SODIUM CHLORIDE 0.9% SOLUTION FOR INJECTION

PL 08828/0178

UKPAR

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LAY SUMMARY

The Medicines and Healthcare products Regulatory Agency (MHRA) granted Fresenius Kabi Limited a Marketing Authorisation (licence) for the medicinal product Sodium chloride 0.9% solution for injection (PL 08828/0178) on 30th August 2007. This is a prescription-only medicine (POM) and is used as a solvent and carrier for injectable drugs.

Sodium chloride 0.9% solution for injection contains the active ingredient sodium chloride, which belongs to a group of medicines called electrolytes. This product is used as a solvent and carrier to deliver drugs.

No new or unexpected safety concerns arose from this application and it was therefore judged that the benefits of using Sodium chloride 0.9% solution for injection outweigh the risks, hence a Marketing Authorisation has been granted.
SODIUM CHLORIDE 0.9% SOLUTION FOR INJECTION

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SCIENTIFIC DISCUSSION

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INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the UK granted a marketing authorisation for the medicinal product Sodium chloride 0.9% solution for injection (PL 08828/0178) on 30th August 2007. The product is a prescription-only medicine.

The application was submitted as a standard abridged application, for an active of well-established use (bibliographic), according to Article 10(a) of Directive 2001/83/EC (as amended).

The product contains the active ingredient sodium chloride, which belongs to a group of medicines called electrolytes. Sodium chloride 0.9% solution for injection is used as a vehicle for the administration of parenteral drugs.
PHARMACEUTICAL ASSESSMENT

DRUG SUBSTANCE

Sodium chloride
NaCl

Structure:

Physical form: White crystalline powder with a salty flavour
Solubility: Soluble in water and slightly soluble in alcohol

The drug substance is a simple and stable inorganic salt with a Ph. Eur. monograph.

An appropriate specification based on the European Pharmacopoeia has been provided.

Analytical methods are as per the Ph. Eur. and, therefore, suitable for ensuring compliance with the relevant specifications. Validation of the analytical procedures is not required as the methods are those of the Ph. Eur.

The drug substance is packed in open-ended, glued flat-bottom, straight-cut 25kg paper bags consisting of three paper layers, and with a polyethylene coating. The polyethylene coating is in direct contact with the drug substance and, satisfying Directive 2002/72/EC (as amended), is suitable for contact with food. The packaging is satisfactory. The specifications and typical analytical test reports are provided and are satisfactory.

Batch analysis data has been provided by the finished product manufacturer and it complies with the specifications.

Satisfactory certificates of analysis have been provided for standards used by the active substance manufacturer and finished product manufacturer.
No stability data have been provided by the applicant. The active substance is known to be very stable. The Ph. Eur. monograph does not include degradation products, thus formal stability studies are not required. The applicant states that if a batch of sodium chloride has been in storage for longer than two years, a re-test will be performed. This is acceptable.

**DRUG PRODUCT**

**Other ingredients**
Other ingredients consist of pharmaceutical excipients, namely sodium hydroxide (solid), hydrochloric acid, and water for injections. Appropriate justification for the inclusion of each excipient has been provided.

All excipients used comply with their respective standards. Satisfactory certificates of analysis have been provided for all excipients.

There are no materials of animal or human origin contained in or used in the manufacturing process for the proposed products.

There were no novel excipients used and no overages.

A satisfactory summary of the development of the product leading to adoption of the manufacturing process has been provided.

**Impurity profiles**
Impurities are within the specification limits.

**Manufacture**
A description and flow-chart of the manufacturing method has been provided.

In-process controls are appropriate considering the nature of the product and the method of manufacture. Process validation has been carried out on batches of each ampoule. The results are satisfactory.

**Finished product specification**
The finished product specification is satisfactory. Acceptance limits have been justified with respect to conventional pharmaceutical requirements and, where appropriate, safety. Test methods have been described and have been adequately validated, as appropriate. Batch data have been provided and comply with the release specification. Certificates of analysis have been provided for any standards used.

