Safeguarding public health

MHRA

Public Assessment Report

Mutual Recognition Procedure

Water for Injections Ph Eur

MRP no: UK/H/0878/001/MR
UK licence no: PL 24598/0001

Applicant: Noridem Enterprises Limited

Water for Injections Ph Eur
PL 24598/0001; UK/H/0878/001/MR

LAY SUMMARY

On 11th November 2007, Austria, Belgium, Denmark, Germany, Greece, Ireland, The Netherlands, Norway, Portugal, Spain and Sweden approved Noridem Enterprises Limited Marketing Authorisations (licences) for the medicinal product Water for Injections Ph Eur (PL 24598/0001). This application was by mutual recognition procedure with the UK as Reference Member State (RMS). A national licence had previously been granted in the UK on 26th August 2004. This is a prescription-only medicine (POM) to be used to dissolve or dilute some medicines so that they can be given as an injection or infusion (a drip) into veins, muscles or other tissues in the body.

Water for injections is a special type of water that is sterile. This means that it is very clean and can be injected.

No new or unexpected safety concerns arose from this application and it was, therefore, judged that the benefits of using Water for Injections Ph Eur outweighed the risks, hence a Marketing Authorisation has been granted.

TABLE OF CONTENTS

Module 1

Product Name	Water for Injections Ph Eur
Type of Application	Known Active Substance Initial application Bibliographic (Article 10a) Chemical substance Prescription only
Active Substance	Water for injections
Form	Solvent for parenteral use, 100%v/v
MA Holder	Noridem Enterprises Ltd, Evagorou & Makariou, Mitsi Building 3, Suite 115, 1065 Nicosia, Cyprus
RMS	United Kingdom
CMS	Austria, Belgium, Denmark, Germany, Greece, Ireland, The Netherlands, Norway, Portugal, Spain, Sweden
Procedure Number	UK/H/0878/001/MR
Timetable	Day 90: 11/11/2007

Module 2

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

UK: Water for Injections Ph.Eur.
BE: Water for Injections Noridem Ph Eur
DK: Sterilt vand "Noridem"
ES: Water for Injections Noridem, solvent for parenteral use.
IE: Water for Injections Ph Eur.
SE: Vatten för injektiosvätskor Noridem
DE: Wasser für Injektionszwecke Noridem 1mg/ml Lösungsmittel zur Herstellung von Parenteralia
NO: Vann til injeksjonsvaesker Noridem
PT: Água para Injectáveis Noridem

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Water for Injections Ph. Eur.

3. PHARMACEUTICAL FORM

Solvent for parenteral use.

A clear liquid.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Water for Injections is used as a vehicle for dilution and reconstitution of suitable medicinal products for parenteral administration.

4.2. Posology and method of administration

Dosage:
The volume given and administration rate are dependent upon the additive.

Administration:
For parenteral use.

The directions for use of the additive will dictate the administration route.

The solution should only be used if it is clear without visible particles.

4.3. Contraindications

Contraindications related to the additive.

4.4 Special Warning and Precautions for Use

Water for Injections is hypotonic and it should not be administered alone, because it may cause haemolysis.

4.5. Interaction with other medicinal products and other forms of interaction

Interactions related to the additive.

4.6 Pregnancy and Lactation

This solvent does not present any hazard to the pregnant woman, to the foetus or to the breast-fed child.

4.7 Effects on Ability to Drive and Use Machines

Not known.

4.8 Undesirable Effects

None are known for Water for Injections, so any undesirable effects may be related to the additive.

4.9 Overdose

Haemolysis may occur following infusion of large volumes of hypotonic solutions using sterile water for injections as diluent.

The signs and symptoms of overdose may also be related to the nature of the additive. In the event of accidental overdose, the treatment should be discontinued and the patient should be observed for the appropriate signs and symptoms related to the additive administered.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

Pharmacotherapeutic group: V07A B01.

Not applicable.

5.2 Pharmacokinetic Properties

Not applicable.

5.3 Preclinical Safety Data

Not applicable.

6 PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

None.

6.2 Incompatibilities

Incompatible with oily liquids.

6.3 Shelf Life

2 years.

6.4 Special Precautions for Storage

Store below 25°C.

