	Collegeville, PA 19426 USA

Marketing Authorization Holder(s)

Marketing Authorization Holder(s)	Pfizer Limited Ramsgate Road, Sandwich, Kent CT13 0NJ United Kingdom
MAH contact person	Kofi Asomaning, Ph.D. Director, Epidemiology Pfizer Inc. 500 Arcola Road, Collegeville, PA 19426 USA

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1. ABSTRACT (STAND-ALONE DOCUMENT)

Protocol A9821002 Version 1.0, 05 July 2018

Title: Effectiveness of the Additional Risk Minimization Measures in Conveying Safety Information to HCPs Dispensing, Administering or Prescribing Fosphenytoin.

Date: 25 November 2019

Name and affiliation of the main author: Kofi Asomaning, PhD.
Director, Epidemiology, Pfizer Inc.

Keywords: Fosphenytoin, survey, healthcare professionals, medication errors.

Rationale and background: Pfizer Inc. conducted a survey of healthcare professionals (HCPs) to evaluate the effectiveness of additional risk minimization measures (aRMMs) that have been implemented across European Union (EU) to mitigate the risks of medication errors in patients prescribed fosphenytoin (Pro-Epanutin®, Prodilantin® in France) and of off-label use of fosphenytoin in children under 5 years of age. Fosphenytoin is a pro-drug of phenytoin supplied in injectable form for intramuscular or intravenous administration and is indicated for short-term use in the control of generalized convulsive Status epilepticus (SE), the prevention and treatment of seizures during neurosurgery, and as substitute for oral phenytoin if oral administration is not possible and/or contra-indicated. In the EU, fosphenytoin is approved in the following countries: the UK, France, Ireland, Denmark, Finland, Sweden, Iceland, and Norway.

To ensure that the risks of medication errors in patients prescribed fosphenytoin and of off-label use of the medicine in children under 5 years of age are adequately minimized, aRMMs were implemented in the EU beginning July 2016. These included 1) distribution of a Direct Healthcare Professional Communication (DHPC) letter to highlight the risk of medication errors in patients prescribed fosphenytoin as well as off-label use in children under 5 years of age, and 2) distribution of dosing aids. The details of these aRMMS tools implemented across the EU along with the updated fosphenytoin Summary of Product Characteristics (SmPC)[1] are described in the current fosphenytoin Risk Management Plan (RMP) version 4.

Research question and objectives:

Research question:

How effective are the additional risk minimization measures that have been implemented across the EU to mitigate the risks of medication errors in patients using fosphenytoin and off-label use in children under 5 years of age?

Objectives:

The overall objective was to evaluate the effectiveness of the aRMMs to mitigate the risks of medication errors in patients using fosphenytoin and of off-label use in children under 5 years of age. The evaluation was conducted in 3 (UK, Sweden, and France) of the 8 countries in the EEA where Risk Minimization (RM) tools have been implemented.

Specifically, the objectives of the study were:

To estimate, among HCPs involved in the prescribing, dispensing and administration of fosphenytoin, the proportion who:

- Received the fosphenytoin DHPC;
- Read the fosphenytoin DHPC;
- Know the risks of medication error and off-label use in children under 5 years of age associated with the use of fosphenytoin as described in the DHPC;
- Understand the appropriate method of fosphenytoin dose calculation/prescription as described in the dosing aid and SmPC;
- Utilized the dosing aid in fosphenytoin dose prescription/dispensing/ administration.

Study design: This was a cross-sectional survey of HCPs (i.e. physicians, pharmacists, nurses) in the UK, Sweden and France. The data from the HCPs were collected using a structured questionnaire.

Setting: HCPs who had prescribed, dispensed, or administered fosphenytoin across the study countries constituted the study population for the survey.

The survey was conducted primarily through online questionnaires, with surveys administered over the phone for HCPs who indicated a phone preference. In each country, HCPs were identified according to their specialty as specified in the proprietary IQVIA OneKey lists (physicians, pharmacists, nurses). All HCPs in the 3 countries with available email and/or phone contact details on the OneKey list and from whom we had obtained prior consent to be contacted regarding surveys of this nature were contacted; there was no random selection of HCPs.

Subjects and study size, including dropouts: The survey was conducted among HCPs meeting the following inclusion criteria:

- HCPs with experience, prior to the survey administration, of prescribing/dispensing/administering at least one dose of fosphenytoin
- Willingness/consent to participate in this survey

Inactive and retired HCPs (when documented information was available to identify them) were deleted from the contact lists.

HCPs who confirmed that they met any of the following criteria at the beginning of the questionnaire were excluded:

- Not involved in patient treatment
- May have conflicts of interest with the survey (ie. self-identifying HCPs employed by regulatory bodies, pharmaceutical industries)
- Have participated in the pre-testing of the questionnaire ahead of the initiation of the survey

A sample size of approximately 200 completed surveys across the 3 countries (UK, Sweden, and France) was targeted, which was based on both statistical and practical considerations.

Variables and data sources:

Variables

The variables for analyses were derived from the survey data. These included HCP practice information (i.e. location, duration of practice, HCP primary profession, and past experience with fosphenytoin) and information related to the HCP knowledge about prescribing conditions and safety information/warnings of fosphenytoin (i.e. receipt and awareness of each of the aRMM tools, utilization of the Pfizer adult and children fosphenytoin dosing aids, and assessment of HCPs' knowledge/understanding of the risks of medication errors and of off-label use in children under 5 years of age).

Data sources

A structured questionnaire comprised of closed-ended questions and statements with multiple response choices (i.e. questions or statements asking the HCPs to choose from a defined list of responses) was used to collect the survey data using an online tool or phone administration.

Results: Overall 36,377 HCPs were targeted across Europe, with 312 (0.9%) HCPs eventually participating. The top three participating HCP specialties were Intensive Care Specialists (21%), and Neurologists and Anesthesiologists (16% each). Most participating HCPs had a duration of practice of more than 15 years (57.1 %), with over half of the HCPs prescribing fosphenytoin 'for adults only' (52.6%), followed by a third prescribing 'for both adults and children (≥5 years)' (34.0%), with the least HCPs prescribing only 'for children (≥5 years)' (13.5%). Participation rate was similar across all three countries (0.8-0.9%), with most HCPs from France (151), followed by the UK (104) and Sweden (57).

Nearly half (148/312 [47%]) of all the participating HCPs reported receiving the aRMM tools. A total of 114 HCPs reported receiving 'the Pfizer adult and children (aged 5 years and older) fosphenytoin dosing aids and 96/114 (84.2%) of the HCPs that received the dosing aids found them helpful. A total of 91/114 (79.8%) HCPs indicated that they prescribed, or administered Pro-Epanutin/Prodilantin (fosphenytoin) since receiving the Pfizer Pro-Epanutin (fosphenytoin) dosing aid(s). Of these 91 HCPs, 86 (94.5%) utilized the dosing aids when prescribing/dispensing/administering fosphenytoin and 68/86 (79.1%) utilized the dosing aidss to reduce the risk of a medication error.

Over two thirds of HCPs (226/312 [72%]) prescribed, dispensed, or administered fosphenytoin without using the Pfizer dosing aid(s). The most common reasons for not using the dosing aids were the lack of awareness of the dosing aid at the time of prescribing 87/226 (38.5%), use of a different dosing tool 77/226 (34.1%), or use of the SmPC 69/226 (30.5%) (multiple responses were allowed in the survey).

Overall, 252/312 (80.8%) of all HCPs who responded to the survey were aware of the association of fosphenytoin with cardiac arrest, and 244/312 (78.2%) knew that fosphenytoin when administered too rapidly can result in death. Two-thirds (211/312 [68%]) of HCPs knew that deaths had occurred when the correct dose of fosphenytoin was not administered. More than half (181/312 [58%]) of all HCPs were aware that fosphenytoin is not indicated for children younger than 5 years of age, and 186/312 (59.6%) HCPs knew that the maximum infusion rates differ between children and adults.

A large proportion of HCPs (299/312 [95.8%]) knew that fosphenytoin dose should be calculated based on the patient's weight, and 276/312 (88.5%) of HCPs were aware that fosphenytoin is dosed in milligrams phenytoin sodium equivalents (PE) per kilogram (mg PE/kg) body weight.

Discussion: The objective of this survey was to evaluate the effectiveness of the aRMMs in conveying safety information to HCPs dispensing, administering or prescribing fosphenytoin across the EU. The aRMMs were focused on mitigating risks of medication errors in all ages and off-label use in children under 5 years of age, associated with the use of fosphenytoin.

Given the 'restricted' indications and limited sale of fosphenytoin, several steps including multiple contact attempts were taken to maximize the anticipated low response rate. As a result, despite the very low response rate, the planned target of 200 HCPs was achieved.

Of those who received the aRMMs, a large proportion found them helpful. However, 47% of the surveyed HCPs reported receiving the aRMMs. Given the completed comprehensive distribution of the aRMMs (DHPC, dosing aids) and the ongoing distribution of the dosing aids as part of the product package insert, two possible explanations for the low receipt of the aRMMs are potential filtering of: 1) the initial distributed mail by administrative staff at the level of the healthcare facility and 2) the dosing aids as part of the product insert by hospital internal pharmacy procedures preventing distribution of dosing aids along with the fosphenytoin vials to the HCP actually administering fosphenytoin. One of the main reasons for not using the dosing aids detected by the survey was that HCPs were unaware of the dosing aids at the time of dispensing, prescribing or administering.

Most HCPs showed good awareness of the risks associated with the administration of fosphenytoin and showed high awareness of appropriate dose and prescription methods. HCPs also showed a good awareness of the appropriate methods of fosphenytoin dose calculation and prescription. On the other hand, a little more than half of responding HCPs were aware that fosphenytoin is not indicated for children under 5 years of age, and that the maximum infusion rates differ between children and adults. These results indicate that it is important to further educate HCPs with the existing aRMMs, focusing on information about

the appropriate dosing and off-label use in the paediatric population of children below the age of 5 years.

The study results should be interpreted with caution due to the low survey response rate. Nonetheless, it is important to note that the aRMMs are an effective way to communicate and raise awareness of risks. Where HCPs are aware of appropriate aRMMs, they are likely to utilize the information provided in the DHPC and dosing aids which were designed to decrease medication errors and off-label use in the paediatric population of children below the age of 5 years.

Marketing Authorization Holder(s): Pfizer Limited

Names and affiliations of principal investigators:

Name, degree(s)	Title	Affiliation	Address
Kofi Asomaning, PhD	Director, Epidemiology	Pfizer Inc.	500 Arcola Road, Collegeville, PA 19426 USA
Massoud Toussi, MD, PhD, MBA	Epidemiology and Drug Safety Lead	IQVIA	Tour D2, 17 bis, Place des Reflets, Courbevoie La Defanse, France

2. LIST OF ABBREVIATIONS

Abbreviation	Definition
AE	Adverse Event
AEM	Adverse Event Monitoring
ANSM	Agence Nationale de Sécurité du Médicament et des Produits de Santé
aRMMs	Additional Risk Minimisation Measures
CFR	Code of Federal Regulations
CIOMS	Council for International Organizations of Medical Sciences
CIs	Confidence Intervals
DHPC	Direct Healthcare Professional Communication

EDC	Electronic Data Capture
EEA	European Economic Area
EMA	European Medicines Agency
ENCePP	European Network of Centres for Pharmacoepidemiology and Pharmacovigilance
EU	European Union
GEP	Good Epidemiological Practice
GPP	Good Pharmacoepidemiology Practices
HCPs	Healthcare Professionals
HSCT	Hematopoietic stem cell transplant
IEA	International Epidemiological Association
IEC	Independent Ethics Committees
ISPOR	International Society for Pharmacoeconomics and Outcomes Research
ISPE	International Society for Pharmacoepidemiology
MAH	Market Authorisation Holder
MHRA	Medicines and Healthcare Products Regulatory Agency
NIS	Non-interventional Study
PASS	Post-Authorisation Safety Studies
PRAC	Pharmacovigilance Risk Assessment Committee
Q&A	Question &Answer
RM	Risk Minimization
RMP	Risk Management Plan
RMS	Reference Member State

SE	Status epilepticus
SmPC	Summary of Product Characteristics
SOPs	Standard Operating Procedures
UK	United Kingdom

3. INVESTIGATORS

Principal Investigator(s) of the Protocol

Name, degree(s)	Title	Affiliation	Address
Kofi Asomaning, PhD	Director, Epidemiology	Pfizer Inc.	500 Arcola Road, Collegeville, PA 19426 USA
Massoud Toussi, MD, PhD, MBA	Epidemiology and Drug Safety Lead	IQVIA	Tour D2, 17 bis, Place des Reflets, Courbevoie La Defanse, France

4. OTHER RESPONSIBLE PARTIES

Not applicable.

5. MILESTONES

Milestone	Planned Date	Actual Date
DHPC dissemination (with dosing aids included)	UK-29 September 2016 Sweden-28 November 2016 France-18 January 2017	UK-29 September 2016 Sweden-28 November 2016 France-18 January 2017
Registration in the EU PASS register	10 November 2018	03 January 2019
Start of data collection	10 December 2018	25 February 2019
End of data collection	04 March 2019	19 May 2019
Final study report	04 September 2019	

6. RATIONALE AND BACKGROUND

Fosphenytoin is a pro-drug of phenytoin supplied in injectable form for intramuscular or intravenous administration and indicated for short-term use in the control of generalized convulsive Status epilepticus (SE) and the prevention and treatment of seizures during neurosurgery. It can also be used as a substitute for oral phenytoin if oral administration is not possible and/or contraindicated.

Status epilepticus is characterized by the failure of mechanisms required for seizure termination, and results in abnormal, prolonged seizures with a risk of long-term consequences, such as neuronal injury and death.[2,3] Incidence rates in European countries range from 10–20/100,000 people.[2] Higher rates were found in men than in women, and in children[1] under 10 years of age and adults over 50 years of age, compared with adolescents and younger adults.[4]

Fosphenytoin received regulatory approval in the European Union (EU) in February 1998. In the EU, Fosphenytoin is registered in the following markets: the UK, France, Ireland, Denmark, Finland, Sweden, Iceland, and Norway. Post-marketing exposure in the form of persons, or person-years exposure, is not available for fosphenytoin. Fosphenytoin is used for short time periods, the duration of which varies between patients. Therefore, it is difficult to estimate patient exposure from volume of drug sales. In clinical studies, fosphenytoin was studied for up to 5 days. Sales data for fosphenytoin are only available from third quarter 2003 and not for the entire time period since fosphenytoin was first marketed.

The estimated European Economic Area (EEA) sales volume for fosphenytoin for all age groups is 766,700 standard units (1 standard unit is equal to 1 vial). The estimated sales volume is based on the number of vials sold as per applicable data provided by IQVIA from the third quarter 2003 through second quarter 2019, with July and August 2019 data extrapolated for Pfizer. Data for Keocyt was provided for 01 January 2008 through 31 August 2019. Keocyt is the license partner for fosphenytoin distribution in France. Fosphenytoin sales data in the EEA are presented in Table 1.

Table 1. Fosphenytoin Vials Sold in the EEA (3Q2003 through 31 August 2019)

Corporation	Country	Vials Sold (Thousands)	Reporting Period
Pfizer	Finland	318.3	3Q2003 – 31 Aug 2019[a]
	Sweden	221.1	3Q2003 – 31 Aug 2019[a]
	Denmark[b]	71.0	3Q2003 – 31 Aug 2019[a]
	Norway	69.4	3Q2003 – 31 Aug 2019[a]
	United Kingdom	26.8	3Q2003 – 31 Aug 2019[a]
	Ireland	7.5	3Q2003 – 31 Aug 2019[a]

[1] Please note that, in this document, unless otherwise stated, the term “children” is used to encompass paediatric ages from birth to less than 5 years of age.

Table 1. Fosphenytoin Vials Sold in the EEA (3Q2003 through 31 August 2019)

Corporation	Country	Vials Sold (Thousands)	Reporting Period
	Slovenia	1.1	3Q2003 – 31 Aug 2019[a]
Keocyt[c]	France	51.5	01 Jan 2008 – 31 Aug 2019
Total	**-**	**766.7**	**-**

a. Data provided by IQVIA for 3Q2003 – 2Q2019. Data extrapolated for July and August 2019. Extrapolation calculation: 2Q2019 data divided by number of days in April, May and June 2019 (91 days) = Number of vials sold per day. Multiply Number of vials sold per day by 61 days (number of days in July and August 2019).
b. Sales data for Denmark combines data for both Denmark and Iceland markets. Data is combined due to sharing the same packaging.
c. Data provided by License Partner.
Source: RMP version 4

Fosphenytoin dosing errors

Medication errors are an important identified risk for fosphenytoin and are due in part to the complexity of its dosing regimen and the measure of fosphenytoin dose using phenytoin sodium equivalents (PE). Fatal dosing errors with fosphenytoin have also been reported. Fosphenytoin overdoses have resulted from confusion stemming from the vial labelling (per mL confused with total vial content), the misinterpretation of a PE dose, confusion over infusion rates versus the total amount of drug to be dispensed or administered, and confusion regarding the loading versus the maintenance dose.

Medication errors with fosphenytoin are an important issue due to the use of this product in emergency situations (where mistakes can often be made), the vulnerable patient group being treated (who are seriously ill), and the potential serious medical sequelae of overdose (cardiac toxicity) or underdosing (prolonged seizures) with the product.

Medication errors with fosphenytoin have been an ongoing issue since the product was first approved in 1996 in the US. Previous regulatory actions included the distribution of ‘Direct Healthcare Professional’ letters in the US in 1999 and 2009, and in the EU in 2000. Prescribing information and package labelling have been revised on several occasions with the aim of reducing the risk of medication errors.

On 21 June 2012, Pfizer received a letter from the Agence Nationale de Sécurité du Médicament et des Produits de Santé (ANSM) requesting a review of off-label use of fosphenytoin in children less than 5 years of age, following ANSM review of reported medication errors associated with fosphenytoin in France between 2007 and 2009. The cumulative review of off-label use in children again highlighted the issue of medication errors with fosphenytoin.

The MAH conducted a cumulative review of medication errors (in patients of all ages) included in the last fosphenytoin Periodic Safety Update Report (PSUR) (covering the period 01 July 2010 through 04 August 2011). Following this assessment, the MAH completed an RMP for fosphenytoin, focused on medication errors and off-label use in children less than 5 years of age, and to investigate what activities beyond labelling may be appropriate to address these issues.

In 2013 Pfizer submitted to the UK (MHRA) a variation to minimize the risk of the off-label use of fosphenytoin in children under 5 years of age and medication errors in all ages via procedure UK/H/250/001/II/053.

During the assessment, questions were received regarding the dosing aids, including suggestions for separating adult and pediatric dosing aids and the use of “weight bands” in place of specific patient weights. User testing was conducted to ensure that the dosing aids provide additional clarity when used concurrently with SmPC, to ensure that it does not create confusion, and to test several options.

On 4th August 2016, the MAH received the end of procedure communication from the Reference Member State (RMS) the Medicines and Healthcare Products Regulatory Agency (MHRA). The approval of variation UK/H/250/001/II/053 included fosphenytoin Risk Management Plan (RMP) version 3.0 and the implementation of related Risk Minimization Measures (updated SmPC/PIL, carton/vial, DHPC, dosing aids).

The fosphenytoin RMP version 3.0 approved as part of the aforementioned variation, refers to required additional Pharmacovigilance Activities to Measure Effectiveness of Risk Minimisation Measures (Guideline on good pharmacovigilance practices (GVP) Module XVI – Risk minimization measures: selection of tools and effectiveness indicators) [5] and that the MAH would conduct a survey to evaluate the effectiveness of the fosphenytoin DHPC and dosing aid in conveying safety information to HCPs dispensing, administering or prescribing fosphenytoin.

The objective of this survey study was to evaluate the effectiveness of the aRMMs across Europe. For the purposes of conducting the effectiveness evaluation survey, the UK, Sweden and France, countries with relatively high use of fosphenytoin use, and/or adequate operational feasibility, were selected.

This non-interventional study is designated as a Post-Authorisation Safety Study (PASS category 3) and is a commitment to the MHRA.

7. RESEARCH QUESTION AND OBJECTIVES

Research question:
How effective are the additional risk minimization measures that have been implemented across the European Union (EU) to mitigate the risks of medication errors in patients using fosphenytoin and off-label use in children under 5 years of age?

