

**SODIUM CHLORIDE 0.9% W/V SOLUTION FOR INJECTION
PL 01502/0068**

UKPAR

TABLE OF CONTENTS

Lay Summary	Page 2
Scientific discussion	Page 3
Steps taken for assessment	Page 10
Steps taken after authorisation – summary	Page 11
Summary of Product Characteristics	Page 12
Product Information Leaflet	Page 27
Labelling	Page 29

SODIUM CHLORIDE 0.9% W/V SOLUTION FOR INJECTION
PL 01502/0068

LAY SUMMARY

The MHRA granted Hameln Pharmaceuticals Limited a Marketing Authorisation (licence) for the medicinal product Sodium Chloride 0.9% w/v Solution for Injection on 14th March 2008. This product, to be available as a prescription-only medicine (POM), contains sodium chloride and is used to replace the loss of sodium from the body. Because it occurs naturally in the body, it is used to make up medicines and can be used to irrigate surfaces of your body.

This application is an identical duplicate of a previously granted application for Sodium Chloride 0.9% Injection which was originally approved on 30th August 1985 to Hameln Pharmaceuticals Limited (PL 01502/0006R).

No new or unexpected safety concerns arose from this simple application and it was, therefore, judged that the benefits of taking Sodium Chloride 0.9% w/v Solution for Injection outweigh the risks, hence a Marketing Authorisation has been granted.

**SODIUM CHLORIDE 0.9% W/V SOLUTION FOR INJECTION
PL 01502/0068**

SCIENTIFIC DISCUSSION

TABLE OF CONTENTS

Introduction	Page 4
Pharmaceutical assessment	Page 5
Preclinical assessment	Page 8
Clinical assessment	Page 9
Overall conclusions and risk benefit assessment	Page 10

INTRODUCTION

The UK granted a marketing authorisation for the medicinal product Sodium Chloride 0.9% w/v Solution for Injection (PL 01502/0068) to Hameln Pharmaceuticals Limited on 14th March 2008. The product is available as a prescription-only medicine (POM).

The application was submitted as a simple abridged application according to Article 10c (formerly Article 10.1(a)(i)) of Directive 2001/83/EC, cross-referring to Sodium Chloride 0.9% Injection which was originally approved on 30th August 1985 to Hameln Pharmaceuticals Limited (PL 01502/0006R).

No new data were submitted nor was it necessary for this simple application, as the data are identical to that of the previously granted cross-reference product. As the cross-reference product was granted prior to the introduction of current legislation, no PAR was generated for it.

The active ingredient is sodium chloride. Sodium Chloride 0.9% w/v Solution for Injection is indicated for use in prophylactic and replacement treatment requiring the use of isotonic saline solution; in the reconstitution, dilution and making up of certain drugs; as a saline irrigant; and as a priming fluid for haemodialysis procedures and to initiate/terminate blood transfusions.

PHARMACEUTICAL ASSESSMENT

LICENCE NO: PL 01502/0068

PROPRIETARY NAME: Sodium Chloride 0.9% w/v Solution for Injection

ACTIVE(S): Sodium Chloride

COMPANY NAME: Hameln Pharmaceuticals Limited

E.C. ARTICLE: Article 10c (formerly Article 10.1(a)(i)) of Directive 2001/83/EC

LEGAL STATUS: POM

1. INTRODUCTION

This is a simple, piggyback application for Sodium Chloride 0.9% w/v Solution for Injection submitted under Article 10c (formerly Article 10.1(a)(i)) of Directive 2001/83/EC. The proposed MA holder is Hameln Pharmaceuticals Limited, Nexus Hurricane Lane, Gloucester Business Park, Gloucester, GL3 4AG, UK.

The application cross-refers to Sodium Chloride 0.9% Injection, which was approved on 30th August 1985 to Hameln Pharmaceuticals Limited (PL 01502/0006R).

The current application is considered valid.

2. MARKETING AUTHORISATION APPLICATION FORM

2.1 Name(s)

The proposed name of the product is Sodium Chloride 0.9% w/v Solution for Injection. The product has been named in line with current requirements.

