SODIUM CHLORIDE 0.9% W/V SOLUTION FOR INTRAVESICAL USE
PL 12070/0028

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SODIUM CHLORIDE 0.9%W/V SOLUTION FOR INTRAVESICAL USE  
PL 12070/0028

LAY SUMMARY

On 6 January 2011, the Medicines and Healthcare products Regulatory Agency (MHRA) granted Cambridge Laboratories Limited a Marketing Authorisation (licence) for the medicinal product Sodium Chloride 0.9% w/v Solution for Intravesical Use (PL 12070/0028). This is a pharmacy (P) product used to reconstitute other medicines for administration into the bladder through a catheter.

The active ingredient sodium chloride belongs to a group of salt-containing drugs that can be placed into the bladder.

No new or unexpected safety concerns arose from this application and it was, therefore, judged that the benefits of taking Sodium Chloride 0.9% w/v Solution for Intravesical Use outweigh the risks; hence a Marketing Authorisation has been granted.
SODIUM CHLORIDE 0.9% W/V SOLUTION FOR INTRAVESICAL USE
PL 12070/0028

SCIENTIFIC DISCUSSION

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INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the MHRA granted Cambridge Laboratories Limited a Marketing Authorisation for the medicinal product Sodium Chloride 0.9% w/v Solution for Intravesical Use (PL 12070/0028) on 6 January 2011. This is a pharmacy (P) product used as a diluent for the administration of drugs within the bladder.

The application was submitted according to Article 10a of Directive 2001/83/EC, as amended, claiming to be a ‘well established use’ application.

Sodium Chloride 0.9% w/v Solution for Intravesical Use belongs to a group of products called irrigation solutions. It is a sterile salt solution that is very similar to bodily fluids.

No new non-clinical or clinical studies were conducted for this application, which is acceptable given that this was a bibliographic application for a product containing an active of well-established use.

No new or unexpected safety concerns were raised during the assessment of this application and it was, therefore, judged that the benefits of using Sodium Chloride 0.9% w/v Solution for Intravesical Use outweigh the risks; hence a Marketing Authorisation has been granted.
PHARMACEUTICAL ASSESSMENT

ACTIVE SUBSTANCE
INN: Sodium Chloride
Chemical Name: Sodium Chloride
Molecular Formula: NaCl
Molecular weight: 58.44
Appearance: A white crystalline powder or colourless crystals or white pearls. It is freely soluble in water, practically insoluble in ethanol.

Sodium chloride is the subject of a European Pharmacopoeia monograph

Manufacture and extraction of the active substance from the designated raw materials have been adequately described and appropriate in-process controls applied. Satisfactory specification tests are in place for all process reagents.

All impurities are as stated in the pharmacopoeia monograph.

An appropriate specification is provided for sodium chloride. The analytical methods used are as stated in the monograph. Batch analysis data are provided and comply with the proposed specification.

Suitable specifications have been provided for all packaging used. The primary packaging has been shown to comply with current guidelines concerning contact with foodstuff.

No re-test period is stated as sodium chloride is an ionic salt; however appropriate storage conditions and in-process testing during manufacture ensure the quality of the drug substance.

MEDICINAL PRODUCT
Other ingredients
Water for injections is the only pharmaceutical excipient. Suitable batch analysis data have been provided for water for injections, showing compliance with its proposed specification.

Pharmaceutical Development
No pharmaceutical development has been undertaken on the basis that the formula is simple and well-known. This is acceptable.

Manufacturing Process
A description and flow-chart of the manufacturing method have been provided. In-process controls are satisfactory based on process validation data and controls on the finished product. Process validation on batches has been provided.
Finished Product Specification
The finished product specification proposed is satisfactory. Test methods have been described and have been adequately validated. Batch data have been provided and comply with the release specifications.

Container Closure System
The finished product is packaged in 50 ml polyvinylchloride infusion bags, with polyamide/polypropylene laminate, polycarbonate sharps system closure and catheter adapter with breakable conus (and polypropylene caps). These are packed into cardboard cartons with product information leaflets in pack sizes of 1 bag.

Satisfactory specifications and certificates of analysis have been provided for all packaging components. All primary packaging is controlled to current European Pharmacopoeia standards and complies with guidelines concerning materials in contact with food products.