Objectives:
The overall objective was to evaluate the effectiveness of the aRMMs to mitigate the risks of medication errors in patients using fosphenytoin and of off-label use in children under 5 years of age. Specifically, the objectives of this research were to estimate, among HCPs who are involved in the prescribing, dispensing and administration of fosphenytoin, the proportion who:

- Received the fosphenytoin DHPC;
- Read the fosphenytoin DHPC;
- Know the risks of medication error and off-label use in children under 5 years of age associated with the use of fosphenytoin as described in the DHPC;
- Understand the appropriate method of fosphenytoin dose calculation/prescription as described by the dosing aid and SmPC;
- Utilized the dosing aid in fosphenytoin dose prescription/dispensing/administration.

8. AMENDMENTS AND UPDATES

None

9. RESEARCH METHODS

9.1. Study design

This survey was a cross-sectional survey of HCPs (i.e. physicians, pharmacists, nurses) in the UK, Sweden and France. Physicians, pharmacists and nurses are all involved in the prescribing, dispensing and administration of fosphenytoin and as medication errors can occur at any of these steps, physicians, pharmacists, and nurses were all included in the study. The data from the HCPs were collected using a structured questionnaire. The UK, Sweden and France represented the highest volume of fosphenytoin users across the EU and/or the most operationally feasible countries and were expected to provide representativeness across the EU in understanding the effectiveness of the aRMMs.

9.2. Setting

In each country, HCPs were identified according to their specialty as specified in the proprietary IQVIA OneKey lists (physicians, pharmacists, nurses). OneKey is a comprehensive worldwide database of healthcare professionals. It is constructed according to ISO 9001: 2015 Quality Management Systems Requirements. All HCPs in the 3 countries with available email and/or phone contact details on the OneKey list and from whom we had obtained prior consent to be contacted regarding surveys of this nature were contacted; there was no random selection of HCPs.

The survey was conducted primarily through online questionnaires. Additionally, administration of the questionnaire by phone was proposed to HCPs who indicated a preference for this.. To ensure that the lists of HCPs in OneKey are comprehensive and representative of the HCPs population in the selected countries, the OneKey list is compared with staff listing for each and every Healthcare facility at least once a year. Per communication with IQVIA, the OneKey list has a coverage of 80-85% per specialty in each country.

Method of HCP recruitment for participation

The survey aimed to recruit approximately 200 HCPs that had prescribed, dispensed, or administered fosphenytoin across the 3 study countries, as determined by use of a screening question at the beginning of the survey.

HCPs in the 3 study countries were invited on a ‘targeted rolling’ basis by IQVIA to participate in the evaluation survey until the target study size was reached. HCPs were informed of the general purpose of the survey, the approximate duration of the survey, how the information obtained from the survey would be used, how their privacy would be protected and were offered compensation if allowable by local law.. The HCPs were then asked if they were willing to partake in a survey given the information provided and once the HCP agreed to partake in the survey, a full disclosure was then provided as described in the survey preamble (see Annex 2. Additional information).

This targeted rolling method of study HCP recruitment was preferred to the usual approach of ‘en masse send out’ of email invitations to all potential study participants due to the very poor response rate experienced in previous ‘en masse’ approach designed surveys. Using the

rolling basis of recruiting study participants was more efficient than an en masse approach as it only expanded to additional HCPs when needed.

The survey response rate was monitored every week by IQVIA and a report was sent to the MAH. Survey data were stratified by country and HCP primary profession (physician vs. pharmacist vs. nurse).

Each invitation to partake in the survey included information on how to access the survey and a unique code for each prescriber to ensure that the invitation was used only once. For the online version of the survey, there was an option available for the HCP to temporarily save an uncompleted survey and come back later to complete the survey prior to submission. Pfizer, Inc. reimbursed HCPs for their time spent completing the survey as governed by local laws and country regulations.

To ensure comprehension of the invitation and survey, all outreach to HCPs was conducted in local language. The survey and invitation as well as any reminder letters were translated by a certified translation vendor and phone interviews were also conducted in local language.

9.3. Subjects

9.3.1. Inclusion Criteria

The survey was conducted among HCPs meeting the following inclusion criteria:

- Prior experience prescribing/administering/dispensing of at least one dose of fosphenytoin
- Willingness/consent to participate in this survey

9.3.2. Exclusion Criteria

Inactive and retired HCPs (when documented information is available to identify them) were deleted from the contact lists.

The following exclusion criteria were checked at the beginning of the online questionnaire:

- HCPs who were not involved in patient treatment
- HCPs who may had conflicts of interest with the survey (i.e., HCPs employed by regulatory bodies or pharmaceutical industries)
- HCPs who had participated in the pre-testing of the questionnaire ahead of initiation of the survey

9.4. Variables

Data regarding the HCPs' practice information, and about their knowledge and awareness of aRMMs for fosphenytoin were collected.

1. HCPs practice information included:

    - Location (city/country)
    - Duration of practice
    - HCP primary profession (e.g. physician, nurse, pharmacist)
    - Past experience with fosphenytoin

2. Information related to the HCP knowledge about the prescribing conditions and safety information/warnings of fosphenytoin data included:

    - Receipt and awareness of each of the aRMM tools (i.e. the Pfizer fosphenytoin DHPC, and the Pfizer adult and children (aged 5 years and older) fosphenytoin dosing aids) among HCPs
    - Utilization of the Pfizer adult and children (aged 5 years and older) fosphenytoin dosing aids
    - Assessment of HCPs' knowledge/understanding of the risks of medication errors and off-label use in children under 5 years of age

9.5. Data sources and measurement

A structured questionnaire (see Annex 2. Additional information) comprised of closed-ended questions or statements with multiple response choices (i.e. questions or statements asking the HCPs to choose from a defined list of responses) was used to collect the survey data. The questionnaire collected data on HCP characteristics and their responses to the risk knowledge questions.

Questionnaires

The HCP questionnaire was developed by Pfizer and pre-tested by IQVIA among 14 HCPs for its comprehensibility, consistency and the appropriateness of medical terms. No changes were made to the questionnaire following pre-testing. The HCP questionnaire completion took 10-12 minutes during pre-testing.

Once approved by the appropriate regulatory agency, the questionnaire was translated into the local languages for Sweden and France.

9.5.1. Data Collection Process

The data collection (fieldwork) period lasted 12 weeks in each country. The survey started approximately 12-28 months after the date of first distribution of the aRMM tools in the individual countries.

Ideally, it is recommended that such a survey is conducted between 6 and 12 months after the distribution of the aRMM material. However, this product is not used commonly, and it was

important to allow sufficient time for HCPs to have used the product after the distribution of the aRMM material before responding to this survey.

HCPs were contacted by emails or phone calls, by the IQVIA Primary Intelligence team. The surveys were completed as follows:

- HCPs willing to participate in the online survey accessed the survey using the information provided in the invitation.

  HCPs could also choose to participate in the survey by phone. In this case, directions for scheduling an appointment for a phone interview were provided to them in the invitation. The phone interviews were also conducted by the IQVIA Primary Intelligence team.

- Those HCPs who self-reported having ever (at any time) prescribed, dispensed, or administered fosphenytoin at least once were eligible to complete the survey.

- If the questionnaire was not completed and submitted to IQVIA Primary Intelligence in one week after the invitation was sent out and no response had been received, the HCP was sent the first reminder by email.

- If the target number of HCPs was not achieved in any country or HCP category (stratum) (as described in section 9.7.2), an additional reminder by phone was conducted 1.5 weeks after the invitations have been sent out targeting HCPs in that particular category.

- If the questionnaire was still not completed and sent to IQVIA Primary Intelligence two weeks after the invitation was sent out, the HCPs were sent a third and last reminder by email. The recruitment was continued in each country until the target in a specific country or HCP category (stratum) was achieved or all potential respondents on the IQVIA OneKey list had been invited.

A HCP was considered as contacted if he/she:

- Answered the online questionnaire and sent it back to IQVIA Primary Intelligence. This includes HCPs that were ‘screen-outs’ i.e. HCPs that were deemed ineligible by their responses to the initial screening questions.

- Refused to participate.

A HCP was considered as unreachable if 5 attempts of contact were made without any response.

For each HCP of the sample, the number of contacts, and the date and time when he/she completed the online questionnaire were recorded. No further recruitment was initiated when the target for that country was reached. If the lists of HCPs were exhausted in any particular

stratum, the recruitments in this stratum was prematurely ended and the MAH adjusted the sample size with associated weighting (section 9.7.3).

9.5.2. Approaches for Increasing Response Rates

People are increasingly contacted to participate in online or phone surveys. The overall response rate of participation remains low according to international studies.[5,6,7] Holbrook et al. showed that in general, as more and more surveys are conducted, the response rate to surveys continues to decline over time, but a lower rate does not appear to reduce the representativeness of a demographic survey.[5] Van Geest et al. conducted a systematic review of 66 published reports on efforts to perform for improving response rates.[8] Two general strategies were explored: incentives-based approaches and survey design-based approaches. Financial incentives, even little ones, were effective in improving physician response rates while non-monetary incentives were less effective. The survey design was a short questionnaire; the questionnaire was personalized according to type of HCP and approved by professional associations.

In order to increase the response rate among HCPs, the following actions were applied to this survey:

- A compensation fee (50 Euros for physicians, 40 Euros pharmacists and nurses) was proposed to HCPs for their participation in the survey.
- Each HCP was emailed reminders or called up to 5 times before being considered as “not reachable”.

9.6. Bias

To quantify any selection bias, the distribution of each stratification criterion of HCPs (country, specialty, and the other available characteristics present in the screening log) was compared between participants and non-participants.

9.7. Study Size

9.7.1. Study Size Calculation

The precision of the sample size estimate calculations was based on the following assumptions:

- The confidence intervals (CIs) around the estimate are 2-sided.
- The probability of type-I error (alpha) is 5%.
- 50% of the HCPs will correctly answer key questions about the risks of medication errors and off-label use in children under 5 years of age with fosphenytoin (or 50% of HCPs’ practices with regard to mitigating the risks of medication errors and off-label use in children under 5 years of age are in accordance with the SmPC[1] prescribing information). Basing the sample size estimate on this assumption of 50% accurate

risks comprehension (or 50% of HCPs practices in accordance with the SmPC[1]) is the most conservative approach, since either a higher or lower percentage than 50% will lead to higher statistical precision for a given sample size.

The table below provides precision of the estimate (width of 95% CI around the estimate) for a range of sample sizes.

Table 2 .Precision of the Estimate for a Range of Sample Sizes

Sample Size	Statistical Precision
100	±9.8
150	±8.0
200	±6.9
250	±6.2
300	±5.7
350	±5.2
400	±4.9
450	±4.6
500	±4.4

A sample size of approximately 200 completed surveys aggregated across 3 countries (UK, France and Sweden) was targeted, which is based on both statistical and practical considerations. With a sample size of 200, the statistical precision around the estimate was ±6.9%; precision increases with larger sample sizes. It is to be noted that the final survey sample size depended on HCPs' willingness to participate in the survey. While the target was 200 respondents, all completed responses received by the cut-off date (12 weeks after the first set of invitations are sent) were included in the analysis.

9.7.2. Sampling Plan

For each selected country, the sample survey included HCPs identified and recruited from OneKey list. A screening question checked whether the HCP had ever prescribed, dispensed, or administered fosphenytoin and therefore could be considered for the survey.

The survey was deployed amongst emergency room physicians, neurologists, pediatricians, anesthesiologists, intensive care specialists, nurses and pharmacists.

As per sample size defined above and the number of selected countries, HCPs were stratified per country and according to the following table:

Table 3. Sampling Plan Stratified per Country and HCP Specialty Group

Country	Emergency room Physicians	Neurologists	Pediatricians	Anesthesi-ologists	IC	Pharmacists	Nurses	Total Sample
France	13	10	8	10	10	14	12	77
UK	13	10	8	10	10	14	12	77
Sweden	9	7	4	5	5	8	8	46
All	**35**	**27**	**20**	**25**	**25**	**36**	**32**	**200**

Abbreviations: IC, intensive care specialists

9.7.3. Sample Adjustment

Since the relative weight of each country and each category of HCPs in the final sample may be different from its real-life proportion, the extrapolation of the raw survey results to the overall target population would not be relevant without adjustment. The survey results were weighted to reflect the real proportion of the countries and the real proportion of each specialty in order to allow the extension of the survey results to the overall target population. Both unweighted (i.e., raw data) and weighted results are presented in the report.

A weight variable was applied to each statistical unit (i.e., the HCPs) during the results calculation in order to correct any over-or under-sampling that may have occurred for a country or specialty. This weight variable indicated how many unit(s) of the population of interest an observation counted in a statistical procedure. Its value varied per country and per specialty. The weights were normalized to obtain their sum equal to the sample size.

9.8. Data transformation

Detailed methodology for data transformations, particularly complex transformations (e.g., many raw variables used to derive an analytic variable), are documented in the statistical analysis plan (SAP) that is dated, filed and maintained by the sponsor (Annex 1. List of stand-alone documents).

9.9. Statistical methods

9.9.1. Main Summary Measures

To extend the survey results to the overall target population, calculations were first performed on raw data per specialty then weighted according to the real proportion of targeted HCPs in each country. The weighting method is described in section 9.9.2.

Descriptive Analysis
Categorical variables were summarized as the number (n) and percentage (%) per category. Percentages were displayed with one decimal place and computed using the number of non-missing data as the denominator.
In addition, 95% CIs are presented for percentages when relevant. Both lower and upper limits carried the same number of decimal places as the percentage (i.e. 1 decimal place).

For continuous variables, descriptive statistics included the number of non-missing observations (n), the mean and standard deviation (SD), median, 1st quartile and 3rd quartile (Q1, Q3), minimum and maximum values (Min, Max). For the mean, median, Q1 and Q3, the number of decimal places was that of the recorded data + 1. For the SD, the number of decimal places was that of the recorded data + 2. For the Min and Max, the same number of decimal places was used as in the recorded data.

In case of results for multiple choice questions, the frequencies of each option selected by the HCPs were reported in the statistical results. Different combinations of the answers provided were not considered.

9.9.2. Main Statistical Methods

Weighting Method for Sampling Adjustment

To account for the sampling design, the results of the survey were weighted back according to the real proportion of HCPs in each country from IQVIA's reference lists. The following weights were computed for the HCPs with submitted questionnaire.

Calculation of weights for each specialty group at country level (j)

$$W_{ij}^{1} = \frac{\frac{t_{ij}}{\sum_{i=1}^{I} t_{ij}}}{\frac{n_{ij}}{\sum_{i=1}^{I} n_{ij}}} \qquad (1)$$

Calculation of weights for each country

$$W_{j} = \frac{\frac{\sum_{i=1}^{I} t_{ij}}{\sum_{j=1}^{J}\sum_{i=1}^{I} t_{ij}}}{\frac{\sum_{i=1}^{I} n_{ij}}{\sum_{j=1}^{J}\sum_{i=1}^{I} n_{ij}}} \qquad (2)$$

$$= \frac{\frac{\sum_{i=1}^{I} t_{ij}}{T}}{\frac{\sum_{i=1}^{I} n_{ij}}{N}} \qquad (3)$$

Weights for each stratum (specialty group (i) in country (j))

$$W_{ij} = W_{ij}^{1} \times W_{j} \qquad (4)$$

$$= \frac{t_{ij}}{\sum_{j=1}^{J}\sum_{i=1}^{I} t_{ij}} \times \frac{\sum_{j=1}^{J}\sum_{i=1}^{I} n_{ij}}{n_{ij}} \qquad (5)$$

$$W_{ij} = \frac{t_{ij}}{T} \times \frac{N}{n_{ij}} \qquad (6)$$

Where,

- t_{ij}: universe size of the specialty group i for the country j
- T: size of the targeted HCPs
- n_{ij}: actual sample size of specialty group i for the country j
- N: size of the sample (HCPs with submitted questionnaire)
- I : number of speciality groups
- J : number of countries

All statistical units (i.e. HCPs) of the same stratum were weighted with the same final weight W_{ij} (defined by equation (6)).

9.9.3. Missing Values

Missing values were not replaced by imputation methods. They were expected to be few and distributed at random.

9.9.4. Sensitivity Analyses

None.

9.9.5. Amendments to the Statistical Analysis Plan

None.

9.10. Quality control

9.10.1. Approaches for Validating the Questionnaire

Questionnaires were tested among 14 HCPs for their comprehensibility, consistency and the appropriateness of medical terms.

9.10.2. Approaches for Validating the Results

The quality control for validating the results was conducted at more than one level:

1. The survey data were collected using a secure online electronic data capture (EDC) survey system. The proposed data entry system has been tested and was found to be secure for receiving and storing survey data. An online-based data repository was used to warehouse survey data and other relevant program information. This EDC system is an ‘EU Annex 11’ and ‘21 Code of Federal Regulations Part 11’ compliant platform for the entry, storage, manipulation, analysis and transmission of electronic information. This platform ensured compliance with all relevant regulatory guidelines and had been already

used in several Pharmacovigilance Risk Assessment Committee (PRAC)-approved surveys.

All data entered were single data entry directly done by the respondent.

- The reliability and security of the online questionnaire interface was verified by a qualified technical expert for each country.

- Monitoring of the quality and datasets definition was conducted by a qualified data manager. In the background of the online questionnaire, real-time checks of the answers provided by the respondents were developed. Non-admissible answers (i.e., incorrect or unusual values, outlying values) were detected and queries (when applicable) sent to the HCP.

2. At the study database level, final data quality checks were applied (beyond data management process):

   - Distribution of each variable in order to count the number of missing values and estimate the associated relative percentage,

   - Identification and count of non-analyzable questionnaires: estimation of the percentage of HCPs without complete analyzable questionnaire.

   Any changes in the database were tracked and documented. The country-datasets were stored in a dedicated database. Once the data were validated and quality checked, the database was locked.

3. At the statistical analysis level: all data management and statistical analysis programs developed and used in the analysis were documented. All versions generated were dated, kept with accompanying documentation and archived. The original database was stored. A derived database was created for the new versions of the data in order to include recoding and computing of new variables, especially stratification of continuous variables, combination of modalities for categorical variables, calculation of composite indicators, etc.

9.10.3. Safeguards, Security and Traceability of Contacts

Operators of the call center specialized in health surveys, were assigned to the project and trained on the survey methodology prior to fieldwork. The emails contacts and phone calls were traced using the management software.

9.11. Protection of human subjects

Healthcare Provider Information and Consent

All parties ensured protection of physician personal data and did not include HCP names on any Sponsor forms, reports, publications, or in any other disclosures, except where required

by laws. In case of data transfer, Pfizer maintained high standards of confidentiality and protection of HCP data.

Additionally, at the beginning of the survey, the respondent was asked if he/she agreed to take part in the survey. If yes, the respondent continued with the survey questions. If no, the survey was terminated.

Independent Ethics Committee (IEC)/Institutional Review Board (IRB)
No IEC/IRB review was required for this study.

Ethical Conduct of the Study
The study was conducted in accordance with legal and regulatory requirements, as well as with scientific purpose, value and rigor and followed generally accepted research practices described in the Guideline on Good Pharmacovigilance Practices (GVP) Module XVI- Risk Minimisation Measures: Selection of Tools and Effectiveness Indicators (EMA), *Good Pharmacoepidemiology Practices* (GPP) issued by the International Society for Pharmacoepidemiology (ISPE), *Good Epidemiological Practice* (GEP) guidelines issued by the International Epidemiological Association (IEA), *Good Outcomes Research Practices* issued by the International Society for Pharmacoeconomics and Outcomes Research (ISPOR), *International Ethical Guidelines for Epidemiological Research* issued by the Council for International Organizations of Medical Sciences (CIOMS), European Medicines Agency (EMA) European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP) *Guide on Methodological Standards in Pharmacoepidemiology* and FDA Guidance for Industry: *Good Pharmacovigilance Practices and Pharmacoepidemiologic Assessment.*

HCPs' information

HCPs participating in the survey were informed about the targets of the investigation, the nature of the transmitted data, the intended use of data, recipients of these data, and their right of access and rectification to their personal data, as well as their right of objection to use their data or to IQVIA keeping their data.

9.12. HCPs' Compensation

HCPs were offered a compensation for the time spent participating in this survey (that they could have refused). The time to complete the survey was estimated between 10-12 minutes.

The amount of this compensation was in line with the Sunshine Act and determined according to the European Pharmaceutical Market Research Association (EphMRA) recommendations and the Association of Opinion and Behavior in health field research companies (ASOCS) charter, and which states:

"When it is necessary to compensate a HCP in return to the time spent during an interview or a group meeting, the compensation must not exceed the fees commonly taken by the HCP for his/her advice or consultation and must be proportional to the time provided. The compensations should be clearly stated prior to the HCPs ' participation in the survey. They must be declared to the tax authorities in accordance with applicable laws".

A compensation fee (50 Euros for physicians, 40 Euros for pharmacists and nurses) was paid to accepting HCPs for their participation in the survey.