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

The product contains sodium chloride, equivalent to 0.9% w/v. It is to be stored in glass Type I ampoules in pack sizes of 2, 5, 10 and 20ml. The proposed shelf-life (5 years unopened) and storage conditions (keep container in outer carton, do not refrigerate or freeze, and store below 25 degrees) are consistent with the details registered for the cross-reference product.

2.3 Legal status

On approval, the products will be available as prescription-only medicines (POM).

2.4 Marketing authorisation holder/Contact Persons/Company

Hameln Pharmaceuticals Limited, Nexus Hurricane Lane, Gloucester Business Park, Gloucester, GL3 4AG, UK.

The QP responsible for pharmacovigilance is stated and his CV is included.

2.5 Manufacturers

The proposed manufacturing sites are consistent with those registered for the cross-reference product and evidence of GMP compliance has been provided.

2.6 Qualitative and quantitative composition

The proposed composition is consistent with the details registered for the cross-reference product.

2.7 Manufacturing process

The proposed manufacturing process is consistent with the details registered for the cross-reference product and the maximum batch size is stated.

2.8 Finished product/shelf-life specification

The proposed finished product specification is in-line with the details registered for the cross-reference product.

2.9 Drug substance specification

The proposed drug substance specification is consistent with the details registered for the cross-reference product.

2.10 TSE Compliance

No materials of animal or human origin are included in the product. This is consistent with the cross reference product.

3. EXPERT REPORTS

The applicant has included detailed expert reports in Module 2 of the application. Signed declarations and copies of the experts' CVs are enclosed in Module 1.4 for the quality, non-clinical and clinical experts. All are considered to have sufficient experience for their responsibilities.

4. PRODUCT NAME & APPEARANCE

See 2.1 for details of the proposed product name. The appearance of the product is identical to the cross-reference product.

5. SUMMARY OF PRODUCT CHARACTERISTICS

The proposed summary is consistent with the details registered for the cross-reference product.

6. PATIENT INFORMATION LEAFLET/CARTON

PIL

The patient information leaflet has been prepared in-line with the details registered for the cross-reference product. The marketing authorisation holder has provided a commitment to update the marketing authorisation no later than 1st July 2008 with a package leaflet in compliance with Article 59 of Council Directive 2001/83/EC and that the leaflet shall reflect the results of consultation with target patient groups.

Carton and blister

The proposed artwork is comparable to the artwork registered for the cross-reference product and complies with statutory requirements. In-line with current legislation, the applicant has also included the name of the product in Braille on the outer packaging and has included sufficient space for a standard UK pharmacy dispensing label.

7. CONCLUSIONS

The data submitted with the application are acceptable. A Marketing Authorisation should be granted.

PRECLINICAL ASSESSMENT

No new preclinical data have been supplied with this application and none are required for an application of this type.

CLINICAL ASSESSMENT

As this is a duplicate application, no new clinical data have been supplied and none are required.

OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT

QUALITY

The data are consistent with that previously assessed for the cross-reference product and as such have been judged to be satisfactory.

PRECLINICAL

No new preclinical data were submitted and none are required for an application of this type.

EFFICACY

This application is identical to a previously granted application for Sodium Chloride 0.9% Injection which was originally approved on 30th August 1985 to Hameln Pharmaceuticals Limited (PL 01502/0006R).

No new or unexpected safety concerns arise from this application.

The SPC, PIL and labelling are satisfactory and consistent with that for the cross-reference product.

RISK BENEFIT ASSESSMENT

The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. The applicant's product is identical to the cross-reference product. 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.

