Medicines & Healthcare products
Regulatory Agency

# Public Assessment Report

# National Procedure

# Sulpiride 200 mg Tablets
# Sulpiride 400 mg Tablets
# sulpiride

## PL 28444/0266-0267

## Activase Pharmaceuticals Limited

# LAY SUMMARY

**Sulpiride 200 mg Tablets**
**Sulpiride 400 mg Tablets**
**sulpiride**

This is a summary of the Public Assessment Report (PAR) for Sulpiride 200 mg and 400 mg Tablets. It explains how these products were assessed and their authorisation recommended, as well as their conditions of use. It is not intended to provide practical advice on how to use these products.

These products will be referred to as Sulpiride tablets in this lay summary for ease of reading.

For practical information about using Sulpiride tablets, patients should read the Patient Information Leaflet (PIL) or contact their doctor or pharmacist.

**What are Sulpiride tablets and what are they used for?**
These applications are the same as Sulpiride 200 mg and 400 mg Tablets (PL 21880/0058-0059) which are already authorised.

The Company responsible for Sulpiride 200 mg and 400 mg Tablets agreed that its scientific data can be used as the basis for the grant of identical licences for Sulpiride tablets.

Sulpiride tablets are used to treat schizophrenia.

**How do Sulpiride tablets work?**
The active substance, sulpiride, belongs to a group of medicines called ‘benzamides’. It works by blocking the effect of a chemical in the brain.

**How are Sulpiride tablets used?**
The pharmaceutical form of these medicines is a tablet, and the route of administration is oral (taken by mouth).

The patient should swallow the tablets whole with a glass of water.

If the patient feels that the effect of their medicine is too weak or too strong, they should not change the dose themself, but ask their doctor.

**The recommended dose is:**
**Adults and children over 14:**
The usual starting dose is 400 mg twice daily. This may be reduced to 200 mg twice daily or increased to a maximum of 1200 mg twice daily, depending on how the patient responds to treatment.

The patient’s doctor may then change the dose depending on the patient’s illness.

**Children:** Not recommended for children under 14 years of age.

**Patients with kidney disease:** The starting dose may be lower and the rate of increasing the dose slower.

For further information on how Sulpiride tablets are used, refer to the PIL and Summaries of Product Characteristics (SmPCs) available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.

These medicines can only be obtained with a prescription.

The patient should always take their medicine(s) exactly as their doctor/pharmacist has told them. The patient should check with their doctor or pharmacist if they are not sure.

**What benefits of Sulpiride tablets have been shown in studies?**
Sulpiride tablets are considered identical to the previously authorised products with the same benefits and risks. No new studies have been provided for Sulpiride tablets; however, reference is made to the studies for Sulpiride 200 mg and 400 mg Tablets.

**What are the possible side effects of Sulpiride tablets?**
For the full list of all side effects reported with these medicines, see Section 4 of the PIL or the SmPCs available on the MHRA website.

If a patient gets any side effects, they should talk to their doctor, pharmacist or nurse. This includes any possible side effects not listed in the product information or the PIL that comes with the medicine. Patients can also report suspected side effects themselves, or a report can be made on their behalf by someone else who cares for them, directly via the Yellow Card scheme at https://yellowcard.mhra.gov.ukor search for 'MHRA Yellow Card' online. By reporting side effects, patients can help provide more information on the safety of these medicines.

**Why were Sulpiride tablets approved?**
The MHRA decided that the benefits of Sulpiride tablets are greater than the risks and recommended that medicines are approved for use.

**What measures are being taken to ensure the safe and effective use of Sulpiride tablets?**
As for all newly authorised medicines, a Risk Management Plan (RMP) has been developed for Sulpiride tablets. The RMP details the important risks of Sulpiride tablets, how these risks can be minimised, any uncertainties about Sulpiride tablets (missing information), and how more information will be obtained about the important risks and uncertainties.

The following safety concerns have been recognised for Sulpiride tablets:

| **Summary of safety concerns** | |
|---|---|
| Important identified risks | • Neuroleptic malignant syndrome<br>• Venous thromboembolism (VTE)<br>• Prolongation of the QT interval<br>• Leukopenia<br>• Neutropenia<br>• Agranulocytosis<br>• Blood dyscrasia |
| Important potential risks | • Increased mortality in elderly people with dementia<br>• Breast cancer<br>• Convulsions<br>• Cerebrovascular events |
| Missing information | • Use in paediatric population |

The information included in the SmPCs and the PIL is compiled based on the available quality, non-clinical and clinical data, and includes appropriate precautions to be followed by healthcare professionals and patients. Side effects of Sulpiride Tablets are continuously monitored and reviewed including all reports of suspected side-effects from patients, their carers, and healthcare professionals.

