

Public Assessment Report

Name of the Product:

Ceftriaxone AptaPharma

1 g and 2 g

powder for solution for injection/infusion

(ceftriaxone sodium)

Procedure number: HU/H/0590/001-002/DC

Marketing authorisation holder: Apta Medica Internacional d.o.o.

Date: 10th March 2021

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LAY SUMMARY

After careful assessment of its quality and therapeutic benefit/risk ratio, the member states have granted the marketing authorisation of the Ceftriaxone AptaPharma 1 g and 2 g powder for solution for injection/infusion. The holder of the marketing authorisation is Apta Medica Internacional d.o.o.

The active substance is ceftriaxone sodium.

Ceftriaxone AptaPharma 1 g powder for solution for injection/infusion

Each vial contains 1 g ceftriaxone (as ceftriaxone sodium).

Ceftriaxone AptaPharma 2 g powder for solution for injection/infusion

Each vial contains 2 g ceftriaxone (as ceftriaxone sodium).

Ceftriaxone AptaPharma does not contain any excipients.

The appearance of the powder for solution for injection/infusion is:

Ceftriaxone AptaPharma is almost white or yellowish powder.

Ceftriaxone AptaPharma 1 g and 2 g powder for solution for injection/infusion are supplied in the following pack sizes:

Ceftriaxone AptaPharma 1 g powder for solution for injection/infusion

Ceftriaxone AptaPharma 1 g powder for solution for injection/infusion in a 10 mL colourless glass vial with a rubber stopper and an aluminium cap with plastic disc.

Packs of 10 vials.

Ceftriaxone AptaPharma 2 g powder for solution for injection/infusion

Ceftriaxone AptaPharma 2 g powder for solution for injection/infusion in a 50 mL colourless glass vial with a rubber stopper and an aluminium cap with plastic disc.

Packs of 5 vials.

Not all pack sizes may be marketed.

Ceftriaxone inhibits bacterial cell wall synthesis following attachment to penicillin binding proteins (PBPs). This results in the interruption of cell wall (peptidoglycan) biosynthesis, which leads to bacterial cell lysis and death.

What patients need to know before using Ceftriaxone AptaPharma

- **Ceftriaxone AptaPharma must not be given:**
 - if the patients are allergic to ceftriaxone or any of the other ingredients of this medicine (listed in section 6);

- if the patients have had sudden or severe allergic reactions to penicillin or to any other similar antibiotics (e.g. cephalosporins, carbapenems or monobactams). The signs include sudden swelling of the throat or face, which may lead to difficulty breathing or swallowing, sudden swelling of the hands, feet and ankles and severe rash, which develops quickly;
- if the patients are allergic to lidocaine and have been prescribed Ceftriaxone AptaPharma to be given as an injection into a muscle.

Ceftriaxone AptaPharma must not be given to:

- preterm newborns;
- full-term newborns (up to 28 days of age) who have certain blood problems or jaundice (yellowing of the skin or the white of the eye) or are to be given a calcium-containing product into their vein.

Warnings and precautions

Patients should talk to their doctor, pharmacist before they take Ceftriaxone AptaPharma if:

- the patient has recently received or are about to receive calcium-containing products;
- the patient has recently had diarrhoea after antibiotic treatment. If the patient has or has had intestinal problems, in particular colitis (bowel inflammation);
- the patient has liver or kidney problems;
- the patient has gall stones or kidney stones;
- the patient has other illnesses, such as haemolytic anaemia (reduced number of red blood cells, which may make the patient's skin look pale yellow and cause weakness or difficulty breathing);
- the patient is on a low sodium diet;
- the patient experiences or has previously experienced a combination of any of the following symptoms: rash, red skin, blistering of the lips eyes and mouth, skin peeling, high fever, flu-like symptoms, increased levels of liver enzymes seen in blood tests and an increase in a type of white blood cell (eosinophilia) and enlarged lymph nodes (signs of severe skin reactions, see also section 4 "Possible side effects").

If the patient requires blood or urine tests

If the patient has been prescribed Ceftriaxone AptaPharma for a long time, he/she may require a regular blood testing. Ceftriaxone AptaPharma may affect the results from sugar testing in blood and urine, known as Coombs test. If the patient is about to have tests:

- he/she should tell the specialist that he/she has received Ceftriaxone AptaPharma.

If the patient is diabetic or need to have his/her blood glucose level monitored he/she should not use certain blood glucose monitoring systems which may estimate blood glucose incorrectly while he/she are receiving ceftriaxone. If the patient use such systems he/she should check the instructions for use and consult his/her doctor, pharmacist or nurse. Alternative testing methods should be used if necessary.

Children

Patients should tell to his/her doctor, pharmacist or nurse before their child is administered Ceftriaxone AptaPharma if:

- their child has recently been given or is to be given a product that contains calcium into their vein.

Other medicines and Ceftriaxone AptaPharma

Patients should tell their doctor or pharmacist if they are taking, have recently taken or might take any other medicines.

In particular, patients should tell their doctor or pharmacist if they are taking any of the following medicines:

- a type of antibiotic called aminoglycoside;
- an antibiotic called chloramphenicol (used to treat infections, especially of the eyes).

Pregnancy, breast-feeding and fertility

- If the patient is pregnant or breast-feeding, think she may be pregnant or are planning to have a baby, she should ask her doctor for advice before taking this medicine.
- The doctor will consider the benefit of treating her with Ceftriaxone AptaPharma against the risk to her baby.