6.5 Nature and Contents of Container

Polypropylene ampoules, of 5 or 10 ml, packed into cartons of 50 ampoules, or of 20 ml, packed into cartons of 20 ampoules.

6.6. Special precautions for disposal and handling

After single use, product should be discarded
Any unused product should be discarded.

7. MARKETING AUTHORISATION HOLDER

Noridem Enterprises Ltd., (trading as Fannin)
Evagorou & Makariou,
Mitsi Building 3, Suit.115,
1065 Nicosia, Cyprus.

8. MARKETING AUTHORISATION NUMBER

PL 24598/0001

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

26 August 2004 / 07 September 2005

10 DATE OF REVISION OF THE TEXT

17/07/2008

Module 3

PACKAGE LEAFLET: INFORMATION FOR THE USER

Water for Injections Ph.Eur.

Water for Injections

Please read all of this leaflet carefully. It includes important information on how you should take this medicine correctly and safely.

- Keep this leaflet. You may need to read it again.
- If you are the parent of a child who is to be given this medicine, read the leaflet replacing 'you' with 'your child' throughout.
- This medicine is prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects get serious, or you notice any side effects not listed in the leaflet, please tell your doctor, nurse or pharmacist.
- If you have any further questions, please ask your doctor, nurse or pharmacist.

In this leaflet:

1. What Water for Injections is and what it is used for

Water for Injections is a special type of water that is sterile. This means that it is very clean and can be injected.

Water for Injections is used to dissolve or dilute some medicines so that they can be given as an injection or an infusion (a drip) into veins, muscles or other tissues in the body.

2. Before you use Water for Injections

Take special care with Water for Injections
Water for Injections is hypotonic (more dilute than your blood) and it should not be given on its own, because it may cause haemolysis (destroy your red blood cells).

Using other medicines
Please tell your doctor if you are taking or have recently taken any other medicines, including medicines obtained with a prescription.
There are no known interactions when Water for Injections is given with other medicines. Please make sure you read the leaflets for all your medicines, as Water for Injections is added to another medicine such as to dissolve or dilute it.

Pregnancy and breast-feeding
Water for Injections is not known to cause problems during pregnancy or breast-feeding.

As Water for Injections is given with other medicines, it is important that:

- If you are pregnant, or think you may be pregnant you must tell your doctor
- If you are breast feeding you must tell your doctor.

Your doctor will advise you if you should have this medicine.

3. How to use Water for Injections

A doctor or a nurse will usually give you this medicine. This product is a solvent for use as an injection.

Your doctor or nurse will use the correct amount to dissolve or dilute another medicine that you are receiving as an injection or a drip (your doctor or nurse may call this an infusion).
Water for injections should not be mixed with oily liquids.

Your doctor will decide the amount (dose) of your medicine that you should receive and how long you will need to take it for.

The dose will depend on what other medicine it is being used to dissolve or dilute.

If you have any further questions on the use of your medicine, ask your doctor, nurse or pharmacist.

4. Possible side effects

Like all medicines, Water for Injections can cause side effects, but not everyone gets them.

Remember that you may also get side effects from the other medicines that Water for Injections is being used to dissolve or dilute.

The expected benefit of your medicine will usually be greater than the risk of you suffering any harmful side effects.

Important: Side effects or sympthoms to look out for, and what to do if you are affected.
The first signs of having too much water in your blood are feeling tired and looking pale.
If you get any of these symptoms you must seek urgent medical advice.

Side effects are not known for Water for Injections so please read the leaflet for all your other medicines that the water is being added to dissolve or dilute.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

Please read the other side of this leaflet.

5. How to store Water for Injections

Keep out of the reach and sight of children.

Do not use Water for injections after the expiry date given on the carton and the label. The expiry date refers to the last day of the month.

Store below 25°C.

After first opening:
Only use your medicine if it is clear and colourless liquid. Open it and use it straight away.

Medicines should not be disposed of via wasterwater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. Further information

What Water for Injections contains
The active substance is Water for Injections.
1ml contains 1g water for injections, 5ml contain 5g water for injections,
10ml contain 10g water for injections, 20ml contain 20g water for injections.

There are no other ingredients in this medicine.