9.13. Confidentiality

Data confidentiality/Data security

Participating HCPs accessed the online site (https secured site) via a secure link using a personalized login and password. This link was unique to each HCP.

The answers provided were collected in an anonymous way, only aggregated data and presented as a synthesis were transmitted to the MAH.

Data were recorded in a central database and tracked using an audit trail. The system enabled retrieving all introduced data at any time and included security elements to prevent others than authorized staff from accessing data. Each user had a specific profile which limited his/her use of the database. A security copy of the database and the application files were made outside the server housing the online-based study. Security copies were periodically made and stored outside this server.

Description of all elements of security and traceability are available upon request.

10. RESULTS

10.1. Participants

10.1.1. HCP Participation Rate

All HCPs in the 3 countries with available email and/or phone contact details on the OneKey list (and from whom we had obtained prior consent to be contacted regarding surveys of this nature) were contacted; there was no random selection of HCPs.

Overall, 36,377 HCPs were targeted for participation with 312 HCPs (0.9%) eventually participating and submitting their data to the survey. Regarding the other HCPs who did not participate, around 64% of HCPs (23,268/36,377) were unreachable within 3-5 contacts, around 34% (12,257/36,377) did not respond within 1-2 contacts, 0.5% (171/36,377) of HCPs refused to participate, and 1% (369/36,377) of the HCPs were screened out due to not meeting the survey eligibility criteria. Within the participating HCPs, most were Intensive Care Specialists (65/312), and Neurologists or Anesthesiologists (49/312, each), with Neurologists and Intensive Care Specialists being the specialty group that participated the most (1.8% and 1.4%, respectively) with respect to the originally targeted HCP population within their specialty.

Most practitioners were targeted in France (17,256) followed by the UK (11,966) and Sweden (7,155). The eventual number of participating HCPs who submitted the survey also followed the same order, with 151 (0.9%) HCPs participating in France, 104 (0.9%) in the UK and 57 (0.8%) in Sweden. Further details on the participation rate of HCPs can be found in Table 4.

Table 4. HCPs Participation Rate

Country	Specialty Group							
	All	**Nurse**	**Pharmacist**	**Neurologist**	**Anesthesiologist**	**Intensive Care Specialist**	**Pediatrician**	**Other**
UK	N=11966	N=2756	N=1477	N=443	N=4922	N=1253	N=1112	N=3
Targeted, n	11966	2756	1477	443	4922	1253	1112	3
HCPs with no response (with 1-2 contacts), n (%) [1]	87 (0.7)	24 (0.9)	8 (0.5)	0 (0)	43 (0.9)	4 (0.3)	8 (0.7)	0 (0)
HCPs unreachable (with 3-5 contacts), n (%) [1]	11509 (96.2)	2655 (96.3)	1397 (94.6)	410 (92.6)	4773 (97)	1206 (96.2)	1068 (96)	0 (0)
HCPs refused to participate, n (%) [1]	75 (0.6)	7 (0.3)	3 (0.2)	5 (1.1)	41 (0.8)	13 (1)	6 (0.5)	0 (0)
HCPs screened out, n (%) [1]	191 (1.6)	38 (1.4)	51 (3.5)	10 (2.3)	54 (1.1)	16 (1.3)	22 (2)	0 (0)
HCPs participated (submitted surveys), n (%) [1]	104 (0.9)	32 (1.2)	18 (1.2)	18 (4.1)	11 (0.2)	14 (1.1)	8 (0.7)	3 (100)
Sweden	N=7155	N=4685	N=641	N=590	N=443	N=456	N=327	N=13
Targeted, n	7155	4685	641	590	443	456	327	13
HCPs with no response (with 1-2 contacts), n (%) [1]	6267 (87.6)	4537 (96.8)	8 (1.2)	563 (95.4)	424 (95.7)	438 (96.1)	297 (90.8)	0 (0)
HCPs unreachable (with 3-5 contacts), n (%) [1]	755 (10.6)	106 (2.3)	615 (95.9)	5 (0.8)	6 (1.4)	6 (1.3)	17 (5.2)	0 (0)
HCPs refused to participate, n (%) [1]	21 (0.3)	4 (0.1)	6 (0.9)	5 (0.8)	2 (0.5)	2 (0.4)	2 (0.6)	0 (0)
HCPs screened out, n (%) [1]	55 (0.8)	30 (0.6)	11 (1.7)	5 (0.8)	2 (0.5)	2 (0.4)	5 (1.5)	0 (0)
HCPs participated (submitted surveys), n (%) [1]	57 (0.8)	8 (0.2)	1 (0.2)	12 (2)	9 (2)	8 (1.8)	6 (1.8)	13 (100)
France	N=17256	N=601	N=2615	N=1683	N=5797	N=2885	N=3660	N=15
Targeted, n	17256	601	2615	1683	5797	2885	3660	15
HCPs with no response (with 1-2 contacts), n (%) [1]	5903 (34.2)	0 (0)	1230 (47)	1394 (82.8)	2708 (46.7)	0 (0)	571 (15.6)	0 (0)

Table 4. HCPs Participation Rate

Country	Specialty Group							
	All	**Nurse**	**Pharmacist**	**Neurologist**	**Anesthesiologist**	**Intensive Care Specialist**	**Pediatrician**	**Other**
HCPs unreachable (with 3-5 contacts), n (%) [1]	11004 (63.8)	570 (94.8)	1326 (50.7)	248 (14.7)	2990 (51.6)	2828 (98)	3042 (83.1)	0 (0)
HCPs refused to participate, n (%) [1]	75 (0.4)	26 (4.3)	1 (0)	7 (0.4)	26 (0.4)	6 (0.2)	9 (0.2)	0 (0)
HCPs screened out, n (%) [1]	123 (0.7)	4 (0.7)	35 (1.3)	15 (0.9)	44 (0.8)	8 (0.3)	17 (0.5)	0 (0)
HCPs participated (submitted surveys), n (%) [1]	151 (0.9)	1 (0.2)	23 (0.9)	19 (1.1)	29 (0.5)	43 (1.5)	21 (0.6)	15 (100)
Overall	N=36377	N=8042	N=4733	N=2716	N=11162	N=4594	N=5099	N=31
Targeted, n	36377	8042	4733	2716	11162	4594	5099	31
HCPs with no response (with 1-2 contacts), n (%) [1]	12257 (33.7)	4561 (56.7)	1246 (26.3)	1957 (72.1)	3175 (28.4)	442 (9.6)	876 (17.2)	0 (0)
HCPs unreachable (with 3-5 contacts), n (%) [1]	23268 (64)	3331 (41.4)	3338 (70.5)	663 (24.4)	7769 (69.6)	4040 (87.9)	4127 (80.9)	0 (0)
HCPs refused to participate, n (%) [1]	171 (0.5)	37 (0.5)	10 (0.2)	17 (0.6)	69 (0.6)	21 (0.5)	17 (0.3)	0 (0)
HCPs screened out, n (%) [1]	369 (1)	72 (0.9)	97 (2)	30 (1.1)	100 (0.9)	26 (0.6)	44 (0.9)	0 (0)
HCPs participated (submitted surveys), n (%) [1]	312 (0.9)	41 (0.5)	42 (0.9)	49 (1.8)	49 (0.4)	65 (1.4)	35 (0.7)	31 (100)

[1] Percentages are calculated using the number of targeted HCPs as the denominator.
HCP: Health Care Professional

10.2. Descriptive data

10.2.1. HCPs Practice information

Table 5 presents HCPs practice information (Q1-Q6 of HCP questionnaire). Regarding the duration of practice, overall most HCPs had a duration of practice of ‘more than 15 years’ (57.1 % [178/312]), followed by a duration of practice of ‘5 to 15 years’ (36.9%[115/312]) and ‘less than 5 years’ (6.1%[19/312]). Most HCPs prescribed, dispensed, or administered fosphenytoin ‘for adults only’ (52.6% [164/312]), followed by prescribing ‘for both adults and children (≥5 years)’ (34.0% [106/312]), with the least HCPs prescribing ‘for children (≥5 years)’ (13.5% [42/312]). Overall, the mean (SD) number of months since last prescription of fosphenytoin was 9.5 (15.34), and the mean (SD) number of patients prescribed, dispensed, or administered with fosphenytoin in the last 6 months was 9.5 (21.26) months.

The UK, Sweden and France followed a similar pattern of duration of practice as reported overall. In all three countries (UK, Sweden, France) HCPs prescribed mostly ‘for adults only’ (47.1%, 56.1% and 55.0% respectively), followed by prescribing ‘for both adults and children (≥5 years)’ (41.3%, 33.3% and 29.1%, respectively), and with the least HCPs prescribing ‘for children (≥5 years)’ across all three countries (11.5%, 10.5% and 15.9%, respectively). The mean (SD) of months since last prescription of fosphenytoin was lowest in the UK (7.4 [14.07]) followed by France (10.1 [15.37]) and Sweden (11.4 [17.22]). The mean (SD) number of patients prescribed,/dispensed or administered with fosphenytoin in the last 6 months was the highest in the UK (14.2 [17.62]), followed by Sweden (8.2 [39.56]) and France (6.7 [10.77]).

Table 5. HCPs Practice Information

Country	All Unweighted	All, Weighted	Specialty Group: Nurse	Pharmacist	Neurologist	Anesthesio-logist	Intensive Care Specialist	Pediatrician	Other
UK	(N=104)	(N=102.6)	(N=32)	(N=18)	(N=18)	(N=11)	(N=14)	(N=8)	(N=3)
Duration of practice, n (%) [1]	104	102.6	32	18	18	11	14	8	3
less than 5 years	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
5 to 15 years	32 (30.8)	30.4 (29.62)	8 (25)	7 (38.9)	9 (50)	4 (36.4)	3 (21.4)	0 (0)	1 (33.3)
>15 years	72 (69.2)	72.2 (70.38)	24 (75)	11 (61.1)	9 (50)	7 (63.6)	11 (78.6)	8 (100)	2 (66.7)
Ever prescribed/dispensed/administered fosphenytoin , n (%) [1]	104	102.6	32	18	18	11	14	8	3
For children (aged 5 years and older)	12 (11.5)	9.9 (9.68)	1 (3.1)	2 (11.1)	3 (16.7)	0 (0)	0 (0)	6 (75)	0 (0)
For adults only	49 (47.1)	55.8 (54.36)	7 (21.9)	10 (55.6)	8 (44.4)	8 (72.7)	13 (92.9)	1 (12.5)	2 (66.7)
For both	43 (41.3)	36.9 (35.96)	24 (75)	6 (33.3)	7 (38.9)	3 (27.3)	1 (7.1)	1 (12.5)	1 (33.3)
Number of months since last prescription of fosphenytoin									
n	104	102.6	32	18	18	11	14	8	3
Mean (SD)	7.4 (14.07)	12.38 (464.96)	2.6 (5.27)	6.2 (7.34)	4.8 (8.33)	20.9 (31.94)	11.2 (9.5)	11.4 (19.84)	2 (1.73)
Median	2	2.37	1	3	1.5	3	12	4	1
Q1, Q3	1 , 7	0.8 , 10.35	0 , 1.8	1 , 8	1 , 6	1 , 36	1 , 24	2 , 8.5	1 , 4
Min, Max	0 , 99	0 , 99	0 , 24	0 , 30	0 , 36	1 , 99	0 , 24	2 , 60	1 , 4
Number of patients prescribed/dispensed/administered with fosphenytoin in the last 6 months									
n	104	102.6	32	18	18	11	14	8	3
Mean (SD)	14.2 (17.62)	10.62 (142.84)	28.6 (18.55)	5.4 (6.89)	17.1 (21.22)	4.7 (6.28)	4.6 (6.91)	3.4 (4.87)	6 (7.81)
Median	5.5	4.03	29.5	2	6	3	2	2	2

Table 5. HCPs Practice Information

Country	All Unweighted	All, Weighted	Specialty Group: Nurse	Pharmacist	Neurologist	Anesthesio-logist	Intensive Care Specialist	Pediatrician	Other
Q1, Q3	2 , 21	0 , 14.11	16.5 , 40	0 , 10	4 , 20	0 , 9	0 , 6	1 , 3	1 , 15
Min, Max	0 , 60	0 , 60	0 , 60	0 , 22	0 , 60	0 , 20	0 , 25	0 , 15	1 , 15
Sweden	(N=57)	(N=61.4)	(N=8)	(N=1)	(N=12)	(N=9)	(N=8)	(N=6)	(N=13)
Duration of practice, n (%) [1]	57	61.4	8	1	12	9	8	6	13
Less than 5 years	2 (3.5)	0.8 (1.37)	0 (0)	0 (0)	2 (16.7)	0 (0)	0 (0)	0 (0)	0 (0)
5 to 15 years	24 (42.1)	36.4 (59.26)	5 (62.5)	1 (100)	5 (41.7)	4 (44.4)	2 (25)	2 (33.3)	5 (38.5)
>15 years	31 (54.4)	24.2 (39.37)	3 (37.5)	0 (0)	5 (41.7)	5 (55.6)	6 (75)	4 (66.7)	8 (61.5)
Ever prescribed/dispensed/administered fosphenytoin , n (%) [1]	57	61.4	8	1	12	9	8	6	13
For children (aged 5 years and older)	6 (10.5)	2.8 (4.57)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	6 (100)	0 (0)
For adults only	32 (56.1)	27 (44.01)	4 (50)	0 (0)	11 (91.7)	4 (44.4)	1 (12.5)	0 (0)	12 (92.3)
For both	19 (33.3)	31.6 (51.42)	4 (50)	1 (100)	1 (8.3)	5 (55.6)	7 (87.5)	0 (0)	1 (7.7)
Number of months since last prescription of fosphenytoin									
n	57	61.4	8	1	12	9	8	6	13
Mean (SD)	11.4 (17.22)	11.28 (261.10)	13.6 (14.31)	1 (-)	9.9 (18.91)	6.1 (5.82)	3 (3.38)	18.7 (13.74)	17.8 (25.97)
Median	3	2.68	7.5	1	2	6	1.5	24	8
Q1, Q3	1 , 18	0.91 , 19.07	2.5 , 24	1 , 1	1 , 11.5	1 , 10	1 , 4.5	3 , 24	3 , 24
Min, Max	0 , 96	0 , 96	1 , 40	1 , 1	0 , 67	0 , 18	0 , 10	1 , 36	1 , 96
Number of patients prescribed/dispensed/administered with fosphenytoin in the last 6 months									
n	57	61.4	8	1	12	9	8	6	13
Mean (SD)	8.2 (39.56)	4.82 (139.26)	2.8 (3.99)	1 (-)	29.7 (85.34)	3.7 (5.36)	3.4 (2.56)	0.8 (1.33)	2 (3)

Table 5. HCPs Practice Information

Country	All Unweighted	All, Weighted	Specialty Group: Nurse	Pharmacist	Neurologist	Anesthesio-logist	Intensive Care Specialist	Pediatrician	Other
Median	2	0.73	1	1	4	1	3.5	0	0
Q1, Q3	0 , 4	0 , 3.51	0 , 5	1 , 1	0 , 10	0 , 4	1 , 6	0 , 2	0 , 3
Min, Max	0 , 300	0 , 300	0 , 10	1 , 1	0 , 300	0 , 15	0 , 6	0 , 3	0 , 10
France	(N=151)	(N=148)	(N=1)	(N=23)	(N=19)	(N=29)	(N=43)	(N=21)	(N=15)
Duration of practice, n (%) [1]	151	148	1	23	19	29	43	21	15
Less than 5 years	17 (11.3)	21.7 (14.64)	0 (0)	2 (8.7)	0 (0)	7 (24.1)	3 (7)	4 (19)	1 (6.7)
5 to 15 years	59 (39.1)	55.1 (37.23)	0 (0)	9 (39.1)	7 (36.8)	11 (37.9)	15 (34.9)	9 (42.9)	8 (53.3)
>15 years	75 (49.7)	71.2 (48.13)	1 (100)	12 (52.2)	12 (63.2)	11 (37.9)	25 (58.1)	8 (38.1)	6 (40)
Ever prescribed/dispensed/administered fosphenytoin , n (%) [1]	151	148	1	23	19	29	43	21	15
For children (aged 5 years and older)	24 (15.9)	32.2 (21.77)	0 (0)	0 (0)	2 (10.5)	1 (3.4)	1 (2.3)	19 (90.5)	1 (6.7)
For adults only	83 (55)	77.2 (52.17)	1 (100)	13 (56.5)	14 (73.7)	18 (62.1)	31 (72.1)	0 (0)	6 (40)
For both	44 (29.1)	38.6 (26.06)	0 (0)	10 (43.5)	3 (15.8)	10 (34.5)	11 (25.6)	2 (9.5)	8 (53.3)
Number of months since last prescription of fosphenytoin									
n	151	148	1	23	19	29	43	21	15
Mean (SD)	10.1 (15.37)	12.88 (305.10)	6 (-)	3.7 (3.27)	9.2 (14.91)	24.4 (23.84)	4.8 (8.03)	10.5 (13.39)	9 (7.82)
Median	3	4.08	6	2	1	15	1	4	9
Q1, Q3	1 , 12	0.89 , 15.59	6 , 6	1 , 6	1 , 8	6 , 36	1 , 3	1 , 12	1 , 12
Min, Max	0 , 90	0 , 90	6 , 6	1 , 12	1 , 48	1 , 90	1 , 36	0 , 48	1 , 24
Number of patients prescribed/dispensed/administered with fosphenytoin in the last 6 months									
n	151	148	1	23	19	29	43	21	15
Mean (SD)	6.7 (10.77)	6.31 (140.386)	12 (-)	7.2 (8.91)	8.7 (12.45)	1.9 (3.08)	9.1 (13.22)	8.5 (13.57)	3.5 (4.61)

Table 5. HCPs Practice Information

Country	All Unweighted	All, Weighted	Specialty Group: Nurse	Pharmacist	Neurologist	Anesthesio-logist	Intensive Care Specialist	Pediatrician	Other
Median	3	2.34	12	4	3	0	5	2	1
Q1, Q3	0 , 8	0 , 5.86	12 , 12	2 , 10	1 , 10	0 , 3	2 , 10	0 , 8	0 , 5
Min, Max	0 , 69	0 , 69	12 , 12	1 , 40	0 , 40	0 , 12	0 , 69	0 , 50	0 , 15
Overall - Unweighted	(N=312)		(N=41)	(N=42)	(N=49)	(N=49)	(N=65)	(N=35)	(N=31)
Duration of practice, n (%) [1]	312		41	42	49	49	65	35	31
Less than 5 years	19 (6.1)		0 (0)	2 (4.8)	2 (4.1)	7 (14.3)	3 (4.6)	4 (11.4)	1 (3.2)
5 to 15 years	115 (36.9)		13 (31.7)	17 (40.5)	21 (42.9)	19 (38.8)	20 (30.8)	11 (31.4)	14 (45.2)
>15 years	178 (57.1)		28 (68.3)	23 (54.8)	26 (53.1)	23 (46.9)	42 (64.6)	20 (57.1)	16 (51.6)
Ever prescribed/dispensed/administered fosphenytoin , n (%) [1]	312		41	42	49	49	65	35	31
For children (aged 5 years and older)	42 (13.5)		1 (2.4)	2 (4.8)	5 (10.2)	1 (2)	1 (1.5)	31 (88.6)	1 (3.2)
For adults only	164 (52.6)		12 (29.3)	23 (54.8)	33 (67.3)	30 (61.2)	45 (69.2)	1 (2.9)	20 (64.5)
For both	106 (34)		28 (68.3)	17 (40.5)	11 (22.4)	18 (36.7)	19 (29.2)	3 (8.6)	10 (32.3)
Number of months since last prescription of fosphenytoin									
n	312		41	42	49	49	65	35	31
Mean (SD)	9.5 (15.34)		4.9 (8.76)	4.7 (5.48)	7.8 (13.97)	20.2 (24.44)	5.9 (8.37)	12.1 (14.95)	12 (18.11)
Median	3		1	3	1	12	2	5	8
Q1, Q3	1 , 12		0 , 3	1 , 6	1 , 6	3 , 30	1 , 6	2 , 24	1 , 15
Min, Max	0 , 99		0 , 40	0 , 30	0 , 67	0 , 99	0 , 36	0 , 60	1 , 96
Number of patients prescribed/dispensed/administ									