Driving and using machines

Ceftriaxone AptaPharma can cause dizziness. If the patient feel dizzy, he/she should not drive or use any tools or machines. Patients should talk to their doctor if they experience these symptoms.

Ceftriaxone AptaPharma contains sodium

Ceftriaxone AptaPharma 1 g powder for solution for injection/infusion:

This medicine contains approximately 82.8 mg sodium (main component of cooking/table salt) in each 1 g. This is equivalent to 4.15 % of the recommended maximum daily dietary intake of sodium for an adult.

Ceftriaxone AptaPharma 2 g powder for solution for injection/infusion:

This medicine contains approximately 165.6 mg sodium (main component of cooking/table salt) in each 2 g. This is equivalent to 8.3 % of the recommended maximum daily dietary intake of sodium for an adult.

How to use Ceftriaxone AptaPharma?

Ceftriaxone AptaPharma is usually given by a doctor or nurse. It can be given as

- a drip (intravenous infusion) or as an injection directly into a vein or
- into a muscle.

Ceftriaxone AptaPharma is made up by the doctor, pharmacist or nurse and will not be mixed with or given to the patient at the same time as calcium-containing injections.

The usual dose

The doctor will decide the correct dose of Ceftriaxone AptaPharma for the patients. The dose will depend on the severity and type of infection; whether the patients are on any other antibiotics; the patient's weight and age; how well their kidneys and liver are working. The number of days or weeks that Ceftriaxone AptaPharma is given to patients depends on what sort of infection they have.

Adults, older people and children aged 12 years and over with a body weight greater than or equal to 50 kilograms (kg):

- 1 to 2 g once a day depending on the severity and type of infection. If the patient has a severe infection, his/her doctor will give he/she a higher dose (up to 4 g once a day). If his/her daily dose is higher than 2 g, the patient may receive it as a single dose once a day or as two separate doses.

Newborn babies, infants and children aged 15 days to 12 years with a body weight of less than 50 kg:

- 50 – 80 mg Ceftriaxone AptaPharma for each kg of the child's body weight once a day depending on the severity and type of infection. If the patient has a severe infection, his/her doctor will give he/she a higher dose up to 100 mg for each kg of body weight to a maximum of 4 g once a day. If his/her daily dose is higher than 2 g, he/she may receive it as a single dose once a day or as two separate doses.
- Children with a body weight of 50 kg or more should be given the usual adult dose.

Newborn babies (0-14 days)

- 20 – 50 mg Ceftriaxone AptaPharma for each kg of the child's body weight once a day depending on the severity and type of infection.
- The maximum daily dose is not to be more than 50 mg for each kg of the baby's weight.

People with liver and kidney problems

These patients may be given a different dose to the usual dose. Their doctor will decide how much Ceftriaxone AptaPharma they will need and will check their closely depending on the severity of the liver and kidney disease.

What to do if more Ceftriaxone AptaPharma was taken than it should have been?

If the patient accidentally receive more than his/her prescribed dose, he/she should contact his/her doctor or nearest hospital straight away.

What to do if taking Ceftriaxone AptaPharma was forgotten?

If the patient misses an injection, he/she should have it as soon as possible. However, if it is almost time for their next injection, skip the missed injection. Patients should not take a double dose (two injections at the same time) to make up for a missed dose.

If the patient stops using Ceftriaxone AptaPharma

Patients should not stop taking Ceftriaxone AptaPharma unless their doctor tells them to. If patients have any further questions on the use of this medicine, they should ask their doctor or nurse.

Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

The following side effects may happen with this medicine:

Severe allergic reactions (not known, frequency cannot be estimated from the available data)

If the patients have a severe allergic reaction, they should tell a doctor straight away.

The signs may include:

- sudden swelling of the face, throat, lips or mouth. This can make it difficult to breathe or swallow;
- sudden swelling of the hands, feet and ankles.

Severe skin reactions (not known, frequency cannot be estimated from the available data)

If the patient gets a severe skin reaction, they should tell a doctor straight away.

The signs may include:

- a severe rash that develops quickly, with blisters or peeling of the skin and possibly blisters in the mouth (Stevens-Johnson syndrome and toxic epidermal necrolysis which are also known as SJS and TEN);
- a combination of any of the following symptoms: widespread rash, high body temperature, liver enzyme elevations, blood abnormalities (eosinophilia), enlarged lymph nodes and other body organs involvement (Drug Reaction with Eosinophilia and Systemic Symptoms which is also known as DRESS or drug hypersensitivity syndrome);
- Jarisch-Herxheimer reaction which causes fever, chills, headache, muscle pain, and skin rash that is usually self-limiting. This occurs shortly after starting Rocephin treatment for infections with spirochete such as Lyme disease.

Other possible side effects:

Common (may affect up to 1 in 10 people)

- Abnormalities with the patient's white blood cells (such as a decrease of leucocytes and an increase of eosinophils) and platelets (decrease of thrombocytes).
- Loose stools or diarrhoea.
- Changes in the results of blood tests for liver functions.
- Rash.

Uncommon (may affect up to 1 in 100 people)

- Fungal infections (for example, thrush).
- A decrease in the number of white blood cells (granulocytopenia).

- Reduction in number of red blood cells (anaemia).
- Problems with the way the patient's blood clots. The signs may include bruising easily and pain and swelling of their joints.
- Headache.
- Dizziness.
- Feeