

Protocol Abstract

Title

Evaluating the utilisation of Urospir® (spironolactone) in paediatric and adult patients in the United Kingdom: A drug utilisation study using the Clinical Practice Research Datalink (CPRD) database.

Rationale and Background

Spironolactone products such as Urospir® are aldosterone antagonists indicated for the treatment of congestive cardiac failure, moderate to severe heart failure, resistant hypertension, hepatic cirrhosis with ascites and oedema, malignant ascites, nephrotic syndrome, and the diagnosis and treatment of primary aldosteronism. Historically, spironolactone products have been occasionally prescribed by specialists for use in conditions outside of the licensed indications (off-label), such as for acne vulgaris, hirsutism in women, alopecia in women, and to reduce testosterone in transwomen (individuals assigned male at birth whose gender identity is female). Spironolactone may be used from birth, however, in the paediatric patient population, spironolactone must be started by a paediatrician. In adults, Urospir® may be initiated in either primary or secondary care, depending on the clinical context and indication. In paediatric patients, treatment should be initiated under the guidance of a paediatric specialist, with subsequent prescribing in primary care usually occurring under shared-care arrangements. Depending on the indication, treatment with Urospir® may be life-long.

Urospir® is available in the United Kingdom (UK) as a non-aqueous oral solution in two strengths: 25mg/5ml and 50mg/5ml. The product is licensed for use in all age groups (paediatrics and adults).

This drug utilisation study forms part of the Risk Management Plan for Urospir® 25mg/5ml and 50mg/5ml. The study is being conducted to fulfil the regulatory requirements of the Medicines and Healthcare products Regulatory Agency (MHRA) in relation to the important potential risk of medication error.

Research Question and Objectives

The overall aim of this drug utilisation study will be to characterise paediatric and adult patients prescribed Urospir® oral solution 25mg/5ml and 50mg/5ml.

The primary objectives are:

- a) To evaluate the demographic and clinical characteristics of patients prescribed Urospir® 25mg/5ml and 50mg/5ml oral solution.
- b) To describe the use of Urospir® 25mg/5ml and 50mg/5ml oral solution from index to end of follow-up, including starting dose, treatment duration, cumulative dose, and number of repeated prescriptions for the medication in patients.
- c) To describe changes to starting dose, reasons for stopping treatment, and which treatment (if any) patients switch to, as well as add-on therapy.

- d) To describe the clinical indications for which Urospir[®] 25mg/5ml and 50mg/5ml oral solution is prescribed and to characterise relevant prior treatments to understand treatment pathways before initiation.
- e) To assess the extent of off-label prescribing of Urospir[®] 25mg/5ml and 50mg/5ml oral solution.

Study Design

A drug utilisation study conducted in the UK primary care (general practice) setting using the Clinical Practice Research Datalink (CPRD) Aurum and CPRD Gold electronic health record databases. The use of both CPRD Aurum and CPRD Gold will ensure geographical representation across the whole of the UK.

Population

The study population will comprise all patients within CPRD Aurum and CPRD Gold who have received at least one prescription of Urospir[®] oral solution 25mg/5ml or 50mg/5ml. The study period will begin on the date of the earliest Urospir[®] prescription recorded in CPRD.

Patients will be included if they meet the 'acceptable' or 'Up to Standard' criteria assigned by CPRD, meaning their records are of acceptable quality for research purposes.

Variables

Data will be collected on the following covariates:

- Baseline characteristics of patients prescribed Urospir[®] oral solution 25mg/5ml or 50mg/5ml, including:
 - Demographics: age, sex, ethnicity, geographical region (practice-level), socioeconomic status
 - Characteristics of the medical condition: the indication for prescribing Urospir[®] oral solution 25mg/5ml or 50mg/5ml, and severity of the condition (where a suitable proxy is available)
 - Comorbidities, prior and concomitant medications
- Characteristics of the treatment sequence, including:
 - Age at which Urospir[®] oral solution 25mg/5ml or 50mg/5ml was initiated
 - Starting dose
 - Changes to the starting dose, and reasons for this (where available)
 - Duration of treatment and number of treatment episodes
 - Instances of switching to another product for the same indication as Urospir[®], including the drug that was prescribed after switching and the reason for switching, as well as add-on therapy.

Data sources

CPRD Aurum and CPRD Gold are databases of de-identified, coded primary care records of UK patients for use in public health research. The CPRD Aurum database contains routinely collected data from primary care practices which use the EMIS Web[®] electronic patient record system software, whereas the CPRD Gold database contains patient data from practices which use the Vision[®] system software. As of September 2025, the regional distribution of practices

currently contributing to CPRD Aurum includes practices in England (1,645 practices, 100%), while CPRD Gold coverage includes Scotland (209 practices, 71.8%), Wales (56 practices, 19.2%), and Northern Ireland (26 practices, 8.9%).

The data contained within CPRD Aurum and CPRD Gold includes primary care diagnoses, symptoms, prescribed medications, referrals, and diagnostic tests requested (including results). CPRD Aurum and CPRD Gold will be used to identify patients prescribed Urospir® 25mg/5ml and 50mg/5ml oral solution. Data will be extracted, to provide demographic information on the patient, disease or condition for which Urospir® has been prescribed, and medicinal product characteristics as outlined below.

CPRD Aurum and CPRD Gold are updated on a quarterly basis, with an approximate three-month lag.

Several datasets can be linked to CPRD Aurum and Gold if needed. For this study, linkage will be performed to the CPRD Aurum and CPRD Gold Ethnicity Records to obtain data on patients' ethnicity. Additionally, for information on socioeconomic factors, the patient- and/or practice-level Index of Multiple Deprivation (IMD) datasets will be used.

Study Size

All eligible patients within the CPRD Aurum and CPRD Gold databases who meet the inclusion criteria will be included in the analyses for this study. Therefore, the study size will be dependent on the uptake of Urospir® oral solution (25mg/5ml or 50mg/5ml) and prescribing in the primary care setting. To ensure adequate numbers of patients exposed to the medicine of interest, if at the initial data extraction time point (anticipated between 18-24 months post licensing, dependent on CPRD study approval), the number of patients exposed is considered insufficient to allow meaningful analyses of the utilisation of Urospir® oral solution in the specified strengths, the study timelines will be extended by 6 months. If usage remains insufficient at this timepoint then study timelines may be extended by another 6 months. A sufficient number of exposed patients is considered to be approximately 200 adults in total and 150–200 paediatric patients in total.

Data Analysis

Descriptive summary statistics will be produced to provide an overall description of the patient characteristics and the medical condition for which Urospir® was prescribed. Patient ages will be categorised. Prescribing patterns of Urospir® 25mg/5ml and 50mg/5ml oral solution will be described, including off-label use. For numerical variables, frequencies and percentages will be presented, along with estimates of the mean (standard deviation) or median (interquartile range) where appropriate. Further details will be provided in the statistical analysis plan (SAP).