Table 5. HCPs Practice Information

Country	All Unweighted	All, Weighted	Specialty Group: Nurse	Pharmacist	Neurologist	Anesthesio-logist	Intensive Care Specialist	Pediatrician	Other
ered with fosphenytoin in the last 6 months									
n	312		41	42	49	49	65	35	31
Mean (SD)	9.5 (21.26)		23.1 (19.48)	6.3 (7.98)	16.9 (44.2)	2.8 (4.48)	7.4 (11.44)	6 (11.11)	3.1 (4.36)
Median	3		20	3	4	0	4	2	1
Q1, Q3	0 , 10		2 , 35	2 , 10	2 , 10	0 , 4	2 , 8	0 , 5	0 , 5
Min, Max	0 , 300		0 , 60	0 , 40	0 , 300	0 , 20	0 , 69	0 , 50	0 , 15
Overall - Weighted		(N=312)	(N=69)	(N=40.6)	(N=23.3)	(N=95.7)	(N=39.4)	(N=43.7)	(N=0.3)
Duration of practice, n (%) [1]		312	69	40.6	23.3	95.7	39.4	43.7	0.3
Less than 5 years		22.5 (7.21)	0 (0)	2 (4.8)	0.8 (3.62)	12 (12.54)	1.7 (4.38)	6 (13.67)	0 (3.23)
5 to 15 years		121.9 (39.06)	31 (44.98)	19.2 (47.3)	9.3 (40.04)	35.9 (37.5)	11.9 (30.23)	14.4 (32.9)	0.1 (45.16)
>15 years		167.6 (53.72)	38 (55.02)	19.4 (47.9)	13.1 (56.34)	47.8 (49.97)	25.8 (65.39)	23.4 (53.43)	0.1 (51.61)
Ever prescribed/dispensed/administered fosphenytoin , n (%) [1]		312	69	40.6	23.3	95.7	39.4	43.7	0.3
For children (aged 5 years and older)		45 (14.41)	0.7 (1.07)	1.4 (3.47)	2.2 (9.24)	1.7 (1.79)	0.6 (1.46)	38.4 (87.71)	0 (3.23)
For adults only		160 (51.29)	30.4 (44.1)	19.7 (48.57)	17 (72.82)	63.3 (66.07)	28.3 (71.84)	1.2 (2.73)	0.2 (64.52)
For both		107 (34.3)	37.8 (54.83)	19.5 (47.97)	4.2 (17.94)	30.8 (32.14)	10.5 (26.7)	4.2 (9.56)	0.1 (32.26)
Number of months since last prescription of fosphenytoin									
n		312	69	40.6	23.3	95.7	39.4	43.7	0.3
Mean (SD)		12.4 (612.19)	9.29 (272.23)	4.12 (35.58)	8.62 (63.97)	22.12 (552.46)	6.34 (52.84)	11.21 (136.11)	12.03 (1.01)
Median		2.88	2.52	1.89	0.97	10.67	1.37	3.91	5

Table 5. HCPs Practice Information

Country	All Unweighted	All, Weighted	Specialty Group: Nurse	Pharmacist	Neurologist	Anesthesio-logist	Intensive Care Specialist	Pediatrician	Other
Q1, Q3		0.88 , 13.84	0.86 , 11.58	0.59 , 4.29	0.46 , 6.22	1.77 , 31.69	0.74 , 7.9	1 , 11.6	1 , 12.75
Min, Max		0 , 99	0 , 40	0 , 30	0 , 67	0 , 99	0 , 36	0 , 60	1 , 96
Number of patients prescribed/dispensed/administered with fosphenytoin in the last 6 months									
n		312	69	40.6	23.3	95.7	39.4	43.7	0.3
Mean (SD)		7.43 (246.02)	12.29 (161.291)	5.78 (57.53)	14.65 (137.238)	3.2 (101.475)	7.33 (62.74)	6.87 (108.22)	3.1 (0.249)
Median		2.05	2.79	2	3.31	0	3.61	1.4	0.63
Q1, Q3		0 , 8.77	0 , 16.97	0.81 , 5.6	0.58 , 8.67	0 , 4.36	1.01 , 7.77	0 , 5.48	0 , 4.08
Min, Max		0 , 300	0 , 60	0 , 40	0 , 300	0 , 20	0 , 69	0 , 50	0 , 15

10.3. Outcome data

See section 10.4

10.4. Main results

Aggregate results are presented below; detailed country level results are presented in corresponding tables.

10.4.1. HCP receipt and awareness of aRMM tools

Table 6 shows information on HCPs' receipt and awareness of aRMM tools (Q7, Q9, Q10 of HCP questionnaire). Nearly half (47% [148/312]) of all the participating HCPs reported having received the aRMM tools. Overall, out of the 148 HCPs that received at least one of the aRMM tools, 70.9% (105/148) reported that they received the DHPC and 77.0% HCPs (114/148) reported that they received 'the Pfizer adult and children (aged 5 years and older) fosphenytoin dosing aids'. Furthermore, from the 114 HCPs that reported receiving 'the Pfizer adult and children (aged 5 years and older) fosphenytoin dosing aids' 41.2% (47/114) reported receiving it with DHPC, 21.9% (25/114) reported receiving it 'with other', 19.3% (22/114) received it with a package inserts and 17.5% (20/114) received both DHPC and a package insert. Across all the countries, overall 84.2% (96/114) HCPs reported the dosing aids as helpful. Across the countries, most HCPs received at least one of the aRMM tools in the UK (57.7% [60/104]), followed by France (45% [68/151]) and Sweden (35.1% [20/57]).

Table 6. HCPs receipt and awareness of aRMM tools

Country	All, Unweighted	All, Weighted	95% Confidence Interval, Weighted percent	Nurse	Pharmacist	Neurologist	Anesthesio-logist	Intensive Care Specialist	Pediatrician	Other
UK	(N=104)	(N=102.6)		(N=32)	(N=18)	(N=18)	(N=11)	(N=14)	(N=8)	(N=3)
Whether received at least one of aRMM tools, n (%) [1]	104	102.6		32	18	18	11	14	8	3
Yes	60 (57.7)	50.4 (49.14)	[35.15 - 63.12]	28 (87.5)	8 (44.4)	12 (66.7)	4 (36.4)	5 (35.7)	2 (25)	1 (33.3)
Received DHPC	48 (80)	32.5 (64.37)	[44.35 - 84.39]	28 (100)	5 (62.5)	10 (83.3)	1 (25)	3 (60)	0 (0)	1 (100)
Received the Pfizer adult and children (aged 5 years and older) fosphenytoin dosing aids	51 (85)	45.6 (90.45)	[83.03 - 97.87]	27 (96.4)	5 (62.5)	10 (83.3)	4 (100)	3 (60)	2 (100)	0 (0)
Received the Pfizer adult and children (aged 5 years and older) fosphenytoin dosing aids, n (%) [1]	51	45.6		27	5	10	4	3	2	0
With DHPC	24 (47.1)	16.6 (36.37)		16 (59.3)	2 (40)	3 (30)	0 (0)	2 (66.7)	1 (50)	
With package insert	9 (17.6)	15.3 (33.55)		0 (0)	2 (40)	2 (20)	3 (75)	1 (33.3)	1 (50)	
With DHPC and package insert	9 (17.6)	8.2 (17.9)		5 (18.5)	0 (0)	3 (30)	1 (25)	0 (0)	0 (0)	
With other	9 (17.6)	5.6 (12.19)		6 (22.2)	1 (20)	2 (20)	0 (0)	0 (0)	0 (0)	
Rated the dosing aids as, n (%) [1]	51	45.6		27	5	10	4	3	2	0
Helpful [2]	43 (84.3)	38.2 (83.67)	[67.23 – 100]	26 (96.3)	4 (80)	7 (70)	3 (75)	1 (33.3)	2 (100)	

Table 6. HCPs receipt and awareness of aRMM tools

Country	All, Unweighted	All, Weighted	95% Confidence Interval, Weighted percent	Nurse	Pharmacist	Neurologist	Anesthesio-logist	Intensive Care Specialist	Pediatrician	Other
Sweden	(N=57)	(N=61.4)		(N=8)	(N=1)	(N=12)	(N=9)	(N=8)	(N=6)	(N=13)
Whether received at least one of aRMM tools, n (%) [1]	57	61.4		8	1	12	9	8	6	13
Yes	20 (35.1)	26.7 (43.54)	[18.3 - 68.78]	4 (50)	0 (0)	6 (50)	4 (44.4)	3 (37.5)	2 (33.3)	1 (7.7)
Received DHPC	4 (20)	6.4 (24.13)	[0 - 59.57]	1 (25)		0 (0)	0 (0)	1 (33.3)	2 (100)	0 (0)
Received the Pfizer adult and children (aged 5 years and older) fosphenytoin dosing aids	17 (85)	20.7 (77.62)	[42.23 - 100]	3 (75)		6 (100)	4 (100)	2 (66.7)	1 (50)	1 (100)
Received the Pfizer adult and children (aged 5 years and older) fosphenytoin dosing aids, n (%) [1]	17	20.7		3	0	6	4	2	1	1
With DHPC	2 (11.8)	0.8 (4.07)		0 (0)		2 (33.3)	0 (0)	0 (0)	0 (0)	0 (0)
With package insert	9 (52.9)	17.8 (85.72)		3 (100)		0 (0)	3 (75)	2 (100)	1 (100)	0 (0)
With DHPC and package insert	1 (5.9)	0.4 (2.04)		0 (0)		0 (0)	1 (25)	0 (0)	0 (0)	0 (0)
With other	5 (29.4)	1.7 (8.17)		0 (0)		4 (66.7)	0 (0)	0 (0)	0 (0)	1 (100)
Rated the dosing aids as, n (%) [1]	17	20.7		3	0	6	4	2	1	1
Helpful [2]	15 (88.2)	15.2 (73.43)	[29.41 - 100]	2 (66.7)		6 (100)	4 (100)	1 (50)	1 (100)	1 (100)
France	(N=151)	(N=148)		(N=1)	(N=23)	(N=19)	(N=29)	(N=43)	(N=21)	(N=15)

Table 6. HCPs receipt and awareness of aRMM tools

Country	All, Unweighted	All, Weighted	95% Confidence Interval, Weighted percent	Nurse	Pharmacist	Neurologist	Anesthesio-logist	Intensive Care Specialist	Pediatrician	Other
Whether received at least one of aRMM tools, n (%) [1]	151	148		1	23	19	29	43	21	15
Yes	68 (45)	65.4 (44.2)	[34.58 - 53.81]	1 (100)	18 (78.3)	9 (47.4)	8 (27.6)	15 (34.9)	9 (42.9)	8 (53.3)
Received DHPC	53 (77.9)	52.9 (80.92)	[69.71 - 92.13]	1 (100)	13 (72.2)	9 (100)	6 (75)	13 (86.7)	7 (77.8)	4 (50)
Received the Pfizer adult and children (aged 5 years and older) fosphenytoin dosing aids	46 (67.6)	42.3 (64.62)	[49 - 80.23]	0 (0)	14 (77.8)	3 (33.3)	5 (62.5)	10 (66.7)	8 (88.9)	6 (75)
Received the Pfizer adult and children (aged 5 years and older) fosphenytoin dosing aids, n (%) [1]	46	42.3		0	14	3	5	10	8	6
With DHPC	21 (45.7)	20.1 (47.49)			7 (50)	2 (66.7)	2 (40)	4 (40)	4 (50)	2 (33.3)
With package insert	4 (8.7)	2.7 (6.39)			1 (7.1)	0 (0)	0 (0)	3 (30)	0 (0)	0 (0)
With DHPC and package insert	10 (21.7)	9.7 (23)			2 (14.3)	1 (33.3)	2 (40)	1 (10)	2 (25)	2 (33.3)
With other	11 (23.9)	9.8 (23.12)			4 (28.6)	0 (0)	1 (20)	2 (20)	2 (25)	2 (33.3)
Rated the dosing aids as, n (%) [1]	46	42.3		0	14	3	5	10	8	6
Helpful [2]	38 (82.6)	34.4 (81.49)	[68.62 - 94.36]		11 (78.6)	2 (66.7)	5 (100)	8 (80)	6 (75)	6 (100)
Overall - Unweighted	(N=312)			(N=41)	(N=42)	(N=49)	(N=49)	(N=65)	(N=35)	(N=31)

Table 6. HCPs receipt and awareness of aRMM tools

Country	All, Unweighted	All, Weighted	95% Confidence Interval, Weighted percent	Nurse	Pharmacist	Neurologist	Anesthesio-logist	Intensive Care Specialist	Pediatrician	Other
Whether received at least one of aRMM tools, n (%) [1]	312			41	42	49	49	65	35	31
Yes	148 (47.4)			33 (80.5)	26 (61.9)	27 (55.1)	16 (32.7)	23 (35.4)	13 (37.1)	10 (32.3)
Received DHPC	105 (70.9)			30 (90.9)	18 (69.2)	19 (70.4)	7 (43.8)	17 (73.9)	9 (69.2)	5 (50)
Received the Pfizer adult and children (aged 5 years and older) fosphenytoin dosing aids	114 (77)			30 (90.9)	19 (73.1)	19 (70.4)	13 (81.3)	15 (65.2)	11 (84.6)	7 (70)
Received the Pfizer adult and children (aged 5 years and older) fosphenytoin dosing aids, n (%) [1]	114			30	19	19	13	15	11	7
With DHPC	47 (41.2)			16 (53.3)	9 (47.4)	7 (36.8)	2 (15.4)	6 (40)	5 (45.5)	2 (28.6)
With package insert	22 (19.3)			3 (10)	3 (15.8)	2 (10.5)	6 (46.2)	6 (40)	2 (18.2)	0 (0)
With DHPC and package insert	20 (17.5)			5 (16.7)	2 (10.5)	4 (21.1)	4 (30.8)	1 (6.7)	2 (18.2)	2 (28.6)
With other	25 (21.9)			6 (20)	5 (26.3)	6 (31.6)	1 (7.7)	2 (13.3)	2 (18.2)	3 (42.9)
Rated the dosing aids as, n (%) [1]	114			30	19	19	13	15	11	7
Helpful [2]	96 (84.2)			28 (93.3)	15 (78.9)	15 (78.9)	12 (92.3)	10 (66.7)	9 (81.8)	7 (100)
Overall - Weighted		(N=312)		(N=69)	(N=40.6)	(N=23.3)	(N=95.7)	(N=39.4)	(N=43.7)	(N=0.3)
Whether received at least one of aRMM tools, n (%) [1]		312		69	40.6	23.3	95.7	39.4	43.7	0.3
Yes		142.56 (45.693)	[37.676 - 53.71]	45.9 (66.59)	23.2 (57.11)	11.9 (51.09)	30.8 (32.13)	13.9 (35.37)	16.8 (38.35)	0.1 (32.26)

Table 6. HCPs receipt and awareness of aRMM tools

Country	All, Unweighted	All, Weighted	95% Confidence Interval, Weighted percent	Nurse	Pharmacist	Neurologist	Anesthesio-logist	Intensive Care Specialist	Pediatrician	Other
Received DHPC		91.84 (64.423)	[52.173 - 76.673]	30.9 (67.19)	16.2 (69.86)	8.9 (75.19)	14.1 (45.93)	10.3 (73.71)	11.4 (67.96)	0 (50)
Received the Pfizer adult and children (aged 5 years and older) fosphenytoin dosing aids		108.62 (76.192)	[65.805 - 86.579]	35 (76.23)	17.2 (74.07)	6.9 (58.15)	25.6 (83.28)	9 (64.83)	14.8 (88.3)	0.1 (70)
Received the Pfizer adult and children (aged 5 years and older) fosphenytoin dosing aids, n (%) [1]		108.62		35	17.2	6.9	25.6	9	14.8	0.1
With DHPC		37.5 (34.526)		11.8 (33.76)	8.2 (47.95)	3 (43.29)	3.4 (13.39)	3.8 (42.47)	7.2 (48.42)	0 (28.57)
With package insert		35.78 (32.944)		15.1 (43.04)	2.4 (13.88)	0.4 (6.1)	12.8 (49.9)	3.5 (38.42)	1.7 (11.21)	0 (0)
With DHPC and package insert		18.31 (16.855)		3.7 (10.55)	2 (11.36)	1.4 (20.13)	7.7 (30.02)	0.6 (6.37)	3 (20.19)	0 (28.57)
With other		17.03 (15.675)		4.4 (12.66)	4.6 (26.81)	2.1 (30.48)	1.7 (6.69)	1.2 (12.74)	3 (20.19)	0 (42.86)
Rated the dosing aids as, n (%) [1]		108.62		35	17.2	6.9	25.6	9	14.8	0.1
Helpful [2]		87.84 (80.864)	[69.387 - 92.341]	29.3 (83.54)	13.5 (78.86)	5.5 (79.87)	21.8 (85.02)	5.9 (64.86)	11.8 (79.81)	0.1 (100)

[1] Percentages are calculated using the number of HCPs who answered this question as the denominator
[2] helpful defined as selecting "very helpful" or "extremely helpful" to Q10
aRMM: Additional Risk Minimization Measures, DHPC: Direct Healthcare Professional Communication, HCPs: Healthcare Professionals, UK: United Kingdom

10.4.2. HCPs knowledge about risks of fosphenytoin medication errors and off-label use

Table 7 presents the answers of the HCPs to Questions 8a-8e of the questionnaire. The questions test the HCPs' knowledge regarding the risks of fosphenytoin medication errors and off-label use in children under 5 years of age. In these questions, HCPs selected one response from 'True', 'False', 'I don't know' to 7 statements regarding fosphenytoin use. Overall, 54.8% (171/312) HCPs correctly answered all the statements asked in Question 8. The highest number of HCPs responded correctly to Q8d (80.8% [252/312]) with the correct response 'True' to 'In some cases, medication errors with Pro-Epanutin/Prodilantin (Fosphenytoin) have been associated with cardiac arrest.' The least HCPs responded correctly to Q8a (58.0% [181/312]) with the correct response 'False' to 'Pro-Epanutin/Prodilantin (Fosphenytoin) is indicated for children less than 5 years of age.'