Stability of the Product
Stability studies were performed in accordance with current guidelines on batches of finished product packed in the packaging proposed for marketing. The data from these studies support a shelf-life of 24 months, with the storage conditions, “Do not store above 25°C. Do not freeze. Store in the original container.”

Bioequivalence/Bioavailability
A bioequivalence study was not necessary to support this type of application.

Summary of Product Characteristics (SmPC), Product Information Leaflet (PIL) and Labelling
The SmPC, PIL and labelling are pharmaceutically satisfactory.

A package leaflet has been submitted to the MHRA along with results of consultations with target patient groups ("user testing"), in accordance with Article 59 of Council Directive 2001/83/EC, as amended. The results indicate that the package leaflet is well-structured and organised, easy to understand and written in a comprehensive manner. The test shows that the patients/users are able to act upon the information that it contains.

MAA Form
The MAA form is satisfactory.

Expert Report
The pharmaceutical expert report is written by an appropriately qualified person and is a suitable summary of the pharmaceutical aspects of the dossier.

Conclusion
The grant of a Marketing Authorisation is recommended.
NON-CLINICAL ASSESSMENT

PHARMACODYNAMICS, PHARMACOKINETICS AND TOXICOLOGY
No new non-clinical data were submitted, which is acceptable given that this was a bibliographic application for a product containing an active substance of well-established use.

NON-CLINICAL EXPERT REPORT
The non-clinical expert report has been written by an appropriately qualified person and is satisfactory, providing an appropriate review of the non-clinical aspects of the dossier.

CONCLUSION
The grant of a Marketing Authorisation is recommended.
CLINICAL ASSESSMENT

CLINICAL PHARMACOLOGY
No new clinical pharmacology data were submitted or required for this application.

EFFICACY
No new efficacy data were submitted or required for this application.

SAFETY
No new safety data were submitted or required for this application. The applicant has provided an acceptable safety review from the literature. No new safety issues have been raised from this application.

SUMMARY OF PRODUCT CHARACTERISTICS (SmPC), PRODUCT FORMATION LEAFLET (PIL) AND LABELS
The SmPC, PIL and labels are medically acceptable.

CLINICAL EXPERT REPORT
The clinical expert report has been written by an appropriately qualified physician and is a suitable summary of the clinical aspects of the dossier.

CONCLUSION
The grant of a Marketing Authorisation is recommended.
OVERALL CONCLUSION AND BENEFIT-RISK ASSESSMENT

QUALITY
The important quality characteristics of Sodium Chloride 0.9% w/v Solution for Intravesical Use 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.

NON-CLINICAL
No new non-clinical data were submitted and none were required for this type of application. A non-clinical overview has been provided by an appropriately qualified person and consists of a review of the published literature.

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

The published literature supports the efficacy of this product in the proposed indication. This product is a bladder irrigation system of isotonic saline for use as a carrier system for appropriate drugs. It is identical in composition to other isotonic saline products that are currently marketed in the UK and these have a long history of clinical use.

SAFETY
The safety profile of sodium chloride is well-known. The literature review identified no new or unexpected safety issues or concerns.

PRODUCT LITERATURE
The approved SmPC is satisfactory. The PIL and labelling texts are satisfactory, and consistent with the approved SmPC.

BENEFIT-RISK ASSESSMENT
The quality of the product is acceptable, and no new non-clinical or clinical safety concerns have been identified. Sodium chloride is a well-known active substance. Extensive clinical experience with sodium chloride is considered to have demonstrated the therapeutic value of the product. The benefit-risk is, therefore, considered to be positive.
SODIUM CHLORIDE 0.9% W/V SOLUTION FOR INTRAVESICAL USE
PL 12070/0028

STEPS TAKEN FOR ASSESSMENT

1. The MHRA received the marketing authorisation applications on 20 January 2003.

2. Following standard checks and communication with the applicant the MHRA considered the applications valid on 11 March 2003.


5. The application was determined on 23 December 2010 and granted on 06 January 2011.
Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT
Sodium Chloride 0.9% w/v Solution for Intravesical Use.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Sodium Chloride 0.9%w/v
Each 50 ml bag contains 0.45 g of sodium chloride.
For a full list of excipients, see 6.1.