**SODIUM CHLORIDE 0.9% W/V SOLUTION FOR INJECTION
PL 01502/0068**

STEPS TAKEN FOR ASSESMENT

1	The MHRA received the marketing authorisation application on 20/12/2005.
2	Following standard checks and communication with the applicant the MHRA considered the application valid on 06/01/2006.
3	Following assessment of the application the MHRA requested further information on 02/02/2006 and 24/07/2007.
4	The applicant responded to the MHRA's requests, providing further information on 24/07/2007 and 02/02/2008.
5	The application was determined on 14/03/2008

**SODIUM CHLORIDE 0.9% W/V SOLUTION FOR INJECTION
PL 01502/0068**

STEPS TAKEN AFTER ASSESSMENT

Date submitted	Application type	Scope	Outcome

SODIUM CHLORIDE 0.9% W/V SOLUTION FOR INJECTION

PL 01502/0068

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Sodium Chloride 0.9% w/v Solution for Injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Sodium Chloride 0.9% w/v

Each 2ml ampoule contains a total content of sodium chloride of 18mg

Each 5ml ampoule contains a total content of sodium chloride of 45mg

Each 10ml ampoule contains a total content of sodium chloride of 90mg

Each 20ml ampoule contains a total content of sodium chloride of 180mg

For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for Injection.

Clear glass ampoules containing, 2ml, 5ml, 10ml or 20ml Sodium Chloride 0.9% w/v Solution for Injection.

Clear colourless solution

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For use in prophylactic and replacement therapy, requiring the use of isotonic saline solution.

In the reconstitution, dilution and making up of certain drugs.

As a saline irrigant.

As a priming fluid for haemodialysis procedures and to initiate and terminate blood transfusions.

4.2 Posology and method of administration

For intravenous, intramuscular or subcutaneous use.

In the prophylaxis or replacement therapy of extracellular fluid deficits, the dosage of sodium chloride 0.9% w/v solution for injection is dependent on the age, weight, clinical status and degree of deficiency, and must be determined on the individual basis.

4.3 Contraindications

There are no absolute contraindications to use of Sodium Chloride 0.9% w/v Solution for Injection

4.4 Special warnings and precautions for use

Sodium Chloride 0.9% w/v Solution for Injection, should be administered with caution to patients with congestive cardiac failure, pre-eclampsia, impaired renal function or oedema with sodium retention. Care is also required with administering this solution to very young or to elderly patients. Pseudohyponatraemia is a condition in which spuriously low concentrations of sodium are found when plasma sodium is measured by conventional methods. It may occur when there is an abnormally high concentration of large molecules and hence an abnormally low percentage of plasma water. This may occur in hyperlipaemia and hyperproteinaemia and has also been reported in patients with diabetes mellitus. Correct values may be obtained by referring the concentration to plasma water.

4.5 Interaction with other medicinal products and other forms of interaction

Concomitant administration of other sodium salts, may contribute to the sodium load. Only use as a pharmaceutical diluent where indicated in the manufacturer's literature.

4.6 Pregnancy and lactation

The solution is physiological saline and may be used during pregnancy and lactation.

4.7 Effects on ability to drive and use machines

None known.

4.8 Undesirable effects

Injudicious intravenous saline therapy (e.g. post-operative and in patients with impaired cardiac or renal function) may cause hypernatraemia. Osmotically induced water shift decreases intracellular volume, resulting in dehydration of internal organs, especially the brain, which may lead to thrombosis and haemorrhage. General adverse effects of sodium chloride excess in the body include: nausea, vomiting, diarrhoea, abdominal cramps, thirst, reduced salivary and lachrymal secretions, sweating, fever, hypotension, tachycardia, renal failure, peripheral and pulmonary oedema, respiratory arrest, headache, dizziness, restlessness, irritability, weakness, muscular twitching and rigidity, convulsions, coma and death. Excess chloride in the body may cause a loss of bicarbonate, with an acidifying effect. With judicious use of intravenous saline therapy these side effects can be avoided. If administered sub-cutaneously, any addition to the isotonic solution could render it hypertonic and cause pain at the site of injection.