Table 7. HCPs knowledge about the risks of fosphenytoin medication errors and off-label use in children under 5 years of age

Country	All, Unweighted	All, Weighted	95% Confidence Interval, Weighted percent	Nurse	Pharmacist	Neurologist	Anesthesio-logist	Intensive Care Specialist	Pediatrician	Other
UK	(N=104)	(N=102.6)		(N=32)	(N=18)	(N=18)	(N=11)	(N=14)	(N=8)	(N=3)
Know the risks of medication errors and off-label use in children under 5, n(%) [1]	104	102.6		32	18	18	11	14	8	3
Correctly answered 80% of all questions below [2]	74 (71.2)	71.2 (69.34)	[56.01 - 82.68]	29 (90.6)	10 (55.6)	12 (66.7)	7 (63.6)	8 (57.1)	6 (75)	2 (66.7)
Correctly answered for Q8a	75 (72.1)	69.5 (67.7)		30 (93.8)	15 (83.3)	13 (72.2)	6 (54.5)	5 (35.7)	6 (75)	0 (0)
Correctly answered for Q8b	91 (87.5)	88.1 (85.82)		32 (100)	13 (72.2)	15 (83.3)	9 (81.8)	12 (85.7)	7 (87.5)	3 (100)
Correctly answered for Q8c	81 (77.9)	85.2 (83.04)		28 (87.5)	12 (66.7)	12 (66.7)	10 (90.9)	12 (85.7)	5 (62.5)	2 (66.7)
Correctly answered for Q8d	94 (90.4)	93.8 (91.44)		31 (96.9)	16 (88.9)	14 (77.8)	10 (90.9)	13 (92.9)	7 (87.5)	3 (100)
Correctly answered for Q8e	77 (74)	68.5 (66.72)		31 (96.9)	10 (55.6)	14 (77.8)	6 (54.5)	7 (50)	6 (75)	3 (100)
Sweden	(N=57)	(N=61.4)		(N=8)	(N=1)	(N=12)	(N=9)	(N=8)	(N=6)	(N=13)
Know the risks of medication errors and off-label use in children under 5, n(%) [1]	57	61.4		8	1	12	9	8	6	13
Correctly answered 80% of all questions below [2]	15 (26.3)	14.7 (23.9)	[2.16 - 45.64]	1 (12.5)	1 (100)	1 (8.3)	3 (33.3)	4 (50)	1 (16.7)	4 (30.8)

Table 7. HCPs knowledge about the risks of fosphenytoin medication errors and off-label use in children under 5 years of age

Country	All, Unweighted	All, Weighted	95% Confidence Interval, Weighted percent	Nurse	Pharmacist	Neurologist	Anesthesio-logist	Intensive Care Specialist	Pediatrician	Other
Correctly answered for Q8a	17 (29.8)	24.1 (39.35)		4 (50)	0 (0)	1 (8.3)	4 (44.4)	2 (25)	2 (33.3)	4 (30.8)
Correctly answered for Q8b	36 (63.2)	31.3 (51.04)		3 (37.5)	1 (100)	8 (66.7)	6 (66.7)	5 (62.5)	5 (83.3)	8 (61.5)
Correctly answered for Q8c	25 (43.9)	18.6 (30.29)		1 (12.5)	1 (100)	3 (25)	8 (88.9)	5 (62.5)	2 (33.3)	5 (38.5)
Correctly answered for Q8d	27 (47.4)	18.6 (30.38)		1 (12.5)	1 (100)	7 (58.3)	3 (33.3)	5 (62.5)	3 (50)	7 (53.8)
Correctly answered for Q8e	28 (49.1)	38.3 (62.41)		5 (62.5)	1 (100)	4 (33.3)	5 (55.6)	5 (62.5)	3 (50)	5 (38.5)
France	(N=151)	(N=148)		(N=1)	(N=23)	(N=19)	(N=29)	(N=43)	(N=21)	(N=15)
Know the risks of medication errors and off-label use in children under 5, n(%) [1]	151	148		1	23	19	29	43	21	15
Correctly answered 80% of all questions below [2]	82 (54.3)	72.2 (48.81)	[39.24 - 58.38]	0 (0)	18 (78.3)	11 (57.9)	10 (34.5)	22 (51.2)	11 (52.4)	10 (66.7)
Correctly answered for Q8a	89 (58.9)	88.8 (59.99)		0 (0)	20 (87)	9 (47.4)	18 (62.1)	21 (48.8)	13 (61.9)	8 (53.3)
Correctly answered for Q8b	117 (77.5)	108.2 (73.12)		1 (100)	17 (73.9)	16 (84.2)	18 (62.1)	39 (90.7)	14 (66.7)	12 (80)
Correctly answered for Q8c	105 (69.5)	103.2 (69.7)		1 (100)	20 (87)	14 (73.7)	20 (69)	27 (62.8)	12 (57.1)	11 (73.3)
Correctly answered for Q8d	131 (86.8)	125.2 (84.62)		1 (100)	19 (82.6)	17 (89.5)	26 (89.7)	40 (93)	14 (66.7)	14 (93.3)
Correctly answered for Q8e	81 (53.6)	77.7 (52.51)		0 (0)	18 (78.3)	11 (57.9)	14 (48.3)	17 (39.5)	12 (57.1)	9 (60)

Table 7. HCPs knowledge about the risks of fosphenytoin medication errors and off-label use in children under 5 years of age

Country	All, Unweighted	All, Weighted	95% Confidence Interval, Weighted percent	Nurse	Pharmacist	Neurologist	Anesthesio-logist	Intensive Care Specialist	Pediatrician	Other
Overall - Unweighted	(N=312)			(N=41)	(N=42)	(N=49)	(N=49)	(N=65)	(N=35)	(N=31)
Know the risks of medication errors and off-label use in children under 5, n(%) [1]	312			41	42	49	49	65	35	31
Correctly answered 80% of all questions below [2]	171 (54.8)			30 (73.2)	29 (69)	24 (49)	20 (40.8)	34 (52.3)	18 (51.4)	16 (51.6)
Correctly answered for Q8a	181 (58)			34 (82.9)	35 (83.3)	23 (46.9)	28 (57.1)	28 (43.1)	21 (60)	12 (38.7)
Correctly answered for Q8b	244 (78.2)			36 (87.8)	31 (73.8)	39 (79.6)	33 (67.3)	56 (86.2)	26 (74.3)	23 (74.2)
Correctly answered for Q8c	211 (67.6)			30 (73.2)	33 (78.6)	29 (59.2)	38 (77.6)	44 (67.7)	19 (54.3)	18 (58.1)
Correctly answered for Q8d	252 (80.8)			33 (80.5)	36 (85.7)	38 (77.6)	39 (79.6)	58 (89.2)	24 (68.6)	24 (77.4)
Correctly answered for Q8e	186 (59.6)			36 (87.8)	29 (69)	29 (59.2)	25 (51)	29 (44.6)	21 (60)	17 (54.8)
Overall - Weighted		(N=312)		(N=69)	(N=40.6)	(N=23.3)	(N=95.7)	(N=39.4)	(N=43.7)	(N=0.3)
Know the risks of medication errors and off-label use in children under 5, n(%) [1]		312		69	40.6	23.3	95.7	39.4	43.7	0.3
Correctly answered 80% of all questions below [2]		158.08 (50.666)	[42.575 - 58.757]	26.4 (38.34)	30.1 (74.12)	11.3 (48.56)	45.3 (47.29)	20.8 (52.68)	24.1 (55.02)	0.1 (51.61)
Correctly answered for Q8a		182.41 (58.466)		42.3 (61.26)	30.1 (74.05)	10 (42.94)	55.6 (58.05)	16.9 (42.89)	27.5 (62.93)	0.1 (38.71)

Table 7. HCPs knowledge about the risks of fosphenytoin medication errors and off-label use in children under 5 years of age

Country	All, Unweighted	All, Weighted	95% Confidence Interval, Weighted percent	Nurse	Pharmacist	Neurologist	Anesthesio-logist	Intensive Care Specialist	Pediatrician	Other
Correctly answered for Q8b		227.62 (72.955)		43.9 (63.59)	31.2 (76.92)	18.7 (80.26)	67.9 (70.96)	34.1 (86.54)	31.6 (72.28)	0.2 (74.19)
Correctly answered for Q8c		206.97 (66.335)		30.9 (44.74)	33.4 (82.39)	14.4 (61.96)	76 (79.43)	27.2 (69.01)	24.8 (56.78)	0.2 (58.06)
Correctly answered for Q8d		237.73 (76.195)		33.1 (47.95)	35.3 (86.92)	18.8 (80.8)	84.2 (87.97)	35.4 (89.95)	30.7 (70.14)	0.2 (77.42)
Correctly answered for Q8e		184.48 (59.128)		48 (69.61)	30.1 (74.12)	13 (55.8)	49.1 (51.33)	17.6 (44.67)	26.5 (60.58)	0.1 (54.84)

[1] Percentages are calculated using the number of HCPs who answered this question as the denominator
[2]Q8 a. Pro-Epanutin/Prodilantin (Fosphenytoin) is indicated for children less than 5 years of age.
b. Too rapid administration of Pro-Epanutin/Prodilantin (Fosphenytoin) can result in death.
c. Fatalities have occurred when Pro-Epanutin/Prodilantin (Fosphenytoin) has not been dispensed or administered at the correct dose.
d. In some cases, medication errors with Pro-Epanutin/Prodilantin (Fosphenytoin) have been associated with cardiac arrest.
e. The maximum infusion rates differ between children and adults.
HCP: Healthcare Professional; UK: United Kingdom

10.4.3. HCPs knowledge about the appropriate method of fosphenytoin dose calculation/prescription

Table 8 summarizes the answers to questions Q8f and Q8g of the questionnaire which test the knowledge of HCPs regarding the appropriate method of fosphenytoin dose calculation/prescription. The correct answer to Q8f was 'True'– 'Pro-Epanutin/Prodilantin (Fosphenytoin) dose should be calculated based on the patient's weight.' Overall, 95.8% (299/312) of all HCPs answered this statement correctly. The correct answer to Q8g was also 'True' – 'Pro-Epanutin/Prodilantin (Fosphenytoin) is dosed in milligrams PE per kilogram (mg PE/kg)'. Overall, 88.5% (276/312) HCPs answered this statement correctly.

Table 8. HCPs knowledge about the appropriate method of fosphenytoin dose calculation/prescription

Country	All, Unweighted	All, Weighted	95% Confidence Interval, Weighted percent	Nurse	Pharmacist	Neurologist	Anesthesio-logist	Intensive Care Specialist	Pediatrician	Other
UK	(N=104)	(N=102.6)		(N=32)	(N=18)	(N=18)	(N=11)	(N=14)	(N=8)	(N=3)
Understand the appropriate method of fosphenytoin dose calculation/prescription, n(%) [1]	104	102.6		32	18	18	11	14	8	3
Correctly answered 80% of all questions below [2]	90 (86.5)	89.3 (87.04)	[78.31 - 95.78]	32 (100)	14 (77.8)	16 (88.9)	10 (90.9)	9 (64.3)	6 (75)	3 (100)
Correctly answered for Q8f	98 (94.2)	95.7 (93.25)		32 (100)	15 (83.3)	17 (94.4)	10 (90.9)	13 (92.9)	8 (100)	3 (100)
Correctly answered for Q8g	94 (90.4)	91.7 (89.31)		32 (100)	17 (94.4)	17 (94.4)	10 (90.9)	9 (64.3)	6 (75)	3 (100)
Sweden	(N=57)	(N=61.4)		(N=8)	(N=1)	(N=12)	(N=9)	(N=8)	(N=6)	(N=13)
Understand the appropriate method of fosphenytoin dose calculation/prescription, n(%) [1]	57	61.4		8	1	12	9	8	6	13
Correctly answered 80% of all questions below [2]	52 (91.2)	55.9 (91.09)	[75.37 – 100]	7 (87.5)	1 (100)	12 (100)	8 (88.9)	8 (100)	6 (100)	10 (76.9)
Correctly answered for Q8f	56 (98.2)	61.4 (99.99)		8 (100)	1 (100)	12 (100)	9 (100)	8 (100)	6 (100)	12 (92.3)
Correctly answered for Q8g	53 (93)	55.9 (91.1)		7 (87.5)	1 (100)	12 (100)	8 (88.9)	8 (100)	6 (100)	11 (84.6)
France	(N=151)	(N=148)		(N=1)	(N=23)	(N=19)	(N=29)	(N=43)	(N=21)	(N=15)

Table 8. HCPs knowledge about the appropriate method of fosphenytoin dose calculation/prescription

Country	All, Unweighted	All, Weighted	95% Confidence Interval, Weighted percent	Nurse	Pharmacist	Neurologist	Anesthesio-logist	Intensive Care Specialist	Pediatrician	Other
Understand the appropriate method of fosphenytoin dose calculation/prescription, n(%) [1]	151	148		1	23	19	29	43	21	15
Correctly answered 80% of all questions below [2]	124 (82.1)	118.6 (80.11)	[72.62 – 87.6]	1 (100)	19 (82.6)	15 (78.9)	24 (82.8)	37 (86)	14 (66.7)	14 (93.3)
Correctly answered for Q8f	145 (96)	140.2 (94.76)		1 (100)	23 (100)	18 (94.7)	27 (93.1)	42 (97.7)	19 (90.5)	15 (100)
Correctly answered for Q8g	129 (85.4)	125.6 (84.84)		1 (100)	19 (82.6)	15 (78.9)	26 (89.7)	38 (88.4)	16 (76.2)	14 (93.3)
Overall - Unweighted	(N=312)			(N=41)	(N=42)	(N=49)	(N=49)	(N=65)	(N=35)	(N=31)
Understand the appropriate method of fosphenytoin dose calculation/prescription, n(%) [1]	312			41	42	49	49	65	35	31
Correctly answered 80% of all questions below [2]	266 (85.3)			40 (97.6)	34 (81)	43 (87.8)	42 (85.7)	54 (83.1)	26 (74.3)	27 (87.1)
Correctly answered for Q8f	299 (95.8)			41 (100)	39 (92.9)	47 (95.9)	46 (93.9)	63 (96.9)	33 (94.3)	30 (96.8)
Correctly answered for Q8g	276 (88.5)			40 (97.6)	37 (88.1)	44 (89.8)	44 (89.8)	55 (84.6)	28 (80)	28 (90.3)
Overall - Weighted		(N=312)		(N=69)	(N=40.6)	(N=23.3)	(N=95.7)	(N=39.4)	(N=43.7)	(N=0.3)
Understand the appropriate method of fosphenytoin dose		312		69	40.6	23.3	95.7	39.4	43.7	0.3

Table 8. HCPs knowledge about the appropriate method of fosphenytoin dose calculation/prescription

Country	All, Unweighted	All, Weighted	95% Confidence Interval, Weighted percent	Nurse	Pharmacist	Neurologist	Anesthesio-logist	Intensive Care Specialist	Pediatrician	Other
calculation/prescription, n(%) [1]										
Correctly answered 80% of all questions below [2]		263.79 (84.55)	[79.067 - 90.032]	64 (92.72)	33.9 (83.46)	19.8 (85.14)	82.9 (86.6)	32.1 (81.5)	30.9 (70.62)	0.2 (87.1)
Correctly answered for Q8f		297.31 (95.292)		69 (100)	38.5 (94.8)	22.3 (95.83)	88.5 (92.41)	38.1 (96.59)	40.7 (93.16)	0.3 (96.77)
Correctly answered for Q8g		273.12 (87.538)		64 (92.72)	36 (88.66)	20 (86.05)	86.3 (90.18)	32.7 (82.96)	33.9 (77.46)	0.2 (90.32)

[1] Percentages are calculated using the number of HCPs who answered this question as the denominator
[2]Q8 f. Pro-Epanutin/Prodilantin (Fosphenytoin) dose should be calculated based on the patient's weight.
g. Pro-Epanutin/Prodilantin (Fosphenytoin) is dosed in milligrams phenytoin sodium equivalents (PE) per kilogram (mg PE/kg)

10.4.4. HCPs utilization of the aRMM tools

Table 9. presents information on the utilization of the aRMM tools by HCPs (Question 11, 12, 13 and 14 of the HCP questionnaire).

Q11 asked 'Have you prescribed, dispensed or administered Pro-Epanutin/Prodilantin (Fosphenytoin) since receiving the Pfizer Pro-Epanutin/Prodilantin (Fosphenytoin) dosing aid(s)?' Approximately a third of all HCPs (114/312) responded to this question and of the 114 respondents, 91 (79.8%) responded yes.

Q12 further investigated whether HCPs used the Pfizer dosing aids when prescribing fosphenytoin. Overall, out of the 91 HCPs that responded 'Yes' to Q12, 94.5% (86/91) HCPs responded 'Yes' to the use of Pfizer dosing aids when prescribing. Of the HCPs that used the Pfizer dosing aids, 59.3% (54/91) always used the child dosing aid, and 48.4% (44/91) always used the adult dosing aid.

Q13 looked into the reasons for the use of Pfizer dosing aids. Overall 86 HCPs responded to this question, and the most common reason (79.1%, or 68/86) given for using the dosing aids was 'To reduce the risk of a medication error'. The second most common reason in 62.8% (54/86) of the HCPs was that they 'found the Pfizer dosing aids easy to use'. Thirdly, 31.4% (27/86) HCPs 'needed a dosing tool to prescribe' and 4.7% (4/86) HCPs 'did not have another dosing tool available'.

Q14 investigated the main reasons for not using the Pfizer dosing aids. Overall 226/312 HCPs responded to this question, as these HCPs had prescribed, or dispensed or administered Pro-Epanutin/Prodilantin (Fosphenytoin) without using the Pfizer dosing aid(s). The most common reason (38.5%, or 87/226 of HCPs) for not using the dosing aids was that they were 'not aware of the dosing aid at the time of prescribing', followed by 34.1% (77/226) HCPs which 'already had a different dosing tool' and 30.5% (69/226) HCPs that 'used the SmPC and did not require additional instruction'. For further reasons for not using the Pfizer dosing aids refer to Table 9.

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Table 9. HCPs utilization of the aRMM tools

Country	All, Unweighted	All, Weighted	95% Confidence Interval, Weighted percent	Specialty Group						
				Nurse	Pharmacist	Neurologist	Anesthesio-logist	Intensive Care Specialist	Pediatrician	Other
UK	(N=104)	(N=102.6)		(N=32)	(N=18)	(N=18)	(N=11)	(N=14)	(N=8)	(N=3)
Have you prescribed/dispensed/administered Pro-Epanutin/Prodilantin (Fosphenytoin) since receiving the Pfizer Pro-Epanutin/Prodilantin (Fosphenytoin) dosing aid(s)?, n(%) [1]	51	45.6		27	5	10	4	3	2	0
Yes	46 (90.2)	42.1 (92.3)		27 (100)	4 (80)	8 (80)	4 (100)	3 (100)	0 (0)	
No	5 (9.8)	3.5 (7.7)		0 (0)	1 (20)	2 (20)	0 (0)	0 (0)	2 (100)	
You indicated that you have prescribed/dispensed/administered Pro-Epanutin/Prodilantin (Fosphenytoin) since receiving the Pfizer Pro-Epanutin/Prodilantin (Fosphenytoin) dosing aid(s). Did you use the Pfizer dosing aid(s)?	46	42.1		27	4	8	4	3	0	0
Yes (defined as "always", "often" or "Sometimes" used for either Adult dosing aids or Child dosing aids)	46 (100)	42.1 (100)	[100 - 100]	27 (100)	4 (100)	8 (100)	4 (100)	3 (100)		
Adult Dosing Aid	46	42.1		27	4	8	4	3	0	0
Always	26 (56.5)	21		21 (77.8)	1 (25)	2 (25)	1 (25)	1 (33.3)		

Table 9. HCPs utilization of the aRMM tools

Country	All, Unweighted	All, Weighted	95% Confidence Interval, Weighted percent	Specialty Group						
				Nurse	Pharmacist	Neurologist	Anesthesio-logist	Intensive Care Specialist	Pediatrician	Other
		.2 (50.46)								
Often	15 (32.6)	14.7 (34.83)		5 (18.5)	1 (25)	5 (62.5)	2 (50)	2 (66.7)		
Sometimes	5 (10.9)	6.2 (14.71)		1 (3.7)	2 (50)	1 (12.5)	1 (25)	0 (0)		
Never	0 (0)	0 (0)		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)		
Child Dosing Aid	46	42.1		27	4	8	4	3	0	0
Always	33 (71.7)	25.3 (60.08)		26 (96.3)	2 (50)	4 (50)	1 (25)	0 (0)		
Often	6 (13)	5.4 (12.94)		0 (0)	0 (0)	4 (50)	1 (25)	1 (33.3)		
Sometimes	5 (10.9)	9.9 (23.4)		0 (0)	2 (50)	0 (0)	2 (50)	1 (33.3)		
Never	2 (4.3)	1.5 (3.58)		1 (3.7)	0 (0)	0 (0)	0 (0)	1 (33.3)		
You prescribed/dispensed/administered Pro-Epanutin/Prodilantin (Fosphenytoin) using the Pfizer dosing aid(s). What were the main reasons why you used the Pfizer dosing aid(s)? n(%) [1]*	46	42.1		27	4	8	4	3	0	0
To reduce the risk of a medication error	37 (80.4)	27.2 (64.65)		25 (92.6)	3 (75)	6 (75)	1 (25)	2 (66.7)		
Find the Pfizer dosing aid easy to use	33 (71.7)	24.8 (58.95)		21 (77.8)	3 (75)	5 (62.5)	1 (25)	3 (100)		
Do not have another dosing tool available	1 (2.2)	0.7 (1.75)		1 (3.7)	0 (0)	0 (0)	0 (0)	0 (0)		
Need a dosing tool to prescribe	11 (23.9)	13.3 (31.51)		7 (25.9)	0 (0)	2 (25)	2 (50)	0 (0)		
Other	0 (0)	0 (0)		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)		

Table 9. HCPs utilization of the aRMM tools

Country	All, Unweighted	All, Weighted	95% Confidence Interval, Weighted percent	Specialty Group						
				Nurse	Pharmacist	Neurologist	Anesthesio-logist	Intensive Care Specialist	Pediatrician	Other
You prescribed/dispensed/administered Pro-Epanutin/Prodilantin (Fosphenytoin) without using the Pfizer dosing aid(s). What were the main reasons for not using the Pfizer dosing aid(s)? n(%) [1]*	58	60.5		5	14	10	7	11	8	3
Already have a different dosing tool	12 (20.7)	10.5 (17.31		1 (20)	1 (7.1)	4 (40)	1 (14.3)	1 (9.1)	3 (37.5)	1 (33.3)
Use the SmPC and do not requiring additional instruction	21 (36.2)	21.8 (36.08)		0 (0)	7 (50)	7 (70)	3 (42.9)	2 (18.2)	2 (25)	0 (0)
No need on a dosing tool	0 (0)	0 (0)		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Not aware of the dosing aid at the time of prescribing, dispensing or administering fosphenytoin	23 (39.7)	27.2 (44.95)		1 (20)	10 (71.4)	2 (20)	3 (42.9)	2 (18.2)	5 (62.5)	0 (0)
Do not find the Pfizer dosing aid(s) helpful	2 (3.4)	0.2 (0.36)		0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	1 (33.3)
Find the Pfizer dosing aid(s) complicated	2 (3.4)	0.8 (1.28)		0 (0)	0 (0)	0 (0)	0 (0)	1 (9.1)	0 (0)	1 (33.3)
Do not have the Pfizer dosing aid(s) readily available	19 (32.8)	23.4 (38.73)		2 (40)	4 (28.6)	1 (10)	3 (42.9)	5 (45.5)	3 (37.5)	1 (33.3)
Other	4 (6.9)	2.4 (4)		1 (20)	1 (7.1)	1 (10)	0 (0)	1 (9.1)	0 (0)	0 (0)
Sweden,	(N=57)	(N=61.4)		(N=8)	(N=1)	(N=12)	(N=9)	(N=8)	(N=6)	(N=13)
Have you prescribed/dispensed/administered Pro-Epanutin/Prodilantin	17	20.7		3	0	6	4	2	1	1

