EPIRUBICIN HYDROCHLORIDE 10 MG AND 50 MG POWDER FOR SOLUTION FOR INJECTION

PL 40378/0153-4

UKPAR

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LAY SUMMARY

On 4th October 2012, the MHRA granted Aptil Pharma Limited Marketing Authorisations (licences) for Epirubicin Hydrochloride 10 mg and 50 mg Powder for Solution for Injection.

Epirubicin Hydrochloride 10 mg and 50 mg Powder for Solution for Injection contain the active ingredient epirubicin hydrochloride.

Epirubicin hydrochloride belongs to a group of medicines called anthracyclines, which are used to treat cancer. Epirubicin hydrochloride is a medicine that acts upon cells that are actively growing (such as cancer cells) in such a way as to slow or stop their growth and increases the likelihood that the cells will die. This medicine helps to selectively kill the cancer tissue rather than normal, healthy tissue.

Epirubicin hydrochloride is used to treat a variety of cancers, either alone or in combination with other drugs. The way in which it is used depends upon the type of cancer that is being treated.

When injected into the bloodstream, epirubicin hydrochloride has been found to be useful in the treatment of cancers of the breast, ovaries, stomach, bowel and lung. Epirubicin hydrochloride can be given in the same way to treat cancers of the blood-forming tissues such as malignant lymphomas, leukaemias and multiple myeloma.

In addition, epirubicin hydrochloride can be injected into the bladder through a tube. This is sometimes used to treat abnormal cells or cancers of the bladder wall. It can also be used after other treatments to try to prevent such cells from growing again.

No new or unexpected safety concerns arose from these applications and it was therefore judged that the benefits of taking Epirubicin Hydrochloride 10 mg and 50 mg Powder for Solution for Injection outweigh the risks and Marketing Authorisations were granted.

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SCIENTIFIC DISCUSSION

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INTRODUCTION

The MHRA granted Marketing Authorisations for the medicinal products Epirubicin Hydrochloride 10 mg and 50 mg Powder for Solution for Injection (PL 40378/0153-4) to Aptil Pharma Limited on 4th October 2012. These prescription-only medicines (POM) have produced responses in a wide range of neoplastic conditions, including breast, ovarian, gastric, lung and colorectal carcinomas, malignant lymphomas, leukaemias and multiple myeloma.

Intravesical administration of Epirubicin Hydrochloride 10 mg and 50 mg Powder for Solution for Injection has been found to be beneficial in the treatment of superficial bladder cancer, carcinoma-in-situ and in the prophylaxis of recurrences after transurethral resection.

These applications for Epirubicin Hydrochloride 10 mg and 50 mg Powder for Solution for Injection were submitted according to Article 10c (informed consent application) of Directive 2001/83/EC, as amended, cross-referring to Epirubicin Hydrochloride 10 mg and 50 mg Powder for Solution for Injection, licensed to Apsla Limited on 14th April 2011 (PL 33410/0010-11).

It is considered that the pharmacovigilance system as described by the applicant fulfils the requirements and provides adequate evidence that the applicant has the services of a qualified person responsible for pharmacovigilance together with the necessary means for notification of any adverse reaction suspected of occurring.

Satisfactory justification was provided for the absence of a Risk Management Plan.

No new data were submitted nor were they necessary for these ‘informed consent’ applications because the data are identical to those of the previously granted cross-reference products.

PHARMACEUTICAL ASSESSMENT

LICENCE NO:	PL 40378/0153-4
PROPRIETARY NAME:	Epirubicin Hydrochloride 10 mg and 50 mg Powder for Solution for Injection
ACTIVE(S):	Epirubicin hydrochloride
COMPANY NAME:	Aptil Pharma Limited
E.C. ARTICLE:	Article 10c of Directive 2001/83/EC, as amended
LEGAL STATUS:	POM

1. INTRODUCTION

These are 'informed consent' applications for Epirubicin Hydrochloride 10 mg and 50 mg Powder for Solution for Injection (PL 40378/0153-4) submitted under Article 10c of Directive 2001/83/EC, as amended. The proposed Marketing Authorisation Holder (MAH) is Aptil Pharma Limited, 9th Floor, CP House, 97 – 107 Uxbridge Road, Ealing, London W5 5TL.

