



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

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Pharmacovigilance and Epidemiology Department

## Retinoids-containing medicinal products Art. 31 referral

### Synopsis of EV data analysis and study planner

#### 1. Aims and Objectives

To analyse case reports of neuropsychiatric adverse reactions related to the use of retinoids-containing medicinal products.

#### 2. Methodology

In July 2016, at the start of the referral, additional data quality verification (de-duplication, recoding of medicinal products) was conducted to ensure a reliable data set is available for the conduct of the analysis.

EudraVigilance will be queried for all case of neuropsychiatric disorders reported to any retinoid-containing medicinal product from inception up to July 2016. From the data extracted, analyses will be run of the distribution of reports per retinoid, route of administration, reporting year (receive date), location (country), demographic characteristics (age groups, gender), medical history (history of psychiatric disorders), concomitant medication (scientific composition (high level)) and duration of treatment and time-to-onset. Where possible, correlations of the abovementioned variables will be provided.

This data will be analysed cumulatively for all retinoids, stratified by individual retinoid and stratified by route of administration. Output tables will be adjusted accordingly.

The analysis pertaining to fatal cases resulting from self-injury will be presented separately. Psychiatric disorders typically only lead to fatal outcome when self-destructive behaviour occurs, i.e. suicide. However, other adverse reactions that led to a fatal outcome may be reported in the case reports, hence a case's seriousness may be coded as fatal but not be related to self-injury. To differentiate cases where the patient died from a different reaction, we will report on the self-injury-specific mortality by selecting the reaction outcome field [ICH E2B(R2) B.2.i.8] rather than reporting on the seriousness field [ICH E2B(R2) A.1.5.2.].

As the exploratory analysis revealed thousands of case reports for the System Organ Class (SOC) Psychiatric disorders, neither individual case safety reviews nor case line listings will be produced.



## 2.1. Case definition

### 2.1.1. Neuropsychiatric reaction

A case report will be considered as reporting a neuropsychiatric reaction if any preferred term from the SOC Psychiatric disorders is reported.

### 2.1.2. Suicidality and self-destructive behaviour

Case reports will be considered as a case of suicidality and self-destructive behaviour where the case report includes an adverse drug reaction preferred term from the Suicide/Self-injury Standardised MedDRA Query (SMQ).

### 2.1.3. Self-injury-specific mortality

Case reports will be considered as a fatal case of self-injury where the outcome of a preferred term from the Suicide/Self-injury Standardised MedDRA Query (SMQ) was fatal.

## 3. Study timelines

Steps	Planned date	Actual date
Draft analysis plan sent to Rapporteurs		20/01/2021
Data quality check (de-duplication, recoding)	22/07/2016	19/07/2016
Exploratory analysis	31/08/2016	31/08/2016
Analysis completed	15/09/2016	
Study report completed	21/09/2016	
Study report signed-off	23/09/2016	

## 4. Roles and allocation of resources

Lead investigator	Luis Pinheiro
Product identification	Loris Piccolo
Data quality	Tom Paternoster-Howe
Data analysis	Luis Pinheiro and Irina Caplanusi
Product team Member	Ana Zanoletty Perez
Sign-off	Peter Arlett