**Container Closure System**
The drug product is packaged in low density polyethylene ampoules of Ph. Eur. Specifications, satisfying Directive 2002/72/EC (as amended), as suitable for contact with parenteral and ophthalmic preparations. The ampoules have volumes of 5ml, 10ml or 20ml. The applicant tests ampoules from different packs for integrity ("tightness"). A satisfactory specification has been included. The ampoules are packed into cartons in four strips of five (20 ampoules per carton) with a patient information leaflet.
Stability
Finished product stability studies have been conducted in accordance with current guidelines. Based on the results, a shelf-life of 2 years has been set, which is satisfactory. Once the ampoule is opened it should be used immediately. Storage conditions have been set as “Do not store above 25 degrees”.

SUMMARY OF PRODUCT CHARACTERISTICS (SPC)
The SPC is satisfactory.

PATIENT INFORMATION LEAFLET (PIL)
The PIL is in line with the SPC and is satisfactory.

LABELLING
The labelling is satisfactory.

Conclusion
The grounds for this application are considered adequate. The product literature is approved.

It is recommended that a Marketing Authorisation is granted for this application.
PRECLINICAL ASSESSMENT

The application was submitted as a standard abridged application, for an active of well-established use.

No new preclinical data have been supplied with this application and none are required for an application of this type. A preclinical expert report has been written by a suitably qualified person and is satisfactory.
CLINICAL ASSESSMENT

CLINICAL PHARMACOLOGY
No new data are submitted and none are required for this type of application.

EFFICACY
No new data are submitted and none are required for this type of application.

SAFETY
No new data are submitted and none are required for this type of application.

Safety is reviewed in the Clinical Expert Report. The safety profile of sodium chloride has been well established by many years of clinical use.

EXPERT REPORT
The expert report is written by a medically qualified pharmaceutical consultant and is satisfactory.
OVERALL CONCLUSIONS AND RISK BENEFIT ASSESSMENT

QUALITY
The important quality characteristics of Sodium chloride 0.9% solution for injection are well-defined and controlled. The specifications and batch analytical results indicate consistency from batch to batch. There are no outstanding quality issues that would have a negative impact on the benefit/risk balance.

PRECLINICAL
No new preclinical data were submitted and none are required for applications of this type.

EFFICACY
The applicant’s Sodium chloride 0.9% solution for injection is considered to be efficacious as a carrier for active drugs. This is due to its inert behaviour, on account of which this substance does not induce interferences with the drugs or substances in the solution, and it also maintains stability.

The approved SPC, PIL and labelling are satisfactory.

RISK BENEFIT ASSESSMENT
The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. Extensive clinical experience with sodium chloride is considered to have demonstrated the therapeutic value of the compound. The risk benefit is, therefore, considered to be positive.
### STEPS TAKEN FOR ASSESSMENT

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<tr>
<td>1</td>
<td>The MHRA received the marketing authorisation application on 19\textsuperscript{th} October 2006.</td>
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<td>2</td>
<td>Following standard checks and communication with the applicant the MHRA considered the application valid on 19\textsuperscript{th} January 2007.</td>
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<td>3</td>
<td>Following assessment of the application the MHRA requested further information relating to the quality dossier on 8\textsuperscript{th} March 2007.</td>
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<td>4</td>
<td>The applicant responded to the MHRA’s requests, providing further information for the quality sections on 10\textsuperscript{th} May 2007.</td>
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<td>5</td>
<td>Following assessment of the response the MHRA requested further information relating to the quality dossier on 20\textsuperscript{th} June 2007.</td>
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<tr>
<td>6</td>
<td>The applicant responded to the MHRA’s requests, providing further information for the quality sections on 8\textsuperscript{th} July 2007.</td>
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<tr>
<td>7</td>
<td>The application was determined on 30\textsuperscript{th} August 2007.</td>
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**STEPS TAKEN AFTER ASSESSMENT**

<table>
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<th>Date submitted</th>
<th>Application type</th>
<th>Description</th>
<th>Outcome</th>
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<tr>
<td>15/01/2008</td>
<td>Label update</td>
<td>To change the colour of the writing on the Sodium Chloride 0.9% Solution for injection ampoules and cartons so that the writing will be black instead of white on the green flash of the product and to make the green flash a lighter green.</td>
<td>Approved 16/01/2008</td>
</tr>
<tr>
<td>22/01/2008</td>
<td>Type II variation</td>
<td>To introduce an additional ampoule type (BP6) for the 10ml product.</td>
<td>Approved 24/01/2008</td>
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<tr>
<td>07/11/2008</td>
<td>Type IB variation</td>
<td>To introduce an additional ampoule type (BP6) for the 5ml product.</td>
<td>Approved 08/07/2009</td>
</tr>
<tr>
<td>17/07/2009</td>
<td>Label update</td>
<td>To update the product labels in line with Article 55(3) of Directive 2001/83/EC.</td>
<td>Approved 30/07/2009</td>
</tr>
<tr>
<td>10/10/2011</td>
<td>Label update</td>
<td>To reposition the lot number and expiry date on the carton of the 5ml presentation only.</td>
<td>Approved 07/11/2011</td>
</tr>
<tr>
<td>28/11/2011</td>
<td>Label update</td>
<td>To reposition the lot number and expiry date on the carton of the 20ml presentation only.</td>
<td>Approved 28/11/2011</td>
</tr>
<tr>
<td>16/02/2013</td>
<td>Type IB variation</td>
<td>To update section 6.6 of the SmPC to correct the previous mistake of including a diagram of an ampoule with the wrong cap. Consequently the PIL has been updated.</td>
<td>Approved 28/02/2013</td>
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SUMMARY OF PRODUCT CHARACTERISTICS

In accordance with Directive 2010/84/EU the Summaries of Product Characteristics (SmPC) for products granted Marketing Authorisations at a national level are available on the MHRA website.
PRODUCT INFORMATION LEAFLET

In accordance with Directive 2010/84/EU the Patient Information Leaflets (PIL) for products granted Marketing Authorisations at a national level are available on the MHRA website.
LABELLING

Labels:

5 ml BP 5 label:

Sodium Chloride 0.9% Solution for injection
5 ml contains: Sodium Chloride 0.045 g
Water for Injections to 5 ml
For iv, im, or sc use 5 ml
PL 08828/0178 V001 POM Fresenius Kabi Limited

5 ml BP 6 label:

Sodium Chloride 0.9% Solution for injection
5 ml contains: Sodium Chloride 0.045 g
Water for Injections to 5 ml
For iv, im, or sc use 5 ml
PL 08828/0178 POM Fresenius Kabi Limited

10 ml BP 5 label:

Sodium Chloride 0.9% Solution for injection
10 ml contains: Sodium Chloride 0.09 g
Water for Injections to 10 ml
For iv, im, or sc use 10 ml
PL 08828/0178 POM Fresenius Kabi Limited

10 ml BP 6 label:

Sodium Chloride 0.9% Solution for injection
10 ml contains: Sodium Chloride 0.09 g
Water for Injections to 10 ml
For iv, im, or sc use 10 ml
PL 08828/0178 POM Fresenius Kabi Limited

20 ml BP 5 label:

Sodium Chloride 0.9% Solution for injection
20 ml contains: Sodium Chloride 0.18 g
Water for Injections to 20 ml
For iv, im, or sc use 20 ml
PL 08828/0178 POM Fresenius Kabi Limited
Cartons:
5 ml BP 5 carton:
5 ml BP 6 carton:

Sodium Chloride 0.9% Solution for Injection

Each 5ml ampoule contains:
Sodium Chloride 0.045 g
Water for Injections to 5 ml

May also contain:
Sodium hydroxide for pH adjustment
Hydrochloric acid for pH adjustment

For intravenous, intramuscular or subcutaneous use.

Fresenius Kabi
10 ml BP 5 carton:
UKPAR Sodium Chloride 0.9% Solution for Injection

PL 08828/0178

10 ml BP 6 carton:

Keep out of the reach and sight of children.
Do not store above 30 °C.
Shake the ampoule before opening.
To be used immediately after opening.
Do not use after the expiry date.
Only use the solution if it is clear, colorless, and in an unopened, undamaged container.

For intravenous, intramuscular or subcutaneous use.

Fresenius Kabi