Table 9. HCPs utilization of the aRMM tools

Country	All, Unweighted	All, Weighted	95% Confidence Interval, Weighted percent	Specialty Group						
				Nurse	Pharmacist	Neurologist	Anesthesio-logist	Intensive Care Specialist	Pediatrician	Other
(Fosphenytoin) since receiving the Pfizer Pro-Epanutin/Prodilantin (Fosphenytoin) dosing aid(s)?, n(%) [1]										
Yes	8 (47.1)	8.1 (39)		1 (33.3)		3 (50)	2 (50)	1 (50)	1 (100)	0 (0)
No	9 (52.9)	12.7 (61)		2 (66.7)		3 (50)	2 (50)	1 (50)	0 (0)	1 (100)
You indicated that you have prescribed/dispensed/administered Pro-Epanutin/Prodilantin (Fosphenytoin) since receiving the Pfizer Pro-Epanutin/Prodilantin (Fosphenytoin) dosing aid(s). Did you use the Pfizer dosing aid(s)?	8	8.1		1	0	3	2	1	1	0
Yes (defined as "always", "often" or "Sometimes" used for either Adult dosing aids or Child dosing aids)	8 (100)	8.1 (100)	[100 - 100]	1 (100)		3 (100)	2 (100)	1 (100)	1 (100)	
Adult Dosing Aid	8	8.1		1	0	3	2	1	1	0
Always	3 (37.5)	5.9 (72.53)		1 (100)		1 (33.3)	1 (50)	0 (0)	0 (0)	
Often	1 (12.5)	0.4 (5.21)		0 (0)		1 (33.3)	0 (0)	0 (0)	0 (0)	
Sometimes	2 (25)	0.8 (10.43)		0 (0)		1 (33.3)	1 (50)	0 (0)	0 (0)	
Never	2 (25)	1 (11.82)		0 (0)		0 (0)	0 (0)	1 (100)	1 (100)	

Table 9. HCPs utilization of the aRMM tools

Country	All, Unweighted	All, Weighted	95% Confidence Interval, Weighted percent	Specialty Group						
				Nurse	Pharmacist	Neurologist	Anesthesio-logist	Intensive Care Specialist	Pediatrician	Other
Child Dosing Aid	8	8.1		1	0	3	2	1	1	0
Always	3 (37.5)	1.3 (15.65)		0 (0)		1 (33.3)	2 (100)	0 (0)	0 (0)	
Often	0 (0)	0 (0)		0 (0)		0 (0)	0 (0)	0 (0)	0 (0)	
Sometimes	2 (25)	1 (11.82)		0 (0)		0 (0)	0 (0)	1 (100)	1 (100)	
Never	3 (37.5)	5.9 (72.52)		1 (100)		2 (66.7)	0 (0)	0 (0)	0 (0)	
You prescribed/dispensed/administered Pro-Epanutin/Prodilantin (Fosphenytoin) using the Pfizer dosing aid(s). What were the main reasons why you used the Pfizer dosing aid(s)? n(%) [1]*	8	8.1		1	0	3	2	1	1	0
To reduce the risk of a medication error	6 (75)	2.6 (32.12)		0 (0)		3 (100)	2 (100)	1 (100)	0 (0)	
Find the Pfizer dosing aid easy to use	5 (62.5)	6.8 (83.52)		1 (100)		2 (66.7)	1 (50)	0 (0)	1 (100)	
Do not have another dosing tool available	2 (25)	0.9 (11)		0 (0)		0 (0)	1 (50)	0 (0)	1 (100)	
Need a dosing tool to prescribe	2 (25)	0.8 (10.43)		0 (0)		1 (33.3)	1 (50)	0 (0)	0 (0)	
Other	0 (0)	0 (0)		0 (0)		0 (0)	0 (0)	0 (0)	0 (0)	
You prescribed/dispensed/administered Pro-Epanutin/Prodilantin (Fosphenytoin) without using the Pfizer dosing aid(s). What were	49	53.3		7	1	9	7	7	5	13

Table 9. HCPs utilization of the aRMM tools

Country	All, Unweighted	All, Weighted	95% Confidence Interval, Weighted percent	Specialty Group						
				Nurse	Pharmacist	Neurologist	Anesthesio-logist	Intensive Care Specialist	Pediatrician	Other
the main reasons for not using the Pfizer dosing aid(s)? n(%) [1]*										
Already have a different dosing tool	33 (67.3)	28.3 (53.05)		3 (42.9)	1 (100)	7 (77.8)	3 (42.9)	5 (71.4)	2 (40)	12 (92.3)
Use the SmPC and do not requiring additional instruction	2 (4.1)	5.9 (11.11)		0 (0)	1 (100)	1 (11.1)	0 (0)	0 (0)	0 (0)	0 (0)
No need on a dosing tool	1 (2)	0.5 (0.92)		0 (0)	0 (0)	0 (0)	0 (0)	1 (14.3)	0 (0)	0 (0)
Not aware of the dosing aid at the time of prescribing, dispensing or administering fosphenytoin	12 (24.5)	13.5 (25.4)		2 (28.6)	0 (0)	1 (11.1)	5 (71.4)	0 (0)	2 (40)	2 (15.4)
Do not find the Pfizer dosing aid(s) helpful	0 (0)	0 (0)		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Find the Pfizer dosing aid(s) complicated	0 (0)	0 (0)		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Do not have the Pfizer dosing aid(s) readily available	14 (28.6)	14.1 (26.54)		2 (28.6)	0 (0)	2 (22.2)	2 (28.6)	2 (28.6)	3 (60)	3 (23.1)
Other	0 (0)	0 (0)		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
France	(N=151)	(N=148)		(N=1)	(N=23)	(N=19)	(N=29)	(N=43)	(N=21)	(N=15)
Have you prescribed/dispensed/administered Pro-Epanutin/Prodilantin (Fosphenytoin) since receiving the Pfizer Pro-Epanutin/Prodilantin (Fosphenytoin) dosing aid(s)?, n(%) [1]	46	42.3		0	14	3	5	10	8	6
Yes	37 (80.4)	34.4 (81.35)			9 (64.3)	3 (100)	5 (100)	10 (100)	6 (75)	4 (66.7)

Table 9. HCPs utilization of the aRMM tools

Country	All, Unweighted	All, Weighted	95% Confidence Interval, Weighted percent	Specialty Group						
				Nurse	Pharmacist	Neurologist	Anesthesio-logist	Intensive Care Specialist	Pediatrician	Other
No	9 (19.6)	7.9 (18.65)			5 (35.7)	0 (0)	0 (0)	0 (0)	2 (25)	2 (33.3)
You indicated that you have prescribed/dispensed/administered Pro-Epanutin/Prodilantin (Fosphenytoin) since receiving the Pfizer Pro-Epanutin/Prodilantin (Fosphenytoin) dosing aid(s). Did you use the Pfizer dosing aid(s)?	37	34.4		0	9	3	5	10	6	4
Yes (defined as "always", "often" or "Sometimes" used for either Adult dosing aids or Child dosing aids)	32 (86.5)	29.8 (86.63)	[74.29 - 98.98]		7 (77.8)	3 (100)	5 (100)	8 (80)	5 (83.3)	4 (100)
Adult Dosing Aid	37	34.4		0	9	3	5	10	6	4
Always	15 (40.5)	10.8 (31.34)			3 (33.3)	2 (66.7)	2 (40)	5 (50)	0 (0)	3 (75)
Often	8 (21.6)	6.6 (19.08)			3 (33.3)	1 (33.3)	1 (20)	2 (20)	0 (0)	1 (25)
Sometimes	5 (13.5)	6.5 (18.83)			1 (11.1)	0 (0)	2 (40)	1 (10)	1 (16.7)	0 (0)
Never	9 (24.3)	10.6 (30.75)			2 (22.2)	0 (0)	0 (0)	2 (20)	5 (83.3)	0 (0)
Child Dosing Aid	37	34.4		0	9	3	5	10	6	4
Always	18 (48.6)	14.4 (41.99)			6 (66.7)	1 (33.3)	2 (40)	5 (50)	1 (16.7)	3 (75)
Often	3 (8.1)	2.1 (6.05)			0 (0)	0 (0)	0 (0)	1 (10)	1 (16.7)	1 (25)
Sometimes	5 (13.5)	7 (20.24)			0 (0)	1 (33.3)	1 (20)	0 (0)	3 (50)	0 (0)

Table 9. HCPs utilization of the aRMM tools

Country	All, Unweighted	All, Weighted	95% Confidence Interval, Weighted percent	Specialty Group						
				Nurse	Pharmacist	Neurologist	Anesthesio-logist	Intensive Care Specialist	Pediatrician	Other
Never	11 (29.7)	10.9 (31.73)			3 (33.3)	1 (33.3)	2 (40)	4 (40)	1 (16.7)	0 (0)
You prescribed/dispensed/administered Pro-Epanutin/Prodilantin (Fosphenytoin) using the Pfizer dosing aid(s). What were the main reasons why you used the Pfizer dosing aid(s)? n(%) [1]*	32	29.8		0	7	3	5	8	5	4
To reduce the risk of a medication error	25 (78.1)	22.9 (77.03)			7 (100)	2 (66.7)	3 (60)	6 (75)	4 (80)	3 (75)
Find the Pfizer dosing aid easy to use	16 (50)	16.2 (54.5)			3 (42.9)	0 (0)	4 (80)	6 (75)	2 (40)	1 (25)
Do not have another dosing tool available	1 (3.1)	1 (3.27)			1 (14.3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Need a dosing tool to prescribe	14 (43.8)	9.8 (32.77)			3 (42.9)	2 (66.7)	0 (0)	4 (50)	2 (40)	3 (75)
Other	0 (0)	0 (0)			0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
You prescribed/dispensed/administered Pro-Epanutin/Prodilantin (Fosphenytoin) without using the Pfizer dosing aid(s). What were the main reasons for not using the Pfizer dosing aid(s)? n(%) [1]*	119	118.2		1	16	16	24	35	16	11
Already have a different dosing tool	32 (26.9)	26.7 (22.59)		0 (0)	4 (25)	2 (12.5)	4 (16.7)	12 (34.3)	5 (31.3)	5 (45.5)
Use the SmPC and do not requiring additional instruction	46 (38.7)	49.3 (41.68)		1 (100)	7 (43.8)	10 (62.5)	10 (41.7)	14 (40)	3 (18.8)	1 (9.1)

Table 9. HCPs utilization of the aRMM tools

Country	All, Unweighted	All, Weighted	95% Confidence Interval, Weighted percent	Specialty Group						
				Nurse	Pharmacist	Neurologist	Anesthesio-logist	Intensive Care Specialist	Pediatrician	Other
No need on a dosing tool	4 (3.4)	1.7 (1.47)		0 (0)	0 (0)	0 (0)	0 (0)	3 (8.6)	0 (0)	1 (9.1)
Not aware of the dosing aid at the time of prescribing, dispensing or administering fosphenytoin	52 (43.7)	54.2 (45.83)		0 (0)	11 (68.8)	6 (37.5)	11 (45.8)	14 (40)	8 (50)	2 (18.2)
Do not find the Pfizer dosing aid(s) helpful	2 (1.7)	1.2 (0.97)		0 (0)	0 (0)	0 (0)	0 (0)	2 (5.7)	0 (0)	0 (0)
Find the Pfizer dosing aid(s) complicated	2 (1.7)	1.3 (1.13)		0 (0)	0 (0)	1 (6.3)	0 (0)	1 (2.9)	0 (0)	0 (0)
Do not have the Pfizer dosing aid(s) readily available	25 (21)	24.5 (20.7)		0 (0)	4 (25)	2 (12.5)	8 (33.3)	4 (11.4)	2 (12.5)	5 (45.5)
Other	9 (7.6)	6.2 (5.22)		0 (0)	2 (12.5)	1 (6.3)	1 (4.2)	3 (8.6)	0 (0)	2 (18.2)
Overall - Unweighted	(N=312)			(N=41)	(N=42)	(N=49)	(N=49)	(N=65)	(N=35)	(N=31)
Have you prescribed/dispensed/administered Pro-Epanutin/Prodilantin (Fosphenytoin) since receiving the Pfizer Pro-Epanutin/Prodilantin (Fosphenytoin) dosing aid(s)?, n(%) [1]	114			30	19	19	13	15	11	7
Yes	91 (79.8)			28 (93.3)	13 (68.4)	14 (73.7)	11 (84.6)	14 (93.3)	7 (63.6)	4 (57.1)
No	23 (20.2)			2 (6.7)	6 (31.6)	5 (26.3)	2 (15.4)	1 (6.7)	4 (36.4)	3 (42.9)
You indicated that you have prescribed/dispensed/administered Pro-Epanutin/Prodilantin	91			28	13	14	11	14	7	4

Table 9. HCPs utilization of the aRMM tools

Country	All, Unweighted	All, Weighted	95% Confidence Interval, Weighted percent	Specialty Group						
				Nurse	Pharmacist	Neurologist	Anesthesio-logist	Intensive Care Specialist	Pediatrician	Other
(Fosphenytoin) since receiving the Pfizer Pro-Epanutin/Prodilantin (Fosphenytoin) dosing aid(s). Did you use the Pfizer dosing aid(s)? Yes (defined as "always", "often" or "Sometimes" used for either Adult dosing aids or Child dosing aids)	86 (94.5)			28 (100)	11 (84.6)	14 (100)	11 (100)	12 (85.7)	6 (85.7)	4 (100)
Adult Dosing Aid	91			28	13	14	11	14	7	4
Always	44 (48.4)			22 (78.6)	4 (30.8)	5 (35.7)	4 (36.4)	6 (42.9)	0 (0)	3 (75)
Often	24 (26.4)			5 (17.9)	4 (30.8)	7 (50)	3 (27.3)	4 (28.6)	0 (0)	1 (25)
Sometimes	12 (13.2)			1 (3.6)	3 (23.1)	2 (14.3)	4 (36.4)	1 (7.1)	1 (14.3)	0 (0)
Never	11 (12.1)			0 (0)	2 (15.4)	0 (0)	0 (0)	3 (21.4)	6 (85.7)	0 (0)
Child Dosing Aid	91			28	13	14	11	14	7	4
Always	54 (59.3)			26 (92.9)	8 (61.5)	6 (42.9)	5 (45.5)	5 (35.7)	1 (14.3)	3 (75)
Often	9 (9.9)			0 (0)	0 (0)	4 (28.6)	1 (9.1)	2 (14.3)	1 (14.3)	1 (25)
Sometimes	12 (13.2)			0 (0)	2 (15.4)	1 (7.1)	3 (27.3)	2 (14.3)	4 (57.1)	0 (0)
Never	16 (17.6)			2 (7.1)	3 (23.1)	3 (21.4)	2 (18.2)	5 (35.7)	1 (14.3)	0 (0)
You prescribed/dispensed/administered Pro-Epanutin/Prodilantin (Fosphenytoin) using the Pfizer	86			28	11	14	11	12	6	4

Table 9. HCPs utilization of the aRMM tools

Country	All, Unweighted	All, Weighted	95% Confidence Interval, Weighted percent	Specialty Group						
				Nurse	Pharmacist	Neurologist	Anesthesio-logist	Intensive Care Specialist	Pediatrician	Other
dosing aid(s). What were the main reasons why you used the Pfizer dosing aid(s)? n(%) [1]*										
To reduce the risk of a medication error	68 (79.1)			25 (89.3)	10 (90.9)	11 (78.6)	6 (54.5)	9 (75)	4 (66.7)	3 (75)
Find the Pfizer dosing aid easy to use	54 (62.8)			22 (78.6)	6 (54.5)	7 (50)	6 (54.5)	9 (75)	3 (50)	1 (25)
Do not have another dosing tool available	4 (4.7)			1 (3.6)	1 (9.1)	0 (0)	1 (9.1)	0 (0)	1 (16.7)	0 (0)
Need a dosing tool to prescribe	27 (31.4)			7 (25)	3 (27.3)	5 (35.7)	3 (27.3)	4 (33.3)	2 (33.3)	3 (75)
Other	0 (0)			0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
You prescribed/dispensed/administered Pro-Epanutin/Prodilantin (Fosphenytoin) without using the Pfizer dosing aid(s). What were the main reasons for not using the Pfizer dosing aid(s)? n(%) [1]*	226			13	31	35	38	53	29	27
Already have a different dosing tool	77 (34.1)			4 (30.8)	6 (19.4)	13 (37.1)	8 (21.1)	18 (34)	10 (34.5)	18 (66.7)
Use the SmPC and do not requiring additional instruction	69 (30.5)			1 (7.7)	15 (48.4)	18 (51.4)	13 (34.2)	16 (30.2)	5 (17.2)	1 (3.7)
No need on a dosing tool	5 (2.2)			0 (0)	0 (0)	0 (0)	0 (0)	4 (7.5)	0 (0)	1 (3.7)
Not aware of the dosing aid at the time of prescribing, dispensing or administering fosphenytoin	87 (38.5)			3 (23.1)	21 (67.7)	9 (25.7)	19 (50)	16 (30.2)	15 (51.7)	4 (14.8)
Do not find the Pfizer dosing aid(s) helpful	4 (1.8)			0 (0)	0 (0)	1 (2.9)	0 (0)	2 (3.8)	0 (0)	1 (3.7)

Table 9. HCPs utilization of the aRMM tools

Country	All, Unweighted	All, Weighted	95% Confidence Interval, Weighted percent	Specialty Group						
				Nurse	Pharmacist	Neurologist	Anesthesio-logist	Intensive Care Specialist	Pediatrician	Other
Find the Pfizer dosing aid(s) complicated	4 (1.8)			0 (0)	0 (0)	1 (2.9)	0 (0)	2 (3.8)	0 (0)	1 (3.7)
Do not have the Pfizer dosing aid(s) readily available	58 (25.7)			4 (30.8)	8 (25.8)	5 (14.3)	13 (34.2)	11 (20.8)	8 (27.6)	9 (33.3)
Other	13 (5.8)			1 (7.7)	3 (9.7)	2 (5.7)	1 (2.6)	4 (7.5)	0 (0)	2 (7.4)
Overall - Weighted		(N=312)		(N=69)	(N=40.6)	(N=23.3)	(N=95.7)	(N=39.4)	(N=43.7)	(N=0.3)
Have you prescribed/dispensed/administered Pro-Epanutin/Prodilantin (Fosphenytoin) since receiving the Pfizer Pro-Epanutin/Prodilantin (Fosphenytoin) dosing aid(s)?, n(%) [1]		108.62		35	17.2	6.9	25.6	9	14.8	0.1
Yes		84.58 (77.863)		25 (71.31)	11.6 (67.51)	5.2 (75.62)	24.8 (96.7)	8.5 (94.59)	9.4 (63.71)	0 (57.14)
No		24.05 (22.137)		10 (28.69)	5.6 (32.49)	1.7 (24.38)	0.8 (3.3)	0.5 (5.41)	5.4 (36.29)	0 (42.86)
You indicated that you have prescribed/dispensed/administered Pro-Epanutin/Prodilantin (Fosphenytoin) since receiving the Pfizer Pro-Epanutin/Prodilantin (Fosphenytoin) dosing aid(s). Did you use the Pfizer dosing aid(s)?		84.58		25	11.6	5.2	24.8	8.5	9.4	0
Yes (defined as "always", "often" or "Sometimes" used		79.98 (94.566)	[89.441 - 99.691]	25 (100)	9.6 (83.17)	5.2 (100)	24.8 (100)	7.4 (86.53)	7.9 (84.16)	0 (100)

Table 9. HCPs utilization of the aRMM tools

Country	All, Unweighted	All, Weighted	95% Confidence Interval, Weighted percent	Specialty Group						
				Nurse	Pharmacist	Neurologist	Anesthesio-logist	Intensive Care Specialist	Pediatrician	Other
for either Adult dosing aids or Child dosing aids)										
Adult Dosing Aid		84.58		25	11.6	5.2	24.8	8.5	9.4	0
Always		37.89 (44.796)		20.5 (82.25)	3.6 (31.31)	2.4 (45.16)	7.7 (31.04)	3.6 (42.65)	0 (0)	0 (75)
Often		21.64 (25.591)		3.7 (14.79)	3.6 (31.31)	2.2 (42.75)	9.4 (37.91)	2.7 (31.43)	0 (0)	0 (25)
Sometimes		13.51 (15.978)		0.7 (2.96)	2.4 (20.56)	0.6 (12.09)	7.7 (31.04)	0.6 (6.73)	1.5 (15.84)	0 (0)
Never		11.53 (13.635)		0 (0)	2 (16.83)	0 (0)	0 (0)	1.6 (19.19)	7.9 (84.16)	0 (0)
Child Dosing Aid		84.58		25	11.6	5.2	24.8	8.5	9.4	0
Always		41 (48.475)		19.2 (76.92)	7.3 (62.62)	2 (38.71)	8.1 (32.75)	2.9 (33.67)	1.5 (15.84)	0 (75)
Often		7.53 (8.902)		0 (0)	0 (0)	0.8 (16.14)	3.8 (15.49)	1.3 (15.72)	1.5 (15.84)	0 (25)
Sometimes		17.77 (21.006)		0 (0)	1.4 (12.14)	0.8 (14.52)	9.4 (37.91)	1.3 (14.7)	5 (52.48)	0 (0)
Never		18.28 (21.617)		5.8 (23.08)	2.9 (25.24)	1.6 (30.64)	3.4 (13.84)	3.1 (35.92)	1.5 (15.84)	0 (0)
You prescribed/dispensed/administered Pro-Epanutin/Prodilantin (Fosphenytoin) using the Pfizer dosing aid(s). What were the main		79.98		25	9.6	5.2	24.8	7.4	7.9	0

Table 9. HCPs utilization of the aRMM tools

Country	All, Unweighted	All, Weighted	95% Confidence Interval, Weighted percent	Specialty Group						
				Nurse	Pharmacist	Neurologist	Anesthesio-logist	Intensive Care Specialist	Pediatrician	Other
reasons why you used the Pfizer dosing aid(s)? n(%) [1]*										
To reduce the risk of a medication error		52.76 (65.97)		18.5 (73.97)	8.9 (92.7)	4.1 (77.41)	9.8 (39.67)	5.5 (74.06)	6 (75.29)	0 (75)
Find the Pfizer dosing aid easy to use		47.81 (59.777)		20.5 (82.25)	5 (52.24)	1.9 (36.29)	11.1 (44.89)	5.8 (77.83)	3.5 (43.53)	0 (25)
Do not have another dosing tool available		2.6 (3.255)		0.7 (2.96)	1 (10.11)	0 (0)	0.4 (1.7)	0 (0)	0.5 (5.89)	0 (0)
Need a dosing tool to prescribe		23.87 (29.85)		5.2 (20.71)	2.9 (30.34)	2.4 (45.16)	8.1 (32.69)	2.3 (31.12)	3 (37.65)	0 (75)
Other		0 (0)		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
You prescribed/dispensed/administered Pro-Epanutin/Prodilantin (Fosphenytoin) without using the Pfizer dosing aid(s). What were the main reasons for not using the Pfizer dosing aid(s)? n(%) [1]*		232.02		44	31	18.1	71	32	35.8	0.2
Already have a different dosing tool		65.44 (28.206)		15.8 (35.92)	10.1 (32.64)	5.3 (29.43)	12 (16.86)	10.1 (31.61)	12 (33.49)	0.2 (66.67)
Use the SmPC and do not requiring additional instruction		77.03 (33.199)		5.2 (11.71)	17.3 (55.73)	9.5 (52.58)	28.7 (40.38)	9.6 (29.97)	6.9 (19.19)	0 (3.7)
No need on a dosing tool		2.22 (0.958)		0 (0)	0 (0)	0 (0)	0 (0)	2.2 (6.92)	0 (0)	0 (3.7)
Not aware of the dosing aid at the time of prescribing, dispensing or administering fosphenytoin		94.91 (40.908)		10.8 (24.51)	17.8 (57.39)	5.4 (29.91)	32.5 (45.77)	9.6 (29.97)	18.9 (52.68)	0 (14.81)
Do not find the Pfizer dosing aid(s) helpful		1.37 (0.591)		0 (0)	0 (0)	0.2 (1.17)	0 (0)	1.2 (3.6)	0 (0)	0 (3.7)

Table 9. HCPs utilization of the aRMM tools

Country	All, Unweighted	All, Weighted	95% Confidence Interval, Weighted percent	Specialty Group						
				Nurse	Pharmacist	Neurologist	Anesthesio-logist	Intensive Care Specialist	Pediatrician	Other
Find the Pfizer dosing aid(s) complicated		2.11 (0.91)		0 (0)	0 (0)	0.8 (4.21)	0 (0)	1.3 (4.2)	0 (0)	0 (3.7)
Do not have the Pfizer dosing aid(s) readily available		62.05 (26.743)		11.5 (26.18)	6.7 (21.7)	2.6 (14.25)	26.1 (36.74)	7.1 (22.24)	8 (22.26)	0.1 (33.33)
Other		8.59 (3.702)		0.7 (1.68)	2.7 (8.57)	1 (5.37)	1.7 (2.42)	2.5 (7.79)	0 (0)	0 (7.41)

[1] Percentages are calculated using the number of HCPs who answered this question as the denominator
* Multiple answers will be possible. Therefore, percentages may add up to more than 100%.
SmPC: Summary of Product Characteristics, UK: United Kingdom

10.4.5. Profile of HCPs

Profile of HCPs with/without receiving aRMM tools

Table 10 presents the profile of HCPs based on whether they received the aRMM (Question 9 of HCP questionnaire). Overall 47.4% (148/312) of the HCPs received aRMM tools.

Profile of HCPs based on rating dosing aid(s) as helpful or not helpful

Table 11 presents the profile of HCPs based on whether they rated the dosing aid(s) as helpful or not helpful (Q10 of HCP questionnaire). In total 114 HCPs responded to this question. Overall, the majority (84.2% [96/114]) of HCPs rated the dosing aid(s) as helpful.

Profile of HCPs with/without knowledge of the risks of fosphenytoin medication errors and off-label use

Table 12 presents data on HCPs with/without knowledge of the risks of fosphenytoin medication errors and off-label use. In total 312 HCPs responded to this. Overall, just over a half (54.8% [171/312]) of HCPs had knowledge of the risks.

Profile of HCPs with/without knowledge for the appropriate method of fosphenytoin dose calculation/prescription

Table 13 presents data on HCPs with/without knowledge for the appropriate method of fosphenytoin dose calculation/prescription. In total 312 HCPs responded to this. Overall, 85.25% (266/312) had knowledge of the appropriate method of fosphenytoin dose calculation/prescription.

Profile of HCPs with/without utilizing fosphenytoin dosing aid(s)

Table 14 presents data on the HCPs with/without utilizing fosphenytoin dosing aid(s). In total 312 HCPs responded to this. Overall, only 27.56% (86/312) of the HCPs utilized fosphenytoin dosing aid(s).

Table 10. Profile of HCPs with/without receiving aRMM tools

Characteristics	Overall		UK		Sweden		France	
	HCPs who received aRMM tools*	HCPs who did not receive aRMM tools**	HCPs who received aRMM tools*	HCPs who did not receive aRMM tools**	HCPs who received aRMM tools*	HCPs who did not receive aRMM tools**	HCPs who received aRMM tools*	HCPs who did not receive aRMM tools**
	(N=148)	(N=164)	(N=60)	(N=44)	(N=20)	(N=37)	(N=68)	(N=83)
Specialty Group, n (%) [1]								
Nurse	33 (22.3)	8 (4.9)	28 (46.7)	4 (9.1)	4 (20)	4 (10.8)	1 (1.5)	0 (0)
Pharmacist	26 (17.6)	16 (9.8)	8 (13.3)	10 (22.7)	0 (0)	1 (2.7)	18 (26.5)	5 (6)
Neurologist	27 (18.2)	22 (13.4)	12 (20)	6 (13.6)	6 (30)	6 (16.2)	9 (13.2)	10 (12)
Anesthesiologist	16 (10.8)	33 (20.1)	4 (6.7)	7 (15.9)	4 (20)	5 (13.5)	8 (11.8)	21 (25.3)
Intensive Care Specialist	23 (15.5)	42 (25.6)	5 (8.3)	9 (20.5)	3 (15)	5 (13.5)	15 (22.1)	28 (33.7)
Pediatrician	13 (8.8)	22 (13.4)	2 (3.3)	6 (13.6)	2 (10)	4 (10.8)	9 (13.2)	12 (14.5)
Other	10 (6.8)	21 (12.8)	1 (1.7)	2 (4.5)	1 (5)	12 (32.4)	8 (11.8)	7 (8.4)
Duration of practice, n (%) [1]								
less than 5 years	5 (3.4)	14 (8.5)	0 (0)	0 (0)	0 (0)	2 (5.4)	5 (7.4)	12 (14.5)
5 to 15 years	50 (33.8)	65 (39.6)	17 (28.3)	15 (34.1)	9 (45)	15 (40.5)	24 (35.3)	35 (42.2)
>15 years	93 (62.8)	85 (51.8)	43 (71.7)	29 (65.9)	11 (55)	20 (54.1)	39 (57.4)	36 (43.4)
Ever prescribed/dispensed/administered fosphenytoin , n (%) [1]								
For children (aged 5 years and older)	14 (9.5)	28 (17.1)	1 (1.7)	11 (25)	2 (10)	4 (10.8)	11 (16.2)	13 (15.7)
For adults only	62 (41.9)	102 (62.2)	20 (33.3)	29 (65.9)	11 (55)	21 (56.8)	31 (45.6)	52 (62.7)
For both	72 (48.6)	34 (20.7)	39 (65)	4 (9.1)	7 (35)	12 (32.4)	26 (38.2)	18 (21.7)

Table 10. Profile of HCPs with/without receiving aRMM tools

Characteristics	Overall		UK		Sweden		France	
	HCPs who received aRMM tools*	HCPs who did not receive aRMM tools**	HCPs who received aRMM tools*	HCPs who did not receive aRMM tools**	HCPs who received aRMM tools*	HCPs who did not receive aRMM tools**	HCPs who received aRMM tools*	HCPs who did not receive aRMM tools**
	(N=148)	(N=164)	(N=60)	(N=44)	(N=20)	(N=37)	(N=68)	(N=83)
Number of months since last prescription of fosphenytoin								
n	148	164	60	44	20	37	68	83
Mean (SD)	4.8 (7.61)	13.6 (18.97)	3.1 (6.45)	13.2 (18.9)	6.6 (7.29)	14.1 (20.32)	5.9 (8.4)	13.7 (18.62)
Median	1	6	1	6	3	3	2	4
Q1, Q3	1 , 6	1 , 24	0.8 , 2.5	3 , 12	1 , 10	1 , 24	1 , 8	1 , 24
Min, Max	0 , 48	0 , 99	0 , 36	1 , 99	0 , 24	0 , 96	0 , 48	1 , 90
Number of patients prescribed/dispensed/administered with fosphenytoin in the last 6 months								
n	148	164	60	44	20	37	68	83
Mean (SD)	14.8 (28.38)	4.8 (9.42)	21.4 (18.81)	4.5 (9.46)	17.7 (66.57)	3.2 (4.41)	8 (10.54)	5.7 (10.9)
Median	5	2	20	2	2	1	4	2
Q1, Q3	2 , 20	0 , 5	5 , 30	0 , 4.5	0 , 4	0 , 4	2 , 10	0 , 5
Min, Max	0 , 300	0 , 69	0 , 60	0 , 60	0 , 300	0 , 20	0 , 50	0 , 69

[1] Percentages are calculated using the number of HCPs who answered this question as the denominator
* HCPs who received aRMM tools defined as receiving either DHPC or dosing aid(s)
** HCPs who did not receive aRMM tools defined as receiving neither DHPC nor dosing aid(s)
aRMM: Additional Risk Minimization Measures, DHPC: Direct Healthcare Professional Communication, HCPs: Healthcare Professionals, Max: Maximum, Min: Minimum, Q1 : First Quarter, Q3: Third Quarter, SD: Standard Deviation, UK: United Kingdom

Table 11. Profile of HCPs rating dosing aid(s) helpful/not helpful

Characteristics	Overall		UK		Sweden		France	
	HCPs who rated dosing aid(s) helpful*	HCPs who rated dosing aid(s) not helpful**	HCPs who rated dosing aid(s) helpful*	HCPs who rated dosing aid(s) not helpful**	HCPs who rated dosing aid(s) helpful*	HCPs who rated dosing aid(s) not helpful**	HCPs who rated dosing aid(s) helpful*	HCPs who rated dosing aid(s) not helpful**
	(N=96)	(N=18)	(N=43)	(N=8)	(N=15)	(N=2)	(N=38)	(N=8)
Specialty Group, n (%) [1]								
Nurse	28 (29.2)	2 (11.1)	26 (60.5)	1 (12.5)	2 (13.3)	1 (50)	0 (0)	0 (0)
Pharmacist	15 (15.6)	4 (22.2)	4 (9.3)	1 (12.5)	0 (0)	0 (0)	11 (28.9)	3 (37.5)
Neurologist	15 (15.6)	4 (22.2)	7 (16.3)	3 (37.5)	6 (40)	0 (0)	2 (5.3)	1 (12.5)
Anesthesiologist	12 (12.5)	1 (5.6)	3 (7)	1 (12.5)	4 (26.7)	0 (0)	5 (13.2)	0 (0)
Intensive Care Specialist	10 (10.4)	5 (27.8)	1 (2.3)	2 (25)	1 (6.7)	1 (50)	8 (21.1)	2 (25)
Pediatrician	9 (9.4)	2 (11.1)	2 (4.7)	0 (0)	1 (6.7)	0 (0)	6 (15.8)	2 (25)
Other	7 (7.3)	0 (0)	0 (0)	0 (0)	1 (6.7)	0 (0)	6 (15.8)	0 (0)
Duration of practice, n (%) [1]								
Less than 5 years	2 (2.1)	1 (5.6)	0 (0)	0 (0)	0 (0)	0 (0)	2 (5.3)	1 (12.5)
5 to 15 years	29 (30.2)	6 (33.3)	12 (27.9)	3 (37.5)	5 (33.3)	1 (50)	12 (31.6)	2 (25)
>15 years	65 (67.7)	11 (61.1)	31 (72.1)	5 (62.5)	10 (66.7)	1 (50)	24 (63.2)	5 (62.5)
Ever prescribed/dispensed/administered fosphenytoin , n (%) [1]								
For children (aged 5 years and older)	7 (7.3)	3 (16.7)	0 (0)	1 (12.5)	1 (6.7)	0 (0)	6 (15.8)	2 (25)
For adults only	33 (34.4)	8 (44.4)	10 (23.3)	4 (50)	10 (66.7)	0 (0)	13 (34.2)	4 (50)
For both	56 (58.3)	7 (38.9)	33 (76.7)	3 (37.5)	4 (26.7)	2 (100)	19 (50)	2 (25)

Table 11. Profile of HCPs rating dosing aid(s) helpful/not helpful

Characteristics	Overall		UK		Sweden		France	
	HCPs who rated dosing aid(s) helpful*	HCPs who rated dosing aid(s) not helpful**	HCPs who rated dosing aid(s) helpful*	HCPs who rated dosing aid(s) not helpful**	HCPs who rated dosing aid(s) helpful*	HCPs who rated dosing aid(s) not helpful**	HCPs who rated dosing aid(s) helpful*	HCPs who rated dosing aid(s) not helpful**
	(N=96)	(N=18)	(N=43)	(N=8)	(N=15)	(N=2)	(N=38)	(N=8)
Number of months since last prescription of fosphenytoin								
n	96	18	43	8	15	2	38	8
Mean (SD)	3.3 (5.48)	2.7 (2.25)	2.1 (5.81)	2.4 (1.6)	4.3 (4.61)	4.5 (2.12)	4.2 (5.29)	2.5 (2.83)
Median	1	1	1	2	3	4.5	2	1
Q1, Q3	1 , 3	1 , 4	0 , 1.5	1 , 3.5	1 , 9	3 , 6	1 , 6	1 , 3.5
Min, Max	0 , 36	1 , 8	0 , 36	1 , 5	0 , 14	3 , 6	0 , 24	1 , 8
Number of patients prescribed/dispensed/administered with fosphenytoin in the last 6 months								
n	96	18	43	8	15	2	38	8
Mean (SD)	19.2 (33.75)	12.6 (13.38)	27.4 (18.81)	8 (5.53)	23.4 (76.63)	1 (1.41)	8.4 (9.78)	20 (16.69)
Median	10	6	25	6	3	1	5	20
Q1, Q3	3 , 25	5 , 20	10 , 40	5 , 10	0 , 6	0 , 2	3 , 10	5 , 35
Min, Max	0 , 300	0 , 40	0 , 60	2 , 20	0 , 300	0 , 2	0 , 50	0 , 40

[1] Percentages are calculated using the number of HCPs who answered this question as the denominator
* helpful defined as selecting "very helpful" or "extremely helpful" to Q10
** Not helpful defined as selecting "no opinion/not sure", "somewhat helpful" or "not helpful" to Q10
HCP: Healthcare professionals. Max: Maximum, Min: Minimum, Q1 : First Quarter, Q3: Third Quarter, SD: Standard Deviation, UK: United Kingdom

Table 12. Profile of HCPs with/without knowledge of the risks of fosphenytoin medication errors and off-label use

Characteristics	Overall		UK		Sweden		France	
	HCPs with knowledge	HCPs without knowledge	HCPs with knowledge	HCPs without knowledge	HCPs with knowledge	HCPs without knowledge	HCPs with knowledge	HCPs without knowledge
	(N=171)	(N=141)	(N=74)	(N=30)	(N=15)	(N=42)	(N=82)	(N=69)
Specialty Group, n (%) [1]								
Nurse	30 (17.5)	11 (7.8)	29 (39.2)	3 (10)	1 (6.7)	7 (16.7)	0 (0)	1 (1.4)
Pharmacist	29 (17)	13 (9.2)	10 (13.5)	8 (26.7)	1 (6.7)	0 (0)	18 (22)	5 (7.2)
Neurologist	24 (14)	25 (17.7)	12 (16.2)	6 (20)	1 (6.7)	11 (26.2)	11 (13.4)	8 (11.6)
Anesthesiologist	20 (11.7)	29 (20.6)	7 (9.5)	4 (13.3)	3 (20)	6 (14.3)	10 (12.2)	19 (27.5)
Intensive Care Specialist	34 (19.9)	31 (22)	8 (10.8)	6 (20)	4 (26.7)	4 (9.5)	22 (26.8)	21 (30.4)
Pediatrician	18 (10.5)	17 (12.1)	6 (8.1)	2 (6.7)	1 (6.7)	5 (11.9)	11 (13.4)	10 (14.5)
Other	16 (9.4)	15 (10.6)	2 (2.7)	1 (3.3)	4 (26.7)	9 (21.4)	10 (12.2)	5 (7.2)
Duration of practice, n (%) [1]								
Less than 5 years	7 (4.1)	12 (8.5)	0 (0)	0 (0)	0 (0)	2 (4.8)	7 (8.5)	10 (14.5)
5 to 15 years	59 (34.5)	56 (39.7)	23 (31.1)	9 (30)	6 (40)	18 (42.9)	30 (36.6)	29 (42)
>15 years	105 (61.4)	73 (51.8)	51 (68.9)	21 (70)	9 (60)	22 (52.4)	45 (54.9)	30 (43.5)
Ever prescribed/dispensed/administered, n (%) [1]								
For children (aged 5 years and older)	22 (12.9)	20 (14.2)	8 (10.8)	4 (13.3)	1 (6.7)	5 (11.9)	13 (15.9)	11 (15.9)
For adults only	70 (40.9)	94 (66.7)	31 (41.9)	18 (60)	5 (33.3)	27 (64.3)	34 (41.5)	49 (71)
For both	79 (46.2)	27 (19.1)	35 (47.3)	8 (26.7)	9 (60)	10 (23.8)	35 (42.7)	9 (13)
Number of months since last prescription of fosphenytoin								

Table 12. Profile of HCPs with/without knowledge of the risks of fosphenytoin medication errors and off-label use