3 PHARMACEUTICAL FORM
Solution for intravesical use.
Clear colourless liquid.
Physico-chemical properties:
- pH: 3.5 – 5.5
- Osmolarity: 15.4 mOsm/50 ml
- Na+ and Cl−: 7.7 mmol/50 ml

4 CLINICAL PARTICULARS
4.1 Therapeutic indications
As a diluent for the administration of drugs within the bladder.

4.2 Posology and method of administration
Adults, children and the elderly:
The volume to be used, frequency and duration of the treatment depend on the nature of the
drug administered and the clinical condition of the patient.
Route of Administration:
Urethral.
Refer to section 6.6, Special precautions for disposal and other handling’ for further
information.

4.3 Contraindications
Hypersensitivity to any of the excipients.

4.4 Special warnings and precautions for use
Caution should be exercised in cases of advanced carcinoma of the bladder, as the bladder
may be fragile.
An intact urethra is required.
Ensure proper mixing of any added medication.
Caution should be exercised in the attachment and clamping of both the active medication and
the urinary catheter.

4.5 Interaction with other medicinal products and other forms of interaction
None.

4.6 Pregnancy and lactation
No known effect.
Caution should be exercised when prescribing to pregnant women.

4.7 Effects on ability to drive and use machines
None known.
4.8 Undesirable effects
None known.

4.9 Overdose
Not applicable.

5 PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties
There are no pharmacodynamic properties of relevance for this product.
ATC Code: B05C B 01
Irrigating solutions, salt solutions

5.2 Pharmacokinetic properties
There are no pharmacokinetic properties applicable for this product.

5.3 Preclinical safety data
There are no preclinical data of relevance to the prescriber, which are additional to that already included elsewhere in the SPC.

6 PHARMACEUTICAL PARTICULARS
6.1 List of excipients
Water for Injections

6.2 Incompatibilities
None known.

6.3 Shelf life
24 months.

6.4 Special precautions for storage
Do not store above 25°C. Do not freeze. Store in original container.

6.5 Nature and contents of container
A 50ml infusion bag constructed from 2 PVC tubes welded at each end. At one end of the bag, 2 PVC tubes are welded in place. At the other end of the bag there is one, centrally placed suspension hole in the weld web. A breakable male luer is located at the end of one of the tubes and a frangible section is located at the other end. A universal vial connector connects on to a male luer. It has a threaded stopper end and a covered needle which can be used to transfer fluid from a vial. A blue connector is fitted into the administration tube of the bladder irrigation bag.

6.6 Special precautions for disposal
1. Do not use unless the solution is clear and the container is intact.
Each 50ml bag is for single use only and any unused portion should be discarded.
INSTRUCTIONS FOR USE
1. Take the bag with the Sodium Chloride 0.9% w/v solution out of the packaging. Check that the bag is at
room temperature and that there are no particles in the
bag. Ensure that both clamps are closed. Remove the
shrink-wrap from the drug vial.
   Check that the luer lock at this junction is secure.
2. Push the spike of the luer colored connector into the
channel of the stopper of the drug vial until all air gaps
are closed. Check once again that the luer lock is secure.
3. Break the line below the luer connector and open the
clamps.
4. Invert the bag with the vial attached and gently squeeze
the bag several times. The sodium chloride solution will
flow into the vial. Gently agitate the vial to disperse the
contents.
5. Turn the bag and vial upwards again and gently press
the air out of the bag into the drug vial. As the pressure
subsides, the dissolved drug solution will flow into the
bag. Remove this step once or twice until the vial.
contents are removed.
6. Close the clamp between the vial and the bag and
check that the clamp below the blue capped catheter
adapter is also closed.
7. Bend the end of the blue cap to break the top of the
catheter adapter and remove the blue cap.
8. Push the connecting piece of the catheter adapter into
the catheter. Release the clamp below the catheter
adapter.
9. Instil the solution slowly into the bladder. Any
equipment or material which has come into contact
with the solution must be disposed of in accordance with
teh policy.

MARKETING AUTHORISATION HOLDER
Cambridge Laboratories Limited
Deltic House
Kingfisher Way
Silverlink Business Park
Wallsend
Tyne & Wear
NE28 9NX

MARKETING AUTHORISATION NUMBER(S)
PL 12070/0028

DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
06/01/2011

DATE OF REVISION OF THE TEXT
06/01/2011
Package Leaflet: Information for the User

Sodium Chloride 0.9% w/v Solution for Intravesical Use (Sodium Chloride)

Read all of this leaflet carefully because it contains important information for you.

This medicine is available without prescription, however, you still need to use Sodium Chloride Solution carefully to get the best results from it. Keep this leaflet. You may need to read it again. Ask your doctor, nurse or pharmacist if you need more information or advice. You must contact a doctor if your symptoms worsen or do not improve. If any of the side effects becomes serious or if you notice any side effect not listed in this leaflet, please talk to your doctor, nurse or pharmacist.

In this leaflet:
1. What Sodium Chloride Solution is and what it is used for
2. Before you use Sodium Chloride Solution
3. How to use Sodium Chloride Solution
4. Possible side effects
5. How to store Sodium Chloride Solution
6. Further information

1. WHAT SODIUM CHLORIDE SOLUTION IS AND WHAT IT IS USED FOR

Your medicine is called Sodium Chloride Solution. It belongs to a group of salt-containing drugs that can be placed into the urinary bladder.

Sodium Chloride Solution is used to reconstitute another drug for administration into the urinary bladder through a catheter.

2. BEFORE YOU USE SODIUM CHLORIDE SOLUTION

Before you start using Sodium Chloride Solution read the information which is given below. If you think that any of this information applies to you, or are unsure, tell your doctor, nurse, or pharmacist.

Do not use Sodium Chloride Solution if:
- You are allergic hypersensitive to sodium chloride or any of the other ingredients of Sodium Chloride Solution.

Take special care with Sodium Chloride Solution

Before treatment with Sodium Chloride Solution extra care will be taken if your bladder or uterine are fragile, for example in cases of advanced bladder cancer.

3. HOW TO USE SODIUM CHLORIDE SOLUTION

Sodium Chloride Solution will be given to you by a doctor or nurse. Each 50ml bag is for single use only and any unused portion will be discarded.

Your doctor will have decided how much and how long you need to be given Sodium Chloride Solution, if you have any further questions on the use of this product, ask your doctor, nurse or pharmacist.

4. POSSIBLE SIDE EFFECTS

There are no known side effects caused by Sodium Chloride Solution.

If you do not notice any side effects please tell your doctor, nurse or pharmacist.

5. HOW TO STORE SODIUM CHLORIDE SOLUTION

Keep out of the reach and sight of children.
- Do not use Sodium Chloride Solution after the expiry date which is stated on the bag. The expiry date refers to the last day of that month.
- Do not store above 25°C and do not freeze.
- Store in the original container.
- Do not use Sodium Chloride Solution if you notice that the solution contains any particles or has become cloudy.
- Do not use if the container has become damaged.

Using other medicines

There are no other medicines known to cause problems when they are taken when you are also using Sodium Chloride Solution.

Tell your doctor, nurse or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

Using Sodium Chloride Solution with food and drink

You can eat and drink as normal when using Sodium Chloride Solution.

Pregnancy and breast feeding

If you are or could be pregnant, tell your doctor before treatment starts.

Ask your doctor, nurse or pharmacist for advice before taking any medicine.

Driving and using machines

Your ability to drive a car or operate machinery will not be affected following administration of Sodium Chloride Solution.

4. CLINICAL PARTICULARS

4.1. THERAPEUTIC INDICATIONS

As a diluent for the administration of drugs within the urinary bladder.

4.2. DOSAGE AND METHOD OF ADMINISTRATION

Adults, children and the elderly:

The volume to be used, frequency and duration of the treatment depend on the nature of the drug administered and the clinical condition of the patient.

Route of Administration:

Urethral.

Refer to section 6.4. Special precautions for disposal and other handling for further information.

4.3. CONTRAINDICATIONS

Hypersensitivity to any of the excipients.

4.4. SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Caution should be exercised in cases of advanced carcinoma of the bladder, as the bladder may be fragile. An intact urethra is required. Ensure proper mixing of any added medication. Caution should be exercised in the attachment and clamping of both the active medication and the urinary catheter.

5. INTERACTIONS WITH OTHER MEDICATIONS AND OTHER FORMS OF INTERACTION

5.1. PHARMACODYNAMIC PROPERTIES

AtC Code: B 03 B 01

5.2. PHARMACOKINETIC PROPERTIES

There are no pharmacokinetic properties applicable for this product.

5.3. PRECAUTIONAL INSTRUCTIONS

There are no medical data of relevance to the prescriber, which are additional to that already included elsewhere in the SPC.

6. PHARMACEUTICAL PARTICULARS

6.1. LIST OF EXCIPIENTS

Water for Injections

6.2. INCOMPATIBILITIES

None known.

6.3. SHELF LIFE

24 months.

6.4. SPECIAL PRECAUTIONS FOR STORAGE

Do not store above 25°C. Do not freeze. Store in original container.

6.5. NATURE AND CONTENTS OF CONTAINER

A 50ml infusion bag constructed from 2 PVC tubes welded at each end. At one end of the bag, 2 PVC tubes are welded in place. At the other end of the bag there is one, centrally placed suspension hole in the weld area. A breakable cap is located at the end of one of the tubes and a tamperproof section is located at the other end. A universal vial connector connects to a male luer, It has a threaded stopper and a covered needle which can be used to transfer fluid from a vial. A blue connector is fitted into the administration tube of the bladder instillation bag.

4.7. EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

None known.

4.8. UNDESIRABLE EFFECTS

None known.

4.9. OVERDOSE

Not applicable.

5.1. PHARMACODYNAMIC PROPERTIES

ATC Code: B 03 B 01

5.2. PHARMACOKINETIC PROPERTIES

There are no pharmacokinetic properties applicable to this product.
6.6. SPECIAL PRECAUTIONS FOR DISPOSAL AND OTHER HANDLING
Do not use unless the solution is clear and the container is intact.
Each 50ml bag is for single use only and any unused portion should be discarded.

INSTRUCTIONS FOR USE
1. Take the bag with the Sodium Chloride 0.9% w/v solution out of the packaging. Check that the bag is at room temperature and that there are no particulates in the bag. Ensure that both clamps are closed. Remove the flip-top cap from the drug vial. Check that the laser lock at this junction is secure.
2. Push the spike of the lilac-coloured connector into the centre of the stopper of the drug vial until all six pins click into place around the neck of the vial. Check once again that the laser lock is secure.
3. Break the cone below the lilac connector and open the clamp.
4. Invert the bag with the vial attached and gently squeeze the bag several times. The sodium chloride solution will flow into the vial. Gently agitate the vial to dissolve the contents.
5. Turn the bag and vial upwards again and gently press the air out of the bag into the drug vial. As the pressure subsides, the dissolved drug solution will flow into the bag. Repeat this step once or twice until the vial contents are removed.
6. Close the clamp between the vial and the bag and check that the clamp below the lilac capped catheter adapter is also closed.
7. Band the end of the blue cap to break the tip of the catheter adapter and remove the blue cap.
8. Push the connecting piece of the catheter adapter into the catheter. Release the clamp below the catheter adapter.
9. Instil the solution slowly into the bladder. Any equipment or material which has come into contact with the solution must be disposed of in accordance with local policy.

ADMINISTRATIVE DATA
7. MARKETING AUTHORISATION HOLDER
Cambridge Laboratories Limited
Deltic House, Ringhier Way, Silverlink Business Park, Wallsend Tyne & Wear NE28 9NX
8. MARKETING AUTHORISATION NUMBER
PL 12070/0028
9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10. DATE OF REVISION OF THE TEXT
Labelling

Sterile  Apyrogenic  Single use container

SODIUM CHLORIDE 0.9% w/v SOLUTION FOR INTRAVESICAL USE

Each 50ml bag contains:
Sodium chloride 0.45g
Water for Injections to 50ml
Osmolarity 15.4 mOsm/50ml
pH 3.5 - 5.5

For dosage see the package leaflet

CAUTION
For intravesical use only.
Do not use unless solution is clear and container is intact.
Each 50ml bag is for single use only.
Discard any unused portion.
Do not store above 25°C.
Store in original container.
Do not freeze.
Keep out of the reach and sight of children.
Read the package leaflet before use.

PL 12070/0028
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BN: Exp