These applications cross-refer to Epirubicin Hydrochloride 10 mg and 50 mg Powder for Solution for Injection, licensed to Apsla Limited on 14th April 2011 (PL 33410/0010-11).

2. MARKETING AUTHORISATION APPLICATION FORM

2.1 NAME(S)

The proposed names of the products are Epirubicin Hydrochloride 10 mg and 50 mg Powder for Solution for Injection. The products have been named in line with current requirements.

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

The products contain 10 mg and 50 mg of epirubicin hydrochloride. The products are sterile, freeze-dried, orange-red coloured, lyophilised cakes (powder for solution for injection). After reconstitution, each vial contains 2 mg/ml epirubicin hydrochloride. The products Epirubicin Hydrochloride 10 mg and 50 mg Powder for Solution for Injection are for intravenous or intravesical administration.

The 10 mg strength presentation is packaged in a 10 ml Type I moulded flint glass vial with a 20 mm bromo butyl rubber stopper and 20 mm aluminium flip-off, tear-off seal.

The 50 mg strength presentation is packaged in a 50 ml Type I moulded flint glass vial with a 20 mm bromo butyl rubber stoppers and 20 mm aluminium flip-off tear-off seal.

There is 1 vial in each pack for both presentations.

The shelf-life of the products as packaged for sale is 2 years with storage conditions 'Store below 30°C. Keep the container in the outer carton'.

The shelf-life of the products after reconstitution is according to directions:
'In-use stability has been demonstrated for 24 hours at 15°C - 25°C and for 48 hours at 2-8°C in water for injections and 0.9 % w/v sodium chloride solution. However from a microbiological point of view, it is recommended that the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8ºC'.

This is consistent with the information registered for the cross-reference products.

2.3 Legal status
Prescription-only medicine (POM).

2.4 Marketing authorisation holder (MAH)/Contact Persons/Company
The proposed MAH is Aptil Pharma Limited, 9th Floor, CP House, 97 – 107 Uxbridge Road, Ealing, London W5 5TL.

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

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

2.6 Qualitative and quantitative composition
The composition is consistent with the details registered for the cross-reference products.

2.7 Manufacturing process
The manufacturing process is consistent with the details registered for the cross-reference products.

2.8 Finished product/shelf-life specifications
The finished product specifications are in line with those registered for the cross-reference products.

2.9 Drug substance specification
The drug substance specification is consistent with that registered for the cross-reference products.

2.10 TSE Compliance
With the exception of lactose monohydrate, none of the excipients used contain material of animal or human origin. The applicant has provided a declaration that the milk used in the production of the lactose monohydrate is sourced from healthy animals under the same conditions as those intended for human consumption.

This information is consistent with that for the cross-reference products.

3. EXPERT REPORTS
Quality, non-clinical and clinical expert statements have been provided 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 Section 2.1 for details of the proposed product names. The appearance of the products is identical to the cross-reference products.

5. SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)
The SmPC is consistent with that registered for the cross-reference products.

6. PATIENT INFORMATION LEAFLET (PIL)/LABELLING

PIL

A satisfactory bridging report to previous 'user testing' of the readability of the PIL has been provided. The report cross-refers to the readability testing for the reference product PIL, which is acceptable since the content, layout, formatting and appearance of the proposed leaflet are identical to that of the reference PIL.

Labelling

The artwork is comparable to the artwork registered for the cross-reference products and complies with statutory requirements.

7. CONCLUSIONS

The data submitted with the applications are acceptable. The grant of these Marketing Authorisations is recommended.

NON-CLINICAL ASSESSMENT

No new non-clinical data have been supplied with these applications and none are required for applications of this type.

An Environmental Risk Assessment was not submitted or required for these generic applications.

CLINICAL ASSESSMENT

No new clinical data have been supplied with these applications and none are required for applications of this type.

OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT

QUALITY

The data for these applications are consistent with those previously approved for the cross-reference products and, as such, have been judged to be satisfactory.

NON-CLINICAL

No new non-clinical data were submitted and none are required for applications of this type.

EFFICACY

These applications are considered identical to the previously granted applications, Epirubicin Hydrochloride 10 mg and 50 mg Powder for Solution for Injection, licensed to Apsla Limited on 14th April 2011 (PL 33410/0010-11).

No new or unexpected safety concerns arose from these applications.

At the time of assessment, the SmPCs, PIL and labelling were satisfactory and consistent with those for the cross-reference products.

RISK BENEFIT ASSESSMENT

The quality of the products is acceptable and no new non-clinical or clinical safety concerns have been identified. The applicant's products are identical to the cross-reference products. Extensive clinical experience with epirubicin hydrochloride is considered to have demonstrated the therapeutic value of the compound. The risk-benefit balance is therefore considered to be positive.

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STEPS TAKEN FOR ASSESMENT

1	The MHRA received the Marketing Authorisation Applications on 20th July 2012.
2	Following standard checks and communication with the applicant the MHRA considered the applications valid on 26th July 2012.
3	The applications were determined on 4th October 2012.

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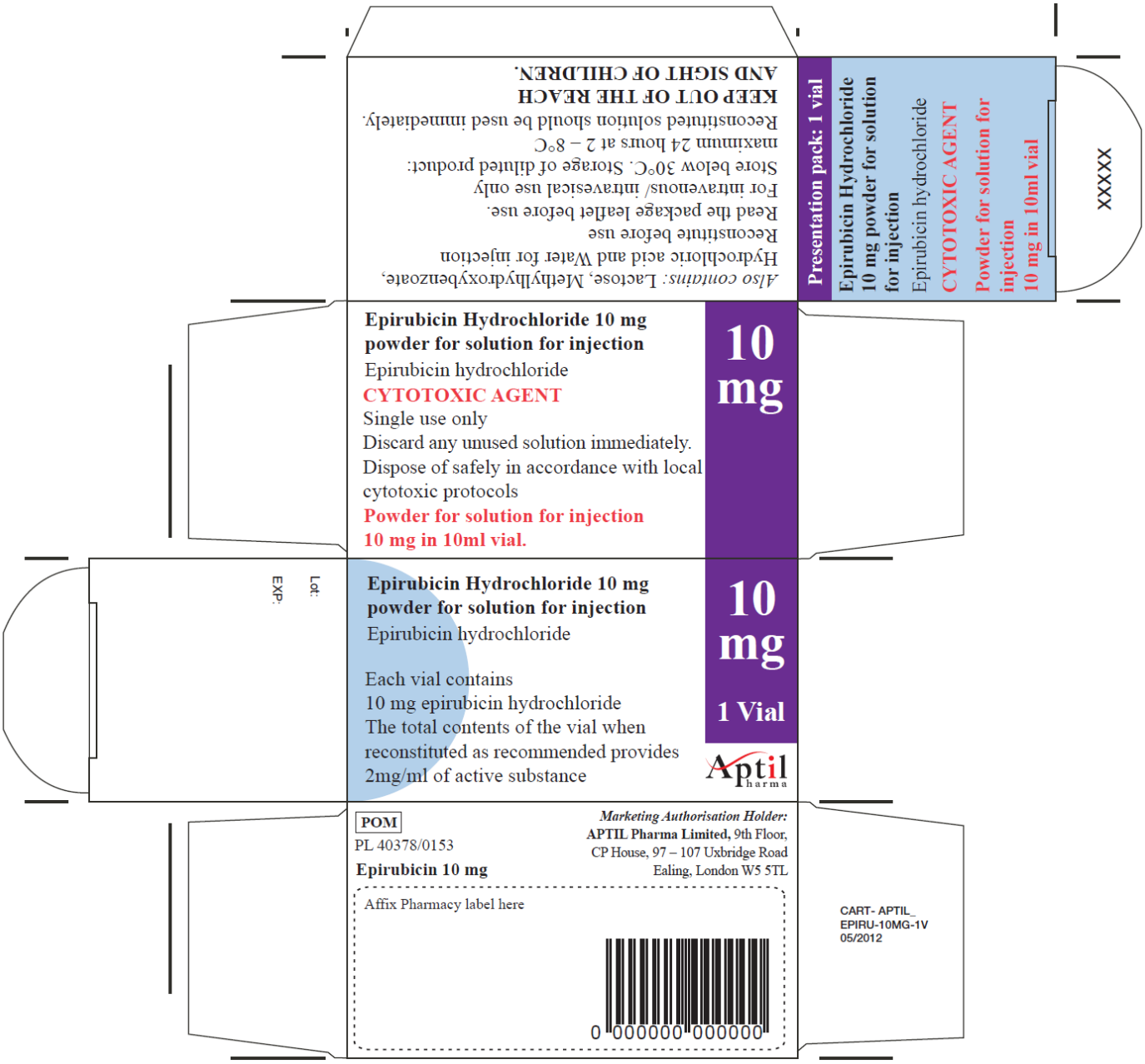
STEPS TAKEN AFTER ASSESSMENT

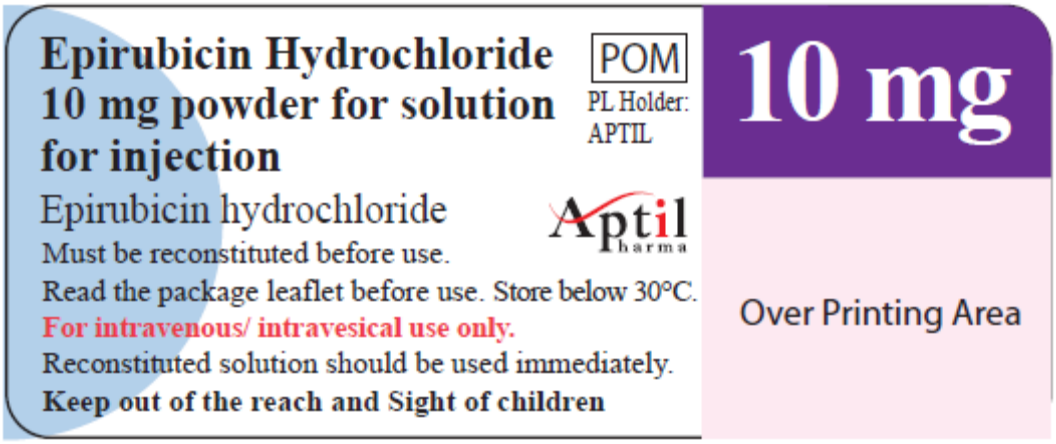
Date submitted	Application type	Scope	Outcome

SUMMARY OF PRODUCT CHARACTERISTICS AND PATIENT INFORMATION LEAFLET

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

LABELLING


Presentation pack: 1 vial
Epirubicin Hydrochloride 10 mg powder for solution for injection
Epirubicin hydrochloride
CYTOTOXIC AGENT
Powder for solution for injection
10 mg in 10ml vial
XXXXX
KEEP OUT OF THE REACH AND SIGHT OF CHILDREN.
Reconstituted solution should be used immediately.
maximum 24 hours at 2 – 8°C
Store below 30°C. Storage of diluted product:
For intravenous/ intravesical use only
Read the package leaflet before use.
Reconstitute before use
Hydrochloric acid and Water for injection
Also contains: Lactose, Methylhydroxybenzoate,
Epirubicin Hydrochloride 10 mg powder for solution for injection
Epirubicin hydrochloride
CYTOTOXIC AGENT
Single use only
Discard any unused solution immediately.
Dispose of safely in accordance with local cytotoxic protocols
Powder for solution for injection
10 mg in 10ml vial.
10 mg
Lot:
EXP:
Epirubicin Hydrochloride 10 mg powder for solution for injection
Epirubicin hydrochloride
Each vial contains
10 mg epirubicin hydrochloride
The total contents of the vial when reconstituted as recommended provides 2mg/ml of active substance
10 mg
1 Vial
Aptil harma
POM
PL 40378/0153
Epirubicin 10 mg
Marketing Authorisation Holder:
APTIL Pharma Limited, 9th Floor, CP House, 97 – 107 Uxbridge Road Ealing, London W5 5TL
Affix Pharmacy label here
0 000000 000000
CART- APTIL_ EPIRU-10MG-1V 05/2012


Epirubicin Hydrochloride 10 mg powder for solution for injection
POM
PL Holder: APTIL
10 mg
Epirubicin hydrochloride
Aptil harma
Must be reconstituted before use.
Read the package leaflet before use. Store below 30°C.
For intravenous/ intravesical use only.
Reconstituted solution should be used immediately.
Keep out of the reach and Sight of children
Over Printing Area