Characteristics	Overall		UK		Sweden		France	
	HCPs with knowledge	HCPs without knowledge	HCPs with knowledge	HCPs without knowledge	HCPs with knowledge	HCPs without knowledge	HCPs with knowledge	HCPs without knowledge
	(N=171)	(N=141)	(N=74)	(N=30)	(N=15)	(N=42)	(N=82)	(N=69)
n	171	141	74	30	15	42	82	69
Mean (SD)	7.3 (12.6)	12 (17.83)	5.5 (10.31)	12.1 (20.1)	8.3 (8.14)	12.5 (19.43)	8.8 (14.85)	11.7 (15.94)
Median	2	4	1.3	6	6	3	2	3
Q1, Q3	1 , 8	1 , 15	1 , 4	2 , 12	1 , 12	1 , 18	1 , 9	1 , 15
Min, Max	0 , 90	0 , 99	0 , 60	1 , 99	0 , 24	0 , 96	0 , 90	1 , 84
Number of patients prescribed/dispensed/administered with fosphenytoin in the last 6 months								
n	171	141	74	30	15	42	82	69
Mean (SD)	11.5 (15.7)	7.1 (26.35)	17.4 (18.73)	6.6 (11.59)	2.7 (5.31)	10.2 (45.96)	7.8 (11.7)	5.4 (9.46)
Median	4	2	10	2	0	2.5	4	3
Q1, Q3	1 , 18	0 , 5	2 , 30	0 , 9	0 , 5	0 , 4	1 , 10	0 , 5
Min, Max	0 , 69	0 , 300	0 , 60	0 , 60	0 , 20	0 , 300	0 , 69	0 , 50

[1] Percentages are calculated using the number of HCPs who answered this question as the denominator
HCP: Healthcare Professionals, Max: Maximum, Min: Minimum, Q1 : First Quarter, Q3: Third Quarter, SD: Standard Deviation, UK: United Kingdom

Table 13. Profile of HCPs with/without knowledge for the appropriate method of fosphenytoin dose calculation/prescription

Characteristics	Overall		UK		Sweden		France	
	HCPs with knowledge	HCPs without knowledge	HCPs with knowledge	HCPs without knowledge	HCPs with knowledge	HCPs without knowledge	HCPs with knowledge	HCPs without knowledge
	(N=266)	(N=46)	(N=90)	(N=14)	(N=52)	(N=5)	(N=124)	(N=27)
Specialty Group, n (%) [1]								
Nurse	40 (15)	1 (2.2)	32 (35.6)	0 (0)	7 (13.5)	1 (20)	1 (0.8)	0 (0)
Pharmacist	34 (12.8)	8 (17.4)	14 (15.6)	4 (28.6)	1 (1.9)	0 (0)	19 (15.3)	4 (14.8)
Neurologist	43 (16.2)	6 (13)	16 (17.8)	2 (14.3)	12 (23.1)	0 (0)	15 (12.1)	4 (14.8)
Anesthesiologist	42 (15.8)	7 (15.2)	10 (11.1)	1 (7.1)	8 (15.4)	1 (20)	24 (19.4)	5 (18.5)
Intensive Care Specialist	54 (20.3)	11 (23.9)	9 (10)	5 (35.7)	8 (15.4)	0 (0)	37 (29.8)	6 (22.2)
Pediatrician	26 (9.8)	9 (19.6)	6 (6.7)	2 (14.3)	6 (11.5)	0 (0)	14 (11.3)	7 (25.9)
Other	27 (10.2)	4 (8.7)	3 (3.3)	0 (0)	10 (19.2)	3 (60)	14 (11.3)	1 (3.7)
Duration of practice, n (%) [1]								
Less than 5 years	14 (5.3)	5 (10.9)	0 (0)	0 (0)	2 (3.8)	0 (0)	12 (9.7)	5 (18.5)
5 to 15 years	99 (37.2)	16 (34.8)	29 (32.2)	3 (21.4)	22 (42.3)	2 (40)	48 (38.7)	11 (40.7)
>15 years	153 (57.5)	25 (54.3)	61 (67.8)	11 (78.6)	28 (53.8)	3 (60)	64 (51.6)	11 (40.7)
Ever prescribed/dispensed/administered fosphenytoin , n (%) [1]								
For children (aged 5 years and older)	33 (12.4)	9 (19.6)	11 (12.2)	1 (7.1)	6 (11.5)	0 (0)	16 (12.9)	8 (29.6)
For adults only	138 (51.9)	26 (56.5)	40 (44.4)	9 (64.3)	28 (53.8)	4 (80)	70 (56.5)	13 (48.1)
For both	95 (35.7)	11 (23.9)	39 (43.3)	4 (28.6)	18 (34.6)	1 (20)	38 (30.6)	6 (22.2)
Number of months since last prescription of fosphenytoin								
n	266	46	90	14	52	5	124	27

Characteristics	Overall		UK		Sweden		France	
	HCPs with knowledge	HCPs without knowledge	HCPs with knowledge	HCPs without knowledge	HCPs with knowledge	HCPs without knowledge	HCPs with knowledge	HCPs without knowledge
	(N=266)	(N=46)	(N=90)	(N=14)	(N=52)	(N=5)	(N=124)	(N=27)
Mean (SD)	9.2 (15.19)	11.2 (16.23)	6.1 (11.16)	15.6 (25.12)	11.5 (17.83)	10.4 (9.91)	10.4 (16.27)	9 (10.45)
Median	2	5.5	1.5	9	3	4	2.5	4
Q1, Q3	1 , 10	2 , 12	1 , 6	3 , 12	1 , 16	3 , 18	1 , 12	1 , 12
Min, Max	0 , 96	0 , 99	0 , 60	1 , 99	0 , 96	3 , 24	1 , 90	0 , 36
Number of patients prescribed/dispensed/administered with fosphenytoin in the last 6 months								
n	266	46	90	14	52	5	124	27
Mean (SD)	10.2 (22.7)	5.4 (8.28)	15.6 (18.4)	5.2 (6.48)	8.9 (41.38)	1.2 (1.3)	6.8 (11.03)	6.3 (9.65)
Median	4	2	6	2.5	2	1	3	2
Q1, Q3	0 , 10	0 , 8	2 , 25	0 , 10	0 , 5	0 , 2	0.5 , 6	0 , 10
Min, Max	0 , 300	0 , 40	0 , 60	0 , 20	0 , 300	0 , 3	0 , 69	0 , 40

[1] Percentages are calculated using the number of HCPs who answered this question as the denominator
HCP: Healthcare Professionals, Max: Maximum, Min: Minimum, Q1 : First Quarter, Q3: Third Quarter, SD: Standard Deviation, UK: United Kingdom

Table 14. Profile of HCPs with/without utilizing fosphenytoin dosing aid(s)

Characteristics	Overall		UK		Sweden		France	
	HCPs who utilized	HCPs who did not utilize	HCPs who utilized	HCPs who did not utilize	HCPs who utilized	HCPs who did not utilize	HCPs who utilized	HCPs who did not utilize
	(N=86)	(N=226)	(N=46)	(N=58)	(N=8)	(N=49)	(N=32)	(N=119)
Specialty Group, n (%) [1]								
Nurse	28 (32.6)	13 (5.8)	27 (58.7)	5 (8.6)	1 (12.5)	7 (14.3)	0 (0)	1 (0.8)
Pharmacist	11 (12.8)	31 (13.7)	4 (8.7)	14 (24.1)	0 (0)	1 (2)	7 (21.9)	16 (13.4)
Neurologist	14 (16.3)	35 (15.5)	8 (17.4)	10 (17.2)	3 (37.5)	9 (18.4)	3 (9.4)	16 (13.4)
Anesthesiologist	11 (12.8)	38 (16.8)	4 (8.7)	7 (12.1)	2 (25)	7 (14.3)	5 (15.6)	24 (20.2)
Intensive Care Specialist	12 (14)	53 (23.5)	3 (6.5)	11 (19)	1 (12.5)	7 (14.3)	8 (25)	35 (29.4)
Pediatrician	6 (7)	29 (12.8)	0 (0)	8 (13.8)	1 (12.5)	5 (10.2)	5 (15.6)	16 (13.4)
Other	4 (4.7)	27 (11.9)	0 (0)	3 (5.2)	0 (0)	13 (26.5)	4 (12.5)	11 (9.2)
Duration of practice, n (%) [1]								
Less than 5 years	1 (1.2)	18 (8)	0 (0)	0 (0)	0 (0)	2 (4.1)	1 (3.1)	16 (13.4)
5 to 15 years	25 (29.1)	90 (39.8)	14 (30.4)	18 (31)	3 (37.5)	21 (42.9)	8 (25)	51 (42.9)
>15 years	60 (69.8)	118 (52.2)	32 (69.6)	40 (69)	5 (62.5)	26 (53.1)	23 (71.9)	52 (43.7)
Ever prescribed/dispensed/administered fosphenytoin , n (%) [1]								
For children (aged 5 years and older)	7 (8.1)	35 (15.5)	1 (2.2)	11 (19)	1 (12.5)	5 (10.2)	5 (15.6)	19 (16)
For adults only	24 (27.9)	140 (61.9)	10 (21.7)	39 (67.2)	5 (62.5)	27 (55.1)	9 (28.1)	74 (62.2)
For both	55 (64)	51 (22.6)	35 (76.1)	8 (13.8)	2 (25)	17 (34.7)	18 (56.3)	26 (21.8)
Number of months since last prescription of fosphenytoin								
n	86	226	46	58	8	49	32	119

Characteristics	Overall		UK		Sweden		France	
	HCPs who utilized	HCPs who did not utilize	HCPs who utilized	HCPs who did not utilize	HCPs who utilized	HCPs who did not utilize	HCPs who utilized	HCPs who did not utilize
	(N=86)	(N=226)	(N=46)	(N=58)	(N=8)	(N=49)	(N=32)	(N=119)
Mean (SD)	1.7 (1.82)	12.4 (17.09)	1.2 (1.34)	12.3 (17.35)	2.3 (1.91)	12.9 (18.14)	2.3 (2.2)	12.3 (16.67)
Median	1	6	1	6	2	6	1	4
Q1, Q3	1 , 2	1 , 18	0 , 1.5	3 , 12	1 , 3	1 , 18	1 , 3	1 , 18
Min, Max	0 , 8	0 , 99	0 , 6	1 , 99	0 , 6	0 , 96	0 , 8	1 , 90
Number of patients prescribed/dispensed/administered with fosphenytoin in the last 6 months								
n	86	226	46	58	8	49	32	119
Mean (SD)	22.4 (34.95)	4.6 (8.68)	26.5 (18.43)	4.5 (8.73)	41.4 (104.6)	2.8 (4.15)	11.9 (12.4)	5.4 (9.89)
Median	12	2	25	2	3	1	8	2
Q1, Q3	5 , 30	0 , 5	10 , 40	0 , 5	2.5 , 10	0 , 4	4 , 16	0 , 5
Min, Max	0 , 300	0 , 69	2 , 60	0 , 60	0 , 300	0 , 20	0 , 50	0 , 69

[1] Percentages are calculated using the number of HCPs who answered this question as the denominator
HCP: Healthcare Professionals, Max: Maximum, Min: Minimum, Q1 : First Quarter, Q3: Third Quarter, SD: Standard Deviation, UK: United Kingdom

10.5. Other analyses

None

10.6. Adverse events / adverse reactions

This study did not involve data collection on clinical endpoints on individual patients. No safety information was identified during the course of data collection and no safety information for an individual patient was volunteered by a study participant (HCP) during the course of this research.

11. DISCUSSION

11.1. Key results

Overall, 312 HCPs participated and submitted their data to the survey. Nearly half (47%) of all the 312 participating HCPs received the aRMM tools, most having received either the Pfizer adult and children (aged 5 years and older) fosphenytoin dosing aids (77.0%) and/or the DHPC (70.9%). Overall 84.2% of the HCPs who received the dosing aids found them helpful and 94.5% of these HCPs subsequently utilized them when prescribing/dispensing/administering fosphenytoin. Dosing aids were most commonly utilized by HPCs to reduce the risk of a medication error (79.1%), which is a significant indicator of the correct utilization of fosphenytoin aRMMs. However, two thirds of HCPs (226/312) prescribed, dispensed or administered fosphenytoin without using the Pfizer dosing aid(s). The most common reasons for not using the dosing aids were the lack of awareness of the dosing aid at the time of prescribing (38.5%), HCPs used a different dosing tool (34.1%), or used the SmPC (30.5%).

The questionnaire further investigated whether HCPs understood the DHPC and knew about the risks of fosphenytoin medication errors and off-label use in children under 5 years. Overall, approximately 80% of all 312 HCPs was aware of the association of fosphenytoin with cardiac arrest, and that fosphenytoin use can result in death if administered too rapidly. Slightly fewer HCPs knew that deaths occurred mainly when the correct dose of fosphenytoin had not been dispensed or administered (67.6%). A total of 181/312 (58%) of all HCPs were aware that fosphenytoin is not indicated for children younger than 5 years old, and 186/312 (59.6%) HCPs knew that the maximum infusion rates differ between children and adults.

HCPs showed better awareness of the appropriate methods of fosphenytoin dose calculation and prescription. A large proportion (95.8%) of the 312 HCPs knew that fosphenytoin dose should be calculated based on the patient’s weight, and 88.5% of HCPs were aware that fosphenytoin is dosed in milligrams phenytoin sodium equivalents (PE) per kilogram (mg PE/kg).

11.2. Limitations

11.2.1. Study Limitations

1. Selection bias

The potential for selection bias of HCPs participating in a survey is an inherent bias/limitation to any study based on volunteer participation. To quantify any selection bias, the distribution of each stratification criterion of HCPs (country, specialty, and the other available characteristics present in the screening log) was compared between participants and non-participants.

Among the survey non-respondents (36,065 HCPs) the country distribution of HCPs was as follows: UK, 33%; Sweden, 20%; France, 47%. Among the survey respondents (312 HCPs), the country distribution of HCPs was as follows: UK, 33%, Sweden 19%, France, 48%. Among the survey non-respondents the proportion of HCPs was as follows: Nurses, 22%; pharmacists, 13%; neurologists, 7%; anesthesiologists, 30%; intensive care specialists, 13%; pediatricians, 14%. No other non-respondent characteristics were available for comparison. No major differences were observed comparing respondents and non-respondents on country and specialty characteristics, and any selection bias of respondents by country and specialty characteristics was expected to be minimal.

The survey response rate was 0.9%. It is not unusual to have survey response rates below 10%.[14] To limit the influence of non-response bias on survey findings and validity, it is recommended that response rates to surveys should be at least 60%.[15] There has been a decrease in clinician survey responses in recent years [15,16,17], which could help shed light on why there was a very low response rate in this survey.

2. Limits inherent to online surveys

In such surveys, the generalization and external validity of the results is restricted to HCPs with internet access and are willing (and able) to answer a questionnaire online. These HCPs may not be fully representative of the whole targeted population.[12]

Non-response bias is a limitation. For instance, targeted HCPs may have had activated filters in their mailbox to block spams and unsolicited emails. They may not even have seen the invitation to participate in the survey if a very strict degree of message filtering was set. Having multiple email addresses could also be responsible for non-responses. For instance, if the email address to which the survey was sent was not the primary address or if the HCPs did not check their email box frequently, they would not have received the invitation during the recruitment period. To minimize bias, the HCPs were also contacted by phone.

Overall 36,377 HCPs were targeted in the UK, Sweden and France for participation in the survey. Participation was voluntary and despite extensive follow-up efforts, a relatively small proportion of HCPs eventually participated in the study and submitted the survey (0.9%

[312/36,377]). However, the survey did exceed its planned target of 200 HCPs which was consider sufficient for a proper interpretation of the study results.

Moreover, online surveys may promote social desirability bias which refers to the tendency of HCPs to give socially desirable/expected responses instead of choosing those reflecting their current knowledge or behavior, e.g. HCPs can reproduce information gathered online instead of giving their own opinions.[12] Social desirability can affect the validity of survey research findings, but as the survey was anonymous and used pre-populated items in the questionnaire, this bias was expected to be minimal.[13]

11.2.2. Study Strengths

1. The information contained in the OneKey file of each country is updated continuously. Quality controls are implemented on a regular basis. OneKey is a comprehensive and representative list of HCPs worldwide with very high coverage in most countries. A survey list based on OneKey is likely to be representative as a result.

1. The access to the online questionnaire interface was strictly limited to the invited participants, with the restriction to participate only once. Thus, stakeholder bias (multiple answers of people who have a personal interest in survey results and/or who incite peers to fulfil the survey in order to influence the results) or unverified respondents (when it is not possible to verify who responds) was mitigated as much as possible.

2. The questionnaire included general questions followed by specific ones in order to limit the learning process during the survey. As the HCPs may understand the right answer in subsequent questions, it was not possible to go back in the questionnaire and edit answers in former questions.

3. The questionnaire, as well as its translations, were tested for clarity before implementation. The questionnaire was checked to ensure that there were no questions which would suggest a specific answer for any reason, for example, social desirability.

5. We applied weights to adjust sample in order to correct any over- or under- sampling, allowing for generalizability to the overall target population. The weighted results were expected to reflect the real proportion of each country and specialty group in the targeted population. For transparency and accuracy, both unweighted (i.e., raw data) and weighted results are presented throughout the report.

11.3. Interpretation

The objective of this survey study was to evaluate the effectiveness of the aRMMs across Europe. The aRMMs have the main aim of mitigating risks of medication errors and off-label use in children under 5 years of age, associated with the use fosphenytoin.

Given the 'restricted' indications and limited sale of fosphenytoin, several steps to maximize survey response rates were taken, including multiple contact attempts. In total, 23,268 HCPs were unreachable within 3-5 contacts and 12,257 did not respond within 1-2 contacts. As a result of the several steps taken, despite the very low response rate, the planned target of 200 HCPs was achieved.

Nearly half (47%) of all the participating HCPs received the aRMM tools. One of the main reasons for not using the dosing aids detected by the survey was that HCPs were unaware of the aids at the time of prescribing. Given the completed comprehensive distribution of the aRMMs (DHPC, dosing aids) and the ongoing distribution of the dosing aids as part of the product package insert, two possible explanations for the low receipt of the aRMMs are potential filtering of: 1) the initial aRMMs mailings by administrative staff at the level of the healthcare facility and 2) the dosing aids as part of the product insert by hospital internal pharmacy procedures preventing distribution of dosing aids along with the fosphenytoin vials to the HCP actually administering fosphenytoin. [18] These potential explanations are to be further investigated by the MAH. One of the main reasons for not using the dosing aids detected by the survey was that HCPs were unaware of the dosing aids at the time of dispensing, prescribing or administering.

Overall a large proportion of the HCPs who received the dosing aids found them helpful. Most HCPs showed good awareness of the risks associated with the administration of fosphenytoin and a large proportion were aware of the appropriate dose and prescription methods. On the other hand, only a little more than a half of responding HCPs were aware that fosphenytoin is not indicated for children under 5 years old, and that the maximum infusion rates differ between children and adults. However, as most HCPs do not administer fosphenytoin in children, the response to these particular questions could have been influenced by that fact. These results indicate the importance of continuously educating HCPs, focusing on among others, information about the appropriate dosing and related risks of off-label use in the paediatric population of children below the age of 5 years, at least until further data in support of the use are gathered and the indication in this population evaluated.

11.4. Generalizability

The weighting method for sampling adjustment factored in under/over sampling that may have occurred for a country or specialty and improves the generalizability of the results.

No major differences were observed comparing respondents and non-respondents on country and specialty characteristics. Any selection bias of respondents by country and specialty characteristics were expected to be minimal. No other limits regarding demographic characteristics, region, or other factors, which could affect the external validity of results, were applied. Due to the low survey response rate, the study results should be interpreted carefully due to the unknown generalizability, which is a recurring challenge in HCP surveys[19]. Nonetheless, a similar proportion of HCPs was recruited in all three participating countries (0.8-0.9%).

12. OTHER INFORMATION

Not applicable

13. CONCLUSIONS

The study results should be interpreted with caution due to the low response rate. Nonetheless, it is important to note that aRMMs are an effective way to communicate risks and raise awareness. Where HCPs are aware of appropriate aRMMs they are likely to utilize the information provided in the DHPC and dosing aids which were designed to decrease medication errors and off-label use in the paediatric population of children below the age of 5 years.

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15. LIST OF SOURCE TABLES AND FIGURES

Not applicable

ANNEX 1. LIST OF STAND-ALONE DOCUMENTS

Appendix 1. PROTOCOL

Appendix 2. STATISTICAL ANALYSIS PLAN

ANNEX 2. ADDITIONAL INFORMATION

Number	Date	Title
1	20 October 2017	Healthcare Professional Questionnaire
2	04 December 2015	Direct Healthcare Professional Communication (DHPC) letter
3	04 December 2015	Pfizer adult fosphenytoin dosing aid
4	04 December 2015	Pfizer children (aged 5 years and older) fosphenytoin dosing aid