What Water for Injections looks like
Water for injections is a solvent for parenteral use.
Water for Injections is a clear, colourless liquid.

Contents of the pack
Each plastic ampoule will contain 5ml (millilitres), 10ml or 20ml of your medicine. 5 and 10ml ampoules come in a box of 50 ampoules. 20ml ampoules come in a box of 20 ampoules. Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer
Marketing Authorisation Holder: Noridem Enterprises Ltd., Evagorou & Makariou, Mitsi Building 3, Suit.115, 1065 Nicosia, Cyprus.
Manufacturer: Demo S.A., 21st Km National Road Athens-Lamia, 14568 Athens, Greece.

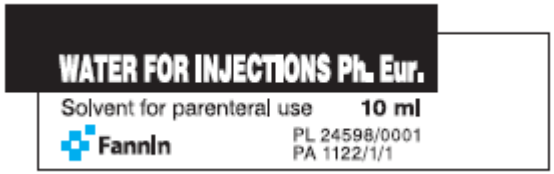
This medicinal product is authorised in the Member States if the EEA under the following names:

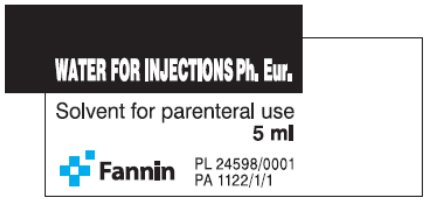
UK: Water for Injections Ph.Eur.
BE: Water for Injections Noridem Ph Eur
DK: Sterilt vand Noridem
ES: Water for Injections Noridem, solvent for parenteral use.
IE: Water for Injections Ph Eur.
SE: Vatten för injektiosvätskor Noridem
DE: Wasser für Injektionszwecke Noridem 1mg/ml Lösungsmittel zur Herstellung von Parenteralia
NO: Vann til injeksjonsvaesker Noridem
PT: Água para Injectáveis Noridem

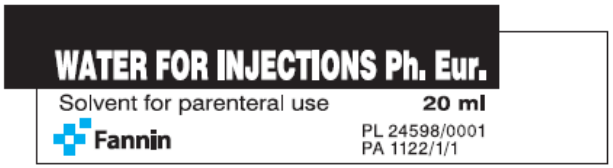
This leaflet was approved in July 2008.

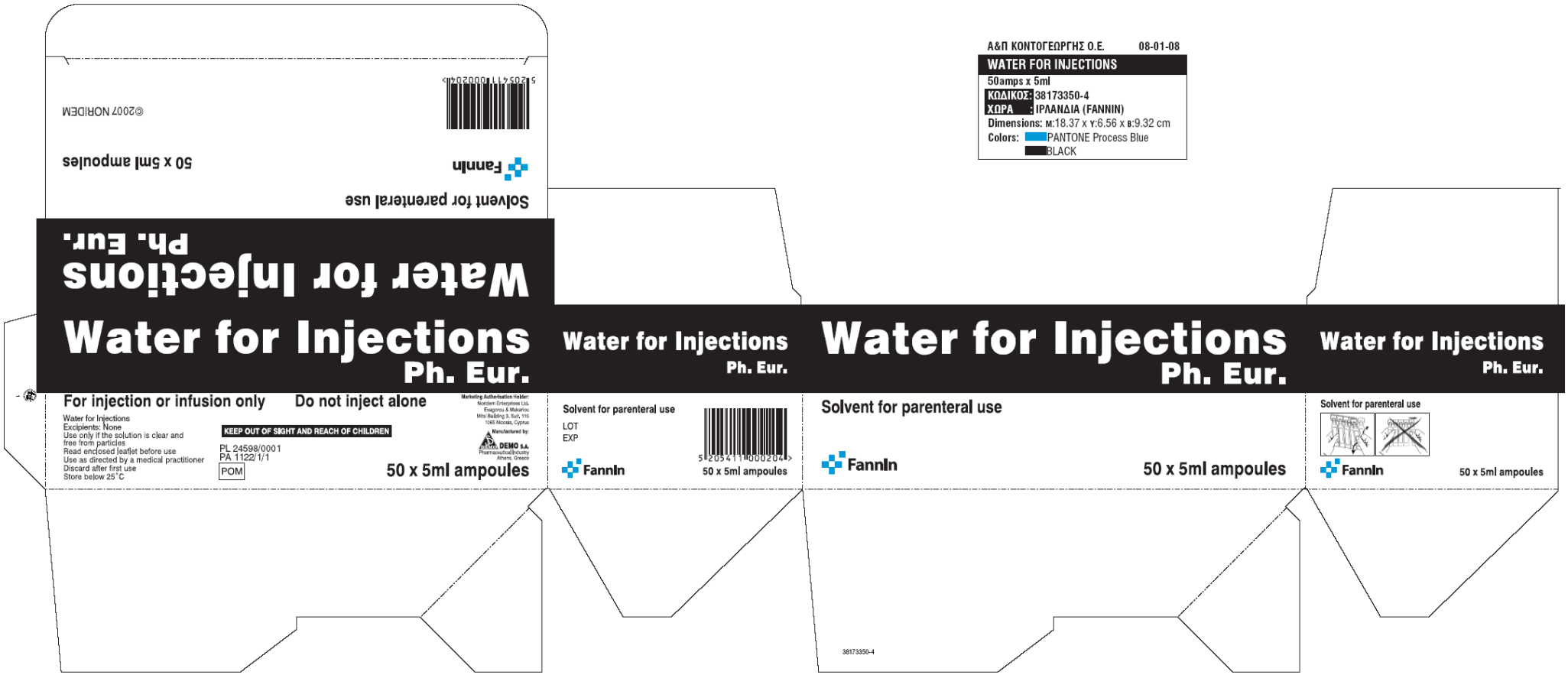
If this leaflet is difficult to see or read please contact the following address for help:
Fannin, Pincent's Kiln Industrial Park, Reading, RG31 7SB, United Kingdom.

