**IPAR**

**Public Assessment Report for a**
**Medicinal Product for Human Use**

Scientific Discussion

Dioralyte Rebalance Citrus Powder for Oral Solution
Sodium chloride
Potassium chloride
Glucose
Disodium hydrogen citrate
PA0540/194/002

The Public Assessment Report reflects the scientific conclusion reached by the Health Products Regulatory Authority (HPRA) at the end of the evaluation process and provides a summary of the grounds for approval of a marketing authorisation for a specific medicinal product for human use. It is made available by the HPRA for information to the public, after deletion of commercially sensitive information. The legal basis for its creation and availability is contained in Article 21 of Directive 2001/83/EC, as amended. It is a concise document which highlights the main parts of the documentation submitted by the applicant and the scientific evaluation carried out by the HPRA leading to the approval of the medicinal product for marketing in Ireland.

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## I. INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the HPRA has granted a marketing authorisation for Dioralyte Blackcurrant, Citrus or Natural, Powder for oral solution, from Sanofi-Aventis Ireland Limited on 03rd of June 1992 (Citrus and Blackcurrant) and the 13th of July 1989 (natural) in the oral correction of fluid and electrolyte loss and in the management of watery diarrhoea.

This application for a marketing authorisation was submitted in accordance with Article 10c of Directive 2001/83/EC and is referred to as an 'informed consent' application. This means that the Marketing Authorisation Holder for Dioralyte Blackcurrant, Citrus or Natural, Powder for oral solution authorised medicinal products in Europe, has permitted the applicant to refer to their dossier to obtain an authorisation for Dioralyte Rebalance Blackcurrant, Citrus or Natural Powder for oral solution PA 0540/194/001-003 which has the same qualitative and quantitative composition in terms of actives substances and the same pharmaceutical form as Dioralyte Blackcurrant, Citrus or Natural, Powder for oral solution PA 0540/098/001-002 & PA 0540/099/001.

The licences for Dioralyte Blackcurrant, Citrus or Natural, Powder for oral solution were issued as national licences by the IMB on the 03rd of June 1992 and 13th of July 1989. The licences last renewal was 2007.
The MOSS is retail through pharmacies only with sales promotion to the general public and healthcare professionals.

The Summary of Product Characteristics for (SmPC) for this medicinal product is available on the HPRA's website at *hpra.ie*

| | |
|---|---|
| Name of the product | Dioralyte Rebalance Blackcurrant, Citrus or Natural |
| Name(s) of the active substance(s) (INN) | Sodium chloride ,Potassium chloride, Glucose, Disodium hydrogen citrate |
| Pharmacotherapeutic classification (ATC code) | A07CA |
| Pharmaceutical form and strength(s) | 0.47/0.30/3.56/0.53 Grams |
| Marketing Authorisation Number(s) in Ireland (PA) | PA0540/194/001-003 |
| Marketing Authorisation Holder | Sanofi-Aventis Ireland Limited |

## II. QUALITY ASPECTS

### II.1. Introduction

This application is for Dioralyte Rebalance Blackcurrant, Citrus or Natural, Powder for oral solution.

### II.2 Drug substance

The active substances are Sodium Chloride, Potassium Chloride, Glucoseand Disodium Hydrogen Citrate all established active substances described in the European/British Pharmacopoeia, and are manufactured in accordance with the principles of Good Manufacturing Practice (GMP)

The active substance specifications are considered adequate to control the quality and meets current pharmacopoeial requirements. Batch analytical data demonstrating compliance with this specification has been provided.

### II.3 Medicinal product

P.1 Composition

The quantity of active and that the excipients are as listed in SmPC section 6.1.
A visual description of the product is included in section 3 of the SmPC.

P.2 Pharmaceutical Development

The product is an established pharmaceutical form and its development is adequately described in accordance with the relevant European guidelines as provided for under dossiers of PA 0540/098/001-002 & PA 0540/099/001.

P.3 Manufacture of the Product

The product is manufactured in accordance with the principles of good manufacturing practice (GMP) at suitably qualified manufacturing sites.

The manufacturing process has been validated according to relevant European/ICH guidelines and the process is considered to be sufficiently validated as provided for under dossiers of PA 0540/098/001-003.

P.4 Control of Other Substances (Excipients/*Ancillary Substances*)

All ingredients comply with Ph. Eur. Or BP and are adequately controlled by the manufacturer's specifications as provided for under dossiers of PA 0540/098/001-002 & PA 0540/099/001.

P.5 Control of Finished Product

The Finished Product Specification is based on the pharmacopoeial monograph for the dosage form, and the tests and control limits are considered appropriate for this type of product based on the reference to the dossiers of PA 0540/098/001-002 & PA 0540/099/001.

The analytical methods used are described in sufficient detail and are supported by validation data as provided for under dossiers of PA 0540/098/001-002& PA 0540/099/001.

Batch analytical data for a number of batches from the proposed production site(s) have been provided, and demonstrate the ability of the manufacturer to produce batches of finished product of consistent quality as provided for under dossiers of PA 0540/098/001-002 & PA 0540/099/001.

P.6 Packaging material

The approved packaging for this product is described in section 6.5 of the SmPC.

Evidence has been provided that the packaging complies with Ph. Eur./EU legislation for use with foodstuffs requirements as provided for under dossiers of PA 0540/098/001-002 & PA 0540/099/001.

