Safety and Incidence of Side Effects in a Cohort of Postmenopausal Women Prescribed Ospemifene Relative to Patients Diagnosed with but not Treated for Vulvar and Vaginal Atrophy (VVA) and Patients on Selective Oestrogen Receptor Modulators (SERMs) for Oestrogen-deficiency Conditions or Breast Cancer Prevention – A Post-Authorisation Safety Study

First published: 11/02/2015

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Study Ongoing

Administrative details

EU PAS number

EUPAS8585

Study ID

41123

DARWIN EU® study

No

Study countries

- [ ] Italy
- [ ] Spain
- [ ] United States

Study description

Oestrogen deficiency leads to a decrease in vaginal lubrication, which is an early hallmark of vulvar and vaginal atrophy (VVA). Ospemifene is a non-steroidal selective oestrogen receptor modulator (SERM) approved in the United States for treatment of moderate to severe dyspareunia, a symptom of VVA due to menopause. The SERM class of drugs has been associated with an increased risk of venous thromboembolism (VTE) and cerebrovascular events (CVE). This post-authorisation safety study (PASS) is being undertaken to assess the safety of ospemifene in real life over a period of five years.The primary objectives are to:a) Compare the incidence of VTE, among postmenopausal women who are newly prescribed ospemifene (ospemifene cohort) to that among patients diagnosed with but not treated for VVA (untreated VVA comparison cohort).b) Compare the incidence of VTE, among postmenopausal women who are newly prescribed ospemifene (ospemifene cohort) to that among postmenopausal women newly prescribed other SERM therapies (SERM comparison cohort) being utilised for oestrogen-deficiency conditions (i.e., non-cancer and non-infertility indications) or breast cancer prevention.This is an observational, retrospective database cohort study using electronic medical records (EMR) and claims databases that will be conducted in 3-EU countries (Italy, Spain and Germany,) and in the United States. All patients with at least one ospemifene prescription or a new diagnosis of VVA with no prescription for VVA (local or systemic oestrogens) or at least one SERM prescription for an oestrogen-deficiency

condition or breast cancer prevention are eligible for the study.The study duration will be up to 5 years, and annual data updates will be obtained from each data source. Annual data updates will continue until the earliest of (1) the target sample size being reached, or (2) 5 years elapsing since first EU launch.

Study status

Ongoing

Research institutions and networks

Institutions

PPD Evidera

- ☐ Sweden
- ☐ United Kingdom
- ☐ United States

First published: 20/11/2013

Last updated: 22/09/2025

Institution | **Laboratory/Research/Testing facility** | **Non-Pharmaceutical company** | **ENCePP partner**

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Beth Nordstrom

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 27/02/2015

Actual: 31/07/2015

Study start date

Planned: 03/06/2013

Actual: 01/05/2013

Data analysis start date

Planned: 01/04/2016

Date of interim report, if expected

Planned: 31/05/2016

Actual: 05/10/2016

Date of final study report

Planned: 31/03/2021

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Shionogi Limited

Regulatory

Was the study required by a regulatory body?

Yes

Is the study required by a Risk Management Plan (RMP)?

EU RMP category 1 (imposed as condition of marketing authorisation)

Methodological aspects

Study type

Study type list

Study type:

Non-interventional study

Scope of the study:

Assessment of risk minimisation measure implementation or effectiveness

Disease epidemiology

Drug utilisation

Main study objective:

a) Compare the incidence of VTE, among postmenopausal women who are newly prescribed ospemifene to that among patients diagnosed with but not treated for VVA.b) Compare the incidence of VTE, among postmenopausal women who are newly prescribed ospemifene to that among postmenopausal women newly prescribed other SERM therapies being utilised for oestrogen-deficiency conditions.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code

(G03XC05) ospemifene

ospemifene

Medical condition to be studied

Dyspareunia

Population studied

Age groups

- Adults (46 to < 65 years)
- Adults (65 to < 75 years)
- Adults (75 to < 85 years)

- Adults (85 years and over)

Estimated number of subjects

35115

Study design details

Outcomes

The primary outcome of the study is the first occurrence of the following events during the follow-up period:• Venous thromboembolic events(VTE), including deep vein thrombosis (DVT), pulmonary embolism, and retinal vein thrombosis, First occurrence of the following events (time to event): Cerebrovascular events, Endometrial hyperplasia, Endometrial cancer, Pelvic organ prolapse, Urinary incontinence, Gall bladder events, Atrial fibrillation, Renal failure, Renal carcinoma, Renal adenoma, Liver tumours, Thymic epithelial tumours, Increased triglycerides, uterine diagnostic tests and procedures, off-label usage of ospemifene.

Data analysis plan

Descriptive statistics will summarise patient demographics, proportion of patients with VTE, proportion of patients prescribed medications related to VTE. Hazard ratios and their 95% confidence intervals will be calculated and appropriate analyses will be conducted for the events of interest. A Cox regression model with time-dependent predictors will be used for the main comparison analysis. The analyses will be carried out separately to compare ospemifene to treatment with SERM and to untreated patients. The analyses would rely on time-dependent indicators to track changes in treatments. The Cox proportional hazard models will be adjusted for confounding factors using fully covariate adjusted models (implemented through inclusion of covariates in

the model).As a secondary analysis, marginal structural models using inverse probability of treatment weighting in time-varying Cox models will be used to compare the risk of each outcome (VTE and stroke) between the treatment cohorts.

Documents

Study publications

Bruyniks N, DeGregorio F, Gibbs T, Carrol R, Fraeman KH, Nordstrom BL. Safety o…

Data management

ENCePP Seal

The use of the ENCePP Seal has been discontinued since February 2025. The ENCePP Seal fields are retained in the display mode for transparency but are no longer maintained.

Data sources

Data source(s)

Health Search/IQVIA Health Longitudinal Patient Database

The Information System for Research in Primary Care (SIDIAP)

Data source(s), other

MarketScan United States

Data sources (types)

Administrative healthcare records (e.g., claims)

Electronic healthcare records (EHR)

Use of a Common Data Model (CDM)

CDM mapping

No

Data quality specifications

Check conformance

Unknown

Check completeness

Unknown

Check stability

Unknown

Check logical consistency

Unknown

Data characterisation

Data characterisation conducted

No