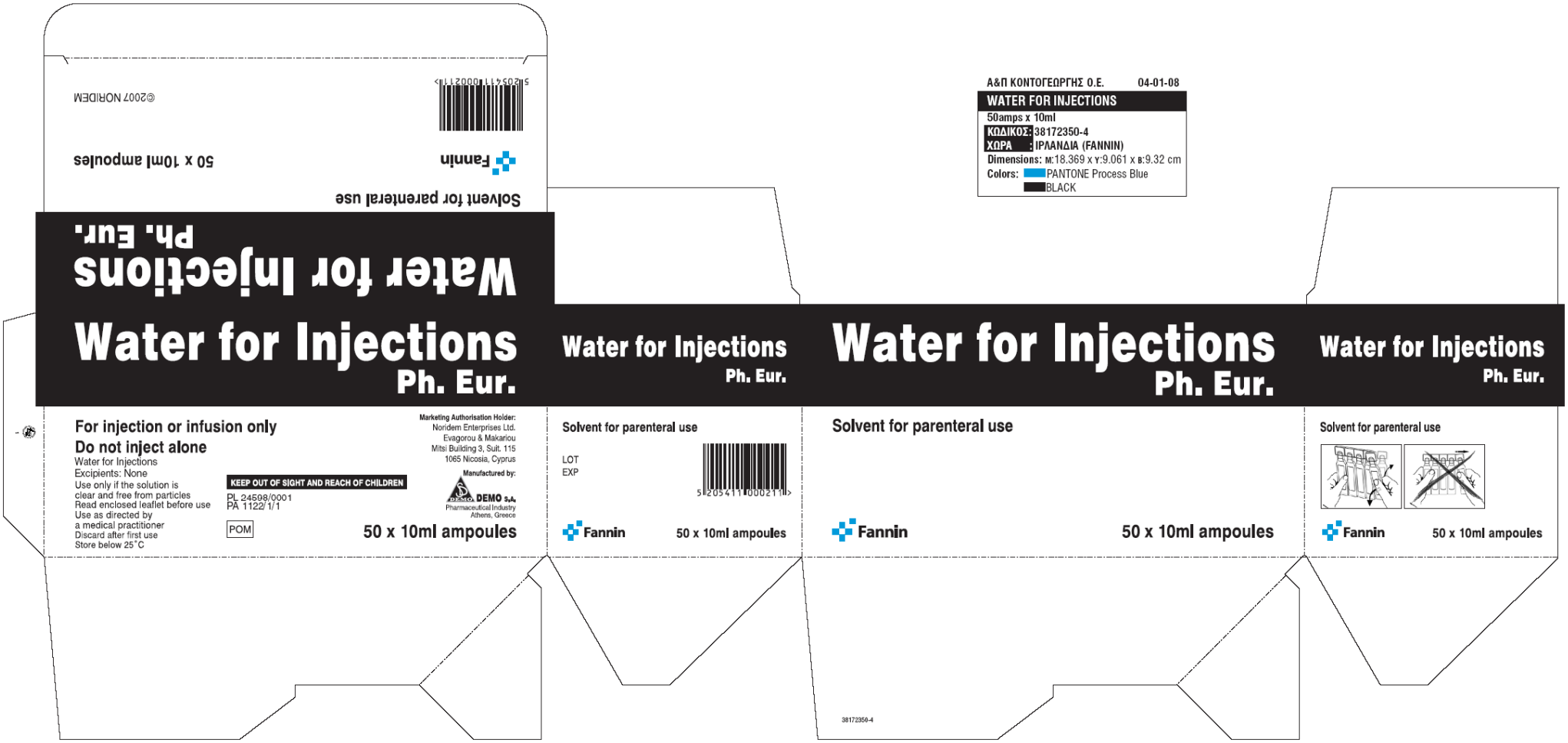
Module 4
Labelling








Α&Π ΚΟΝΤΟΓΕΩΡΓΗΣ Ο.Ε. 08-01-08
WATER FOR INJECTIONS
50amps x 5ml
ΚΩΔΙΚΟΣ: 38173350-4
ΧΩΡΑ : ΙΡΛΑΝΔΙΑ (FANNIN)
Dimensions: Μ:18.37 x Υ:6.56 x Β:9.32 cm
Colors: PANTONE Process Blue
BLACK
Water for Injections Ph. Eur.
Solvent for parenteral use
Fannin
50 x 5ml ampoules
©2007 NORIDEM
Water for Injections Ph. Eur.
For injection or infusion only
Do not inject alone
Water for Injections
Excipients: None
Use only if the solution is clear and free from particles
Read enclosed leaflet before use
Use as directed by a medical practitioner
Discard after first use
Store below 25˚C
KEEP OUT OF SIGHT AND REACH OF CHILDREN
PL 24598/0001
PA 1122/1/1
POM
Marketing Authorisation Holder:
Noridem Enterprises Ltd.
Evagorou & Makariou
Mitsi Building 3, Suit, 115
1065 Nicosia, Cyprus
Manufactured by:
DEMO S.A.
Pharmaceutical Industry
Athens, Greece
50 x 5ml ampoules
Water for Injections Ph. Eur.
Solvent for parenteral use
LOT
EXP
Fannin
50 x 5ml ampoules
Water for Injections Ph. Eur.
Solvent for parenteral use
Fannin
50 x 5ml ampoules
38173350-4
Water for Injections Ph. Eur.
Solvent for parenteral use
Fannin
50 x 5ml ampoules