P.7 Stability of the Finished Product

Stability data on the finished product in the proposed packaging have been provided in accordance with EU guidelines and support the shelf-life and storage conditions listed in sections 6.3 and 6.4 of the SmPC.

*Adventitious Agent Safety*

Certificates of suitability issued by EDQM have been provided for Dioralyte Rebalance Blackcurrant/ Citrus and Natural actives declaring them free of material of animal or human origin, where no CEP is available, a statement that the actives are free of material of animal or human origin has been provided. Compliance with the Note For Guidance on Minimising the Risk if Transmitting Animal Spongiform Encephalopathy Agents via Medicinal Products has been satisfactorily demonstrated

### II.4 Discussion on Chemical, Pharmaceutical and Biological Aspects

The important quality characteristics of the product are well-defined and controlled. Satisfactory chemical and pharmaceutical documentation has been provided, assuring consistent quality of Dioralyte Blackcurrant, Citrus or Natural, Powder for oral solution PA 0540/098/001-002& PA 0540/099/001.

## III. NON-CLINICAL ASPECTS

### III.1 Introduction

These active substances are the same as that present in Dioralyte Natural on the Irish market. No new preclinical data have been submitted. As such, no pre-clinical assessment has been made on the application. This is acceptable for this type of application.

### III.5 Ecotoxicity/environmental risk assessment

The active substance is a natural substance, the use of which will not alter the concentration or distribution of the substance in the environment. Therefore, glucose, sodium chloride, potassium chloride and disodium hydrogen citrate are not expected to pose a risk to the environment.

### III.6 Discussion on the non-clinical aspects

The marketing authorisation is approvable from a nonclinical perspective.

## IV. CLINICAL ASPECTS

### IV.1 Introduction

Sodium chloride, potassium chloride, glucose and disodium hydrogren citrate are well known active substances with established efficacy and tolerability. These medicinal products are the same as Diorolyte Natural Powder for Oral Solution (PA0540/099/001), Dioralyte Blackcurrant Powder for Oral Solution (PA0540/098/001) and Dioralyte Citrus Oral Solution (PA0540/098/002) on the European (Irish) market.

The content of the SmPC approved during the national procedure is in accordance with that accepted for the reference product Diorolyte Natural Powder for Oral Solution (PA0540/099/001), Dioralyte Blackcurrant Powder for Oral Solution (PA0540/098/001) and Dioralyte Citrus Oral Solution (PA0540/098/002) marketed by sanofi-aventis Ireland Ltd., T/A SANOFI.

### IV.2 Pharmacokinetics

The pharmacokinetics of sodium chloride, potassium chloride, glucose and disodium hydrogren citrate are well characterised (see SmPC).

### IV.3 Pharmacodynamics

The pharmacodynamics of sodium chloride, potassium chloride, glucose and disodium hydrogren citrate are well characterised (see SmPC).

### IV.4 Clinical Efficacy

The clinical efficacy of sodium chloride, potassium chloride, glucose and disodium hydrogren citrate are well characterised.

### IV.5 Clinical Safety

The clinical safety of sodium chloride, potassium chloride, glucose and disodium hydrogren citrate are well characterised.

**Risk Management Plan**

The Applicant submitted a Risk Management Plan to support this application. The following table outlines the summary of safety concerns:

| **Summary of safety concerns** | |
|---|---|
| **Important identified risks** | • Hyperkalaemia<br>• Gastrointestinal obstruction |
| **Important potential risks** | - |
| **Missing information** | • Hepatic Disease |

Routine risk minimisation measures and routine pharmacovigilance activities were proposed to address the safety concerns outlined above and this is considered acceptable.

The Applicant should submit Periodic Safety Update Reports (PSUR) in accordance with the requirements set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and published on the European medicines web-portal.

## IV.6 Discussion on the clinical aspects

This is an informed consent (Article 10c of Directive 2001/83/EC) application.S odium chloride, potassium chloride, glucose and disodium hydrogren citrate are well known active substances with established efficacy and tolerability. These medicinal products are the same as Diorolyte Natural Powder for Oral Solution, Dioralyte Blackcurrant Powder for Oral Solution and Dioralyte Citrus Oral Solution respectively (which are the originator products for this informed consent application) on the European market.

## V. OVERALL CONCLUSIONS

Dioralyte Rebalance Blackcurrant, Citrus or Natural Powder for Oral Solution is the same as Dioralyte Blackcurrant, Citrus or Natural Powder for Oral Solution is a well-known medicinal product with a proven chemical-pharmaceutical quality and an established favourable efficacy and safety profile.

The MAH has provided written confirmation that systems and services are in place to ensure compliance with their pharmacovigilance obligations.

The HPRA, on the basis of the data submitted considered that Dioralyte Rebalance Blackcurrant, Citrus or Natural Powder for Oral Solution was the same as the reference product and therefore granted a marketing authorisation.

## VI. REVISION DATE

October 2021

**VII. UPDATES**

| SCOPE | PROCEDURE NUMBER | PRODUCT INFORMATION AFFECTED | DATE OF START OF PROCEDURE | DATE OF END OF PROCEDURE |
|---|---|---|---|---|
| MA Transfer | CRN00C654 | SmPC section 7, 8, 10<br>Package Leaflet<br><br>**New MA Holder:**<br><br>Opella Healthcare France SAS T/A Sanofi<br><br>**New PA number:**<br><br>PA23180/023/001-003 | N/A | 29/10/2021 |