4.9 Overdose

Injudicious intravenous saline therapy (e.g. post-operatively or in patients with impaired cardiac or renal function) may cause hypernatraemia. Osmotically induced water shift decreases intracellular volume, resulting in dehydration of internal organs, especially the brain, which may lead to thrombosis and haemorrhage. General adverse effects of sodium chloride excess in the body include: nausea, vomiting, diarrhoea, abdominal cramps, thirst, reduced salivary and lachrymal secretions, sweating, fever, hypotension, tachycardia, renal failure, peripheral and pulmonary oedema, respiratory arrest, headache, dizziness, restlessness, irritability, weakness, muscular twitching and rigidity, convulsions, coma and death. Excess chloride in the body may cause a loss of bicarbonate, with an acidifying effect. With judicious use of intravenous saline therapy these side effects can be avoided.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC code B05XA03 - Electrolyte solutions

The principal determinant of the effective osmolality of the extracellular fluids (and also of the intracellular fluids, since they remain in osmotic equilibrium with the extracellular fluids) is the extracellular fluid sodium concentration. The reason for this is that sodium is the most abundant positive ion of the extracellular fluid. Negative ion concentrations of the body fluids are adjusted to equal those of the positive ions by renal acid-base control mechanisms. Furthermore, glucose and urea, the most abundant of the non-ionic osmolar solutes in extracellular fluids, normally only represent about 3% of the total osmolality. Therefore, in effect, the extracellular fluid sodium ion concentration controls over 90% of the effective osmotic pressure of the extracellular fluid. Sodium Chloride remains the most important single salt for prophylaxis or replacement therapy of deficits of extracellular fluid. Volume contraction, whether isotonic, hypotonic or hypertonic, may seriously impair the circulation (cardiac output falls and microcirculation is compromised) and prompt infusion of isotonic sodium chloride solution is indicated.

5.2 Pharmacokinetic properties

The homeostatic mechanisms involved in maintaining constant ion concentrations are well described in standard text books of physiology and biochemistry and are not, therefore, included here.

5.3 Preclinical safety data

No further information other than that which is included in the Summary of Product Characteristics.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Water for Injections

Sodium hydroxide (for pH adjustment)

Hydrochloric acid (for pH adjustment)

- 6.2 Incompatibilities**
The addition of sodium chloride to mannitol 20 or 25% may cause precipitation of the mannitol.
- 6.3 Shelf life**
5 years
- 6.4 Special precautions for storage**
Store below 25° C. Keep the ampoules in the outer carton. Do not refrigerate or freeze
- 6.5 Nature and contents of container**
Type I clear glass ampoules, 2ml, 5ml, 10ml and 20ml.
Packed in cardboard cartons to contain 10 or 20 ampoules.
- 6.6 Special precautions for disposal**
Before use, ensure that the container is undamaged and the contents clear in appearance. After use, discard any remaining solution.
- 7 MARKETING AUTHORISATION HOLDER**
hameln pharmaceuticals ltd
Gloucester
GL3 4AG
UK
- 8 MARKETING AUTHORISATION NUMBER(S)**
PL 1502 / 0068
- 9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**
14/03/2008
- 10 DATE OF REVISION OF THE TEXT**
14/03/2008
- 11 DOSIMETRY (IF APPLICABLE)**
- 12 INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS (IF APPLICABLE)**

SODIUM CHLORIDE 0.9% W/V SOLUTION FOR INJECTION

PL 01502/0068

PATIENT INFORMATION LEAFLET

SODIUM CHLORIDE 0.9% W/V SOLUTION FOR INJECTION

Read all of this leaflet carefully before you start using this medicine.

- Keep this leaflet. You may need to read it again. In some circumstances this may not be possible if you are given this injection in an emergency and this leaflet will be kept in a safe place should you wish to read it.
- If you have any further questions, please ask your doctor or your pharmacist.
- This medicine has been prescribed for you personally and you should not pass it on to others. It may harm them, even if their symptoms are the same as yours.

1. What Sodium Chloride 0.9% w/v Solution for Injection is and what it is used for
2. Before you are given Sodium Chloride 0.9% w/v Solution for Injection
3. How to use Sodium Chloride 0.9% w/v Solution for Injection
4. Possible side effects
5. Storing Sodium Chloride 0.9% w/v Solution for Injection
6. Further information

1. What Sodium Chloride 0.9% w/v Solution for Injection is and what it is used for

This solution for injection contains the active ingredient sodium chloride (common salt) in a sterile solution. Each ml contains 9mg of sodium chloride. This injection also contains the following inactive ingredients: sodium hydroxide, hydrochloric acid and water for injections. The injection is supplied in 2, 5, 10 and 20 ml clear glass ampoules. 10 or 20 ampoules supplied in each carton.