Α&Π ΚΟΝΤΟΓΕΩΡΓΗΣ Ο.Ε. 04-01-08
WATER FOR INJECTIONS
50amps x 10ml
ΚΩΔΙΚΟΣ: 38172350-4
ΧΩΡΑ : ΙΡΛΑΝΔΙΑ (FANNIN)
Dimensions: Μ:18.369 x Υ:9.061 x Β:9.32 cm
Colors: PANTONE Process Blue
BLACK
Water for Injections Ph. Eur.
Water for Injections
Ph. Eur.
Solvent for parenteral use
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50 x 10ml ampoules
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For injection or infusion only
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Excipients: None
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POM
Marketing Authorisation Holder:
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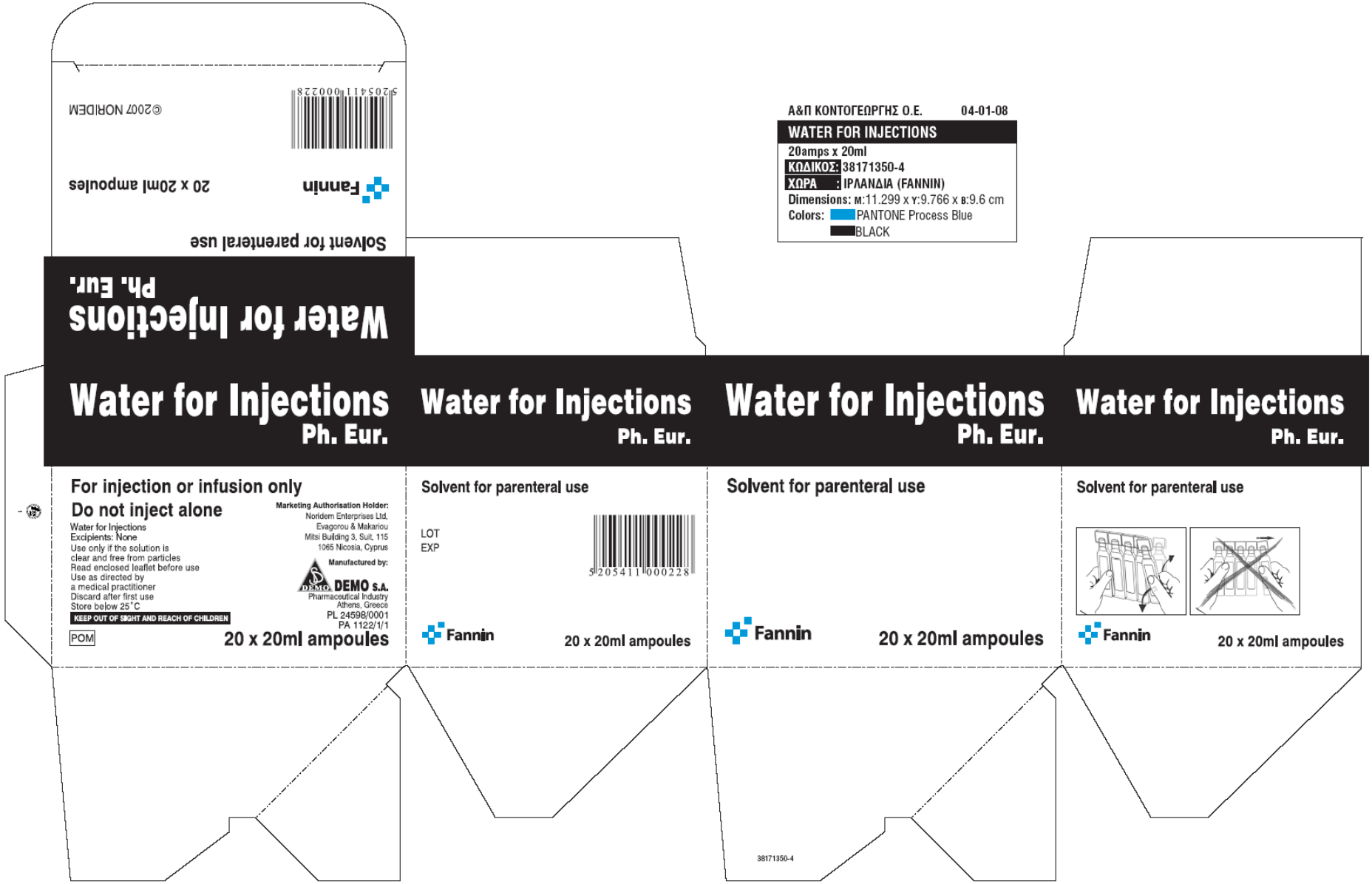
Evagorou & Makariou
Mitsi Building 3, Suit. 115
1065 Nicosia, Cyprus
Manufactured by:
DEMO S.A.
Pharmaceutical Industry
Athens, Greece
50 x 10ml ampoules
LOT
EXP
38172350-4



A&Π ΚΟΝΤΟΓΕΩΡΓΗΣ Ο.Ε. 04-01-08

WATER FOR INJECTIONS
20amps x 20ml
ΚΩΔΙΚΟΣ: 38171350-4
ΧΩΡΑ : ΙΡΛΑΝΔΙΑ (FANNIN)
Dimensions: Μ:11.299 x Υ:9.766 x Β:9.6 cm
Colors: PANTONE Process Blue
BLACK

Module 5
Scientific discussion during initial procedure

1. INTRODUCTION

Background

This application was submitted by Noridem Enterprises Limited for Water for Injections Ph Eur, via the Mutual Recognition Procedure. The UK acted as Reference Member State for the procedure, which was granted a UK licence on 26th August 2004.