An RMP and a summary of the pharmacovigilance system have been provided with these applications and are satisfactory.

**Other information about Sulpiride tablets**
Marketing Authorisations were granted in the United Kingdom on 21 July 2023.

The full PAR for Sulpiride tablets follows this summary.

This summary was last updated in September 2023.

# TABLE OF CONTENTS

I. INTRODUCTION .....6
II. EXPERT REPORT .....7
III. ASSESSOR'S COMMENTS ON THE PRODUCT INFORMATION .....7
IV. QUALITY ASPECTS .....7
V. NON-CLINICAL ASPECTS .....8
VI. CLINICAL ASPECTS .....8
VII. RISK MANAGEMENT PLAN (RMP) .....8
VIII. USER CONSULTATION .....8
IX. OVERALL CONCLUSION, BENEFIT/RISK AND RECOMMENDATION .....9
TABLE OF CONTENT OF THE PAR UPDATE .....10

## I. INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the Medicines and Healthcare products Regulatory Agency (MHRA) considered that the applications for Sulpiride 200 mg and 400 mg Tablets (PL 28444/0266-0267) could be approved.

The products are approved for the following indication:

- treatment of acute and chronic schizophrenia.

The active substance, sulpiride, is a member of the group of substituted benzamides, which are structurally distinct from the phenothiazines, butyrophenones and thioxanthenes. Current evidence suggests that the actions of sulpiride hint at an important distinction between different types of dopamine receptors or receptor mechanisms in the brain.

Behaviourally and biochemically, sulpiride shares with classical neuroleptics a number of properties indicative of cerebral dopamine receptor antagonism.

Essential and intriguing differences include lack of catalepsy at doses active in other behavioural tests, lack of effect in the dopamine sensitive adenylate cyclase systems, lack of effect upon noradrenaline or 5HT turnover, negligible anticholinesterase activity, no effect on muscarinic or GABA receptor binding, and a radical difference in the binding of tritiated sulpiride to striatal preparations in-vitro, compared to 3H-spiperone or 3H-haloperidol. These findings indicate a major differentiation between sulpiride and classical neuroleptics, which lack such specificity.

One of the characteristics of sulpiride is its bimodal activity, as it has both antidepressant and antipsychotic properties. Schizophrenia characterised by a lack of social contact can benefit strikingly.

Mood elevation is observed after a few days' treatment, followed by disappearance of the florid schizophrenic symptoms. The sedative, anti-muscarinic, alpha-blocking and extrapyramidal effects of sulpiride are less pronounced than those characteristically associated with classical neuroleptics of the phenothiazine type.

These are national abridged applications approved under Regulation 56 of The Human Medicines Regulation 2012, as amended (previously Article 10c of Directive 2001/83/EC, as amended) as informed consent applications. The applications cross-refer to the reference products Sulpiride 200 mg and 400 mg Tablets (PL 21880/0058-0059).

No new non-clinical or clinical data have been supplied and none are required for these informed consent applications.

Suitable justification has been provided for non-submission of an Environmental Risk Assessment (ERA). As the applications are identical versions of already authorised products, no increase in environmental exposure is anticipated and no ERA is required.

The MHRA has been assured that acceptable standards of Good Manufacturing Practice (GMP) are in place for these products at all sites responsible for the manufacture, assembly and batch release of these products.

A Risk Management Plan (RMP) and a summary of the pharmacovigilance system have been provided with these applications and are satisfactory.

National marketing authorisations were granted in the United Kingdom on 21 July 2023

## II. EXPERT REPORT

The applicant cross-refers to the data for Sulpiride 200 mg and 400 mg Tablets, to which these applications are claimed to be identical. This is acceptable.

## III. ASSESSOR'S COMMENTS ON THE PRODUCT INFORMATION

### SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

The SmPCs are in line with those for Sulpiride 200 mg and 400 mg Tablets, dated February 2017.

### PATIENT INFORMATION LEAFLET (PIL)

A leaflet mock-up has been provided which has been aligned with that for Sulpiride 200 mg and 400 mg Tablets, dated for January 2017. The user test report submitted for PL 21880/0058-0059 has been provided.