Sodium chloride (common salt) occurs naturally in your body. A solution of 0.9% sodium chloride in water for injections is the same strength as your blood and is used to prime giving sets before blood or other medicines are given to you. It is used to replace the loss of sodium from your body. Because it occurs naturally in the body, it is used to make up medicines that may be injected into you. It can also be used to irrigate surfaces of your body.

2. Before you are given Sodium Chloride 0.9% w/v Solution for Injection

Please tell your doctor or pharmacist, if you know you have any of the following:

Heart disease or heart failure
Impaired kidney function
Diabetes
Pre-eclampsia (high blood pressure during pregnancy)
Fluid retention resulting in swelling of

parts of the body, particularly your feet and ankles.

Pseudohyponatraemia (a low level of salt in your blood caused by levels of fat or protein in your blood that are too high), hyperlipaemia (a raised level of fat in your blood) or hyperproteinaemia (a raised level of protein in your blood).

3. How to use Sodium Chloride 0.9% w/v Solution for Injection

Your doctor or nurse will give you the injection. Sodium Chloride Injection may be given by intramuscular (into the muscle) intravenous (into the vein) or subcutaneous injection (underneath the skin).

Your doctor will decide the correct dosage for you and when and how the injection will be given. The dose will depend on your age, weight and on your clinical condition, and will be determined on an individual basis.

4. Possible side effects

Because sodium chloride occurs naturally in your body, it is unlikely that the small volumes of these injections will by themselves cause you any unwanted effects. If you already have a high level of sodium in your body, your doctor may need to restrict the volume of this injection given to you.

You may find that you have pain at the site of injection if administered underneath the skin. It is also possible for dehydration of internal organs to develop, particularly

the brain, which may result in the development of blood clots and internal bleeding.

Someone who has too much sodium chloride in their body may also feel or be sick, have diarrhoea, stomach pain, low blood pressure, an elevated heart rate, excess sweating, headache, dizziness or fever. Other symptoms of excess sodium chloride include thirst, dry mouth or eyes, swollen legs or chest pain, difficulty breathing, irritability, restlessness, feeling weak, twitching or other unusual muscle movements.

If you think this injection is causing you any problems, or you are at all worried, talk to your doctor, nurse or pharmacist.

5. Storing Sodium Chloride 0.9% w/v Solution for Injection

Your injection will be stored under 25°C and protected from light. It should not be refrigerated or frozen. The doctor or nurse will check that the injection is not past its expiry date before giving you the injection. Keep out of the reach and sight of children.