Water for Injections is a well-known and widely used solvent. It is compatible with an extensive number of substances and can be used as a vehicle/diluent for the parenteral administration of other medicinal products.

Based on the review of the data on quality, safety and efficacy, the RMS considered that the application for Water for Injections Ph Eur could be approved for use as a vehicle for dilution and reconstitution of suitable medicinal products for parenteral administration.

Day 90 for the procedure was 11th November 2007, subsequent to which Marketing Authorisations were approved in Austria, Belgium, Denmark, Germany, Greece, Ireland, The Netherlands, Norway, Portugal, Spain and Sweden.

Overall Benefit/Risk Assessment

Water for Injections is a well known and widely used solvent. It is compatible with an extensive number of substances and can be used as a vehicle/diluent for the parenteral administration of other medicinal products.

No preclinical studies were conducted, and none are required as the product is well established for medicinal use.

No clinical studies were conducted, and none are required as the product is well established for medicinal use.

The RMS has been assured that acceptable standards of GMP are in place at all sites responsible for the manufacture and assembly of this product prior to granting its national authorisation.

For manufacturing sites within the community, the RMS has accepted copies of current manufacturer authorisations issued by inspection services of the competent authorities as certification that acceptable standards of GMP are in place at those sites.

2. QUALITY ASPECTS

S. Active Substance

As the only constituent in this product is water for injections, no active substance data was submitted or required.

P. Medicinal Product

Other Ingredients

The only constituent of this product is water for injections. No materials of human or animal origin are used in the production of water for injections. No genetically modified organisms are used in the production of water for injections.

Pharmaceutical Development
Water for Injections has been developed according to the corresponding European Pharmacopoeia monograph as a vehicle for dilution and reconstitution of suitable medicinal products for parenteral administration.

Manufacturing Process
An appropriate account of the manufacturing process has been provided. The manufacturing process has been validated and has shown satisfactory results.

Finished Product Specification
The finished product specification is satisfactory and in-line with the current European Pharmacopoeia for water for injections. 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 working standards used.

Container-Closure System
The product is packed into polypropylene 5 or 10ml ampoules packed into cartons of 50 or 20ml ampoules packed into cartons of 20.

Satisfactory specifications and certificates of analysis have been provided for all packaging components. All primary packaging complies with the relevant regulations regarding materials for parenteral use.

Product Stability
Stability studies were performed in the packaging proposed for marketing and in accordance with current guidelines. All results from stability studies were within specified limits. These data support a shelf-life of 2 years with the storage condition ‘Store below 25°C’.

Bioequivalence/Bioavailability
No bioequivalence studies have been submitted for this application and none were required.

Summary of Product Characteristics (SPC), Patient Information Leaflet (PIL), Labels
The SPC, PIL and Labels are pharmaceutically acceptable.

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 Forms
The MAA forms are pharmaceutically satisfactory.
Expert Report
The pharmaceutical expert report has been written by an appropriately qualified person and is a suitable summary of the pharmaceutical dossier.

Conclusion
The grant of a marketing authorisation is recommended.

3. PRE-CLINICAL ASPECTS

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

4. CLINICAL ASPECTS

Clinical Pharmacology

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

Efficacy

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

Safety

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

Summary of Product Characteristics (SPC), Patient Information Leaflet (PIL), Labels

The SPC, PIL and labels are medically acceptable. The SPC is consistent with that for other similar products.

Conclusion

The grant of a marketing authorisation is recommended.

5. OVERALL CONCLUSION

QUALITY

The important quality characteristics of Water for Injections Ph Eur 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 preclinical data were submitted and none were required for an application of this type.

EFFICACY

No significant new or unexpected safety concerns were found during the clinical development.

The SPC, PIL and labelling are appropriate for a product of this type.

BENEFIT-RISK ASSESSMENT

The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. Extensive clinical experience with Water for Injections is considered to have demonstrated the therapeutic value of the compound. The benefit-risk is considered to be positive.