### LABEL

Label mock-ups have been provided.

## IV. QUALITY ASPECTS

### IV.1 Drug Substance

**Drug substance specifications**

The sources of the active substance are in line with the cross-reference products. The proposed drug substance specification is consistent with the details registered for the cross-reference products.

### IV.2. Drug Products

**Name**

The products have been named in line with current requirements.

**Strength, pharmaceutical form, route of administration, container and pack sizes**

Sulpiride 200 mg and 400 mg Tablets are available in:

1. aluminium and polyvinylchloride blisters, in pack sizes of 10, 20, 28, 30, 40, 50, 56, 60, 70, 80, 84, 90, 100, 112, 500 and 1000 tablets
2. Polypropylene tablet containers, each with polyethylene tamper-evident lids, in pack sizes of 10, 20, 28, 30, 40, 50, 56, 60, 70, 80, 84, 90, 100, 112, 500 and 1000 tablets.

The appearance of the products is identical to that of the cross-reference products.

The proposed shelf life of the product is 3 years with the recommended storage condition 'Do not store above 25°C'.

The proposed packaging, shelf life and storage conditions are consistent with the details registered for the reference products.

**Legal status**

Prescription only medicine (POM).

**Manufacturers**

The proposed manufacturing sites are consistent with the details registered for the cross-reference products and evidence of Good Manufacturing Practice (GMP) compliance has been provided.

**Qualitative and quantitative compositions**
The composition of the proposed products is consistent with the details registered for the cross-reference products.

**Manufacturing process & control of critical steps**
The proposed manufacturing processes and process controls are consistent with the details registered for the reference products and the maximum batch size is stated.

**Finished product release/shelf life specifications**
The finished product specifications at release and shelf-life are in line with the details registered for the cross-reference products.

**TSE Compliance**
With the exception of lactose monohydrate, no excipients of animal or human origin are used in the final products.

The supplier of lactose monohydrate has confirmed that it is sourced from healthy animals under the same conditions as milk for human consumption.

Confirmation has been given that the magnesium stearate used in the tablets is of vegetable origin.

These products do not contain or consist of genetically modified organisms (GMO).

## V. NON-CLINICAL ASPECTS
As these applications are submitted under Regulation 56 of The Human Medicines Regulation 2012, as amended, (as informed consent applications) no new non-clinical data have been supplied and none are required.

## VI. CLINICAL ASPECTS
As these applications are submitted under Regulation 56 of The Human Medicines Regulation 2012, as amended, (as informed consent applications) no new clinical data have been supplied and none are required.

## VII. RISK MANAGEMENT PLAN (RMP)
The applicant has submitted an RMP, in accordance with the requirements of Regulation 182 of The Human Medicines Regulation 2012, as amended. The applicant proposes only routine pharmacovigilance and routine risk minimisation measures for all safety concerns. This is acceptable.

## VIII. USER CONSULTATION
A full colour mock-up of the Patient Information Leaflet (PIL) has been provided with the applications, in accordance with legal requirements.

The PIL has been evaluated via a user consultation with target patient groups, in accordance with legal requirements, on the basis of a bridging report making reference to Sulpiride 200 mg and 400 mg Tablets (PL 21880/0058-59). The bridging report submitted by the applicant is acceptable.

## IX. OVERALL CONCLUSION, BENEFIT/RISK AND RECOMMENDATION

The quality of the products is acceptable, and no new non-clinical or clinical safety concerns have been identified. The applicant's products are identical to the cross-reference products. The benefit/risk balance is, therefore, considered to be the same as for the cross-reference products and positive.

The SmPCs, PIL and labelling are satisfactory, in line with current guidelines and consistent with the cross-reference products.

In accordance with legal requirements, the current approved UK versions of the SmPCs and PIL for these products are available on the MHRA website.

# TABLE OF CONTENT OF THE PAR UPDATE

Steps taken after the initial procedure with an influence on the Public Assessment Report (non-safety variations of clinical significance).

Please note that only non-safety variations of clinical significance are recorded below and in the annexes to this PAR. The assessment of safety variations, where significant changes are made, is recorded on the MHRA website or European Medicines Agency (EMA) website. Minor changes to the marketing authorisations are recorded in the current SmPCs and/or PIL available on the MHRA website.

| **Application type** | **Scope** | **Product information affected** | **Date of grant** | **Outcome** | **Assessment report attached Y/N** |
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