6. Further information

The marketing authorization number of this medicine is:
PL 01502/0068

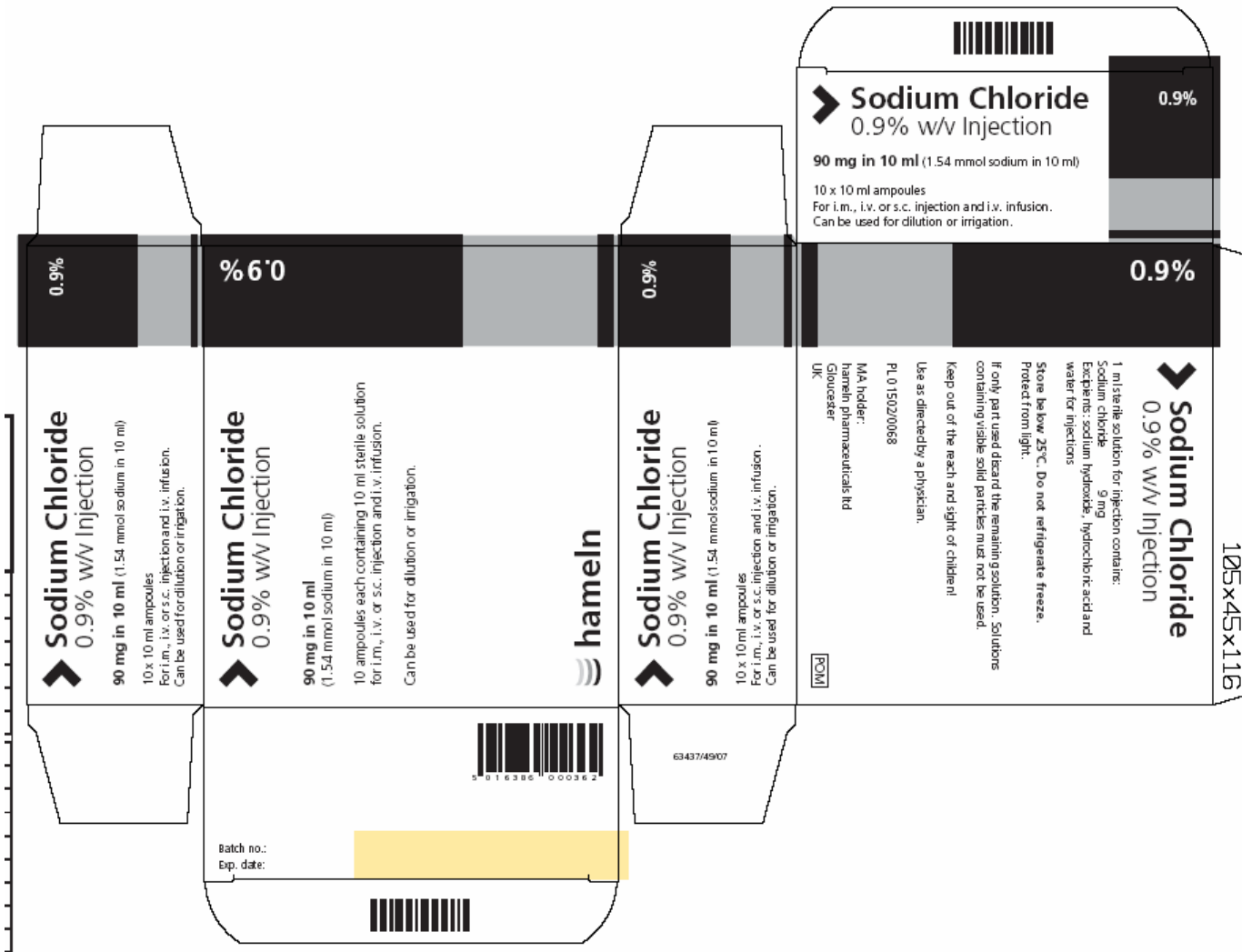
The marketing authorization holder of this medicine is:
hameln pharmaceuticals ltd
Gloucester
UK

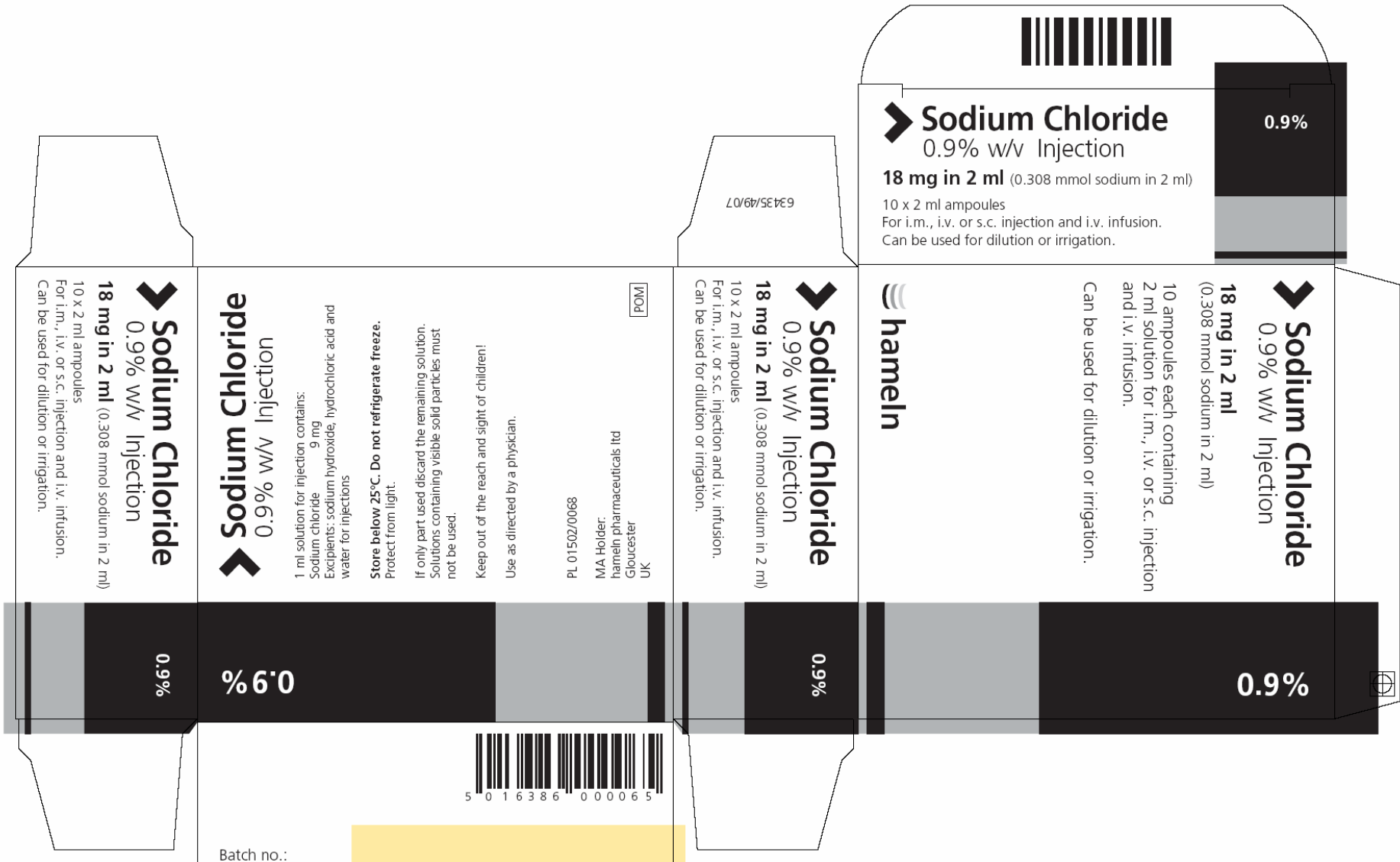
The medicine is manufactured by:
hameln pharmaceuticals gmbh
Langes Feld 13 Hameln,
31789 Germany

Revised December 2007

**SODIUM CHLORIDE 0.9% W/V SOLUTION FOR INJECTION
PL 01502/0068**


LABELLING










0.9%

 **Sodium Chloride**
0.9% w/v Injection

 **90 mg in 10 ml**

 For i.m., i.v. or s.c. injection and i.v. infusion. Can be used for dilution or irrigation.

 PL 01502/0068

 hameln pharmaceuticals ltd

POM

44185/11/08

Batch no.:

Exp. date:

0.9%

Sodium Chloride
0.9% w/v Injection

18 mg in 2 ml

For i.m., i.v. or s.c. injection
and i.v. infusion. Can be
used for dilution or irrigation.

PL 01502/0068

hameln pharmaceuticals ltd **POM**

44183/11/08

Batch no.:

Exp. date:



➤ **Sodium Chloride**
0.9% w/v Injection

45 mg in 5 ml

For i.m., i.v. or s.c. injection
and i.v. infusion. Can be used
for dilution or irrigation.

PL 01502/0068

hameln pharmaceuticals ltd

POM

44184/11/08

Batch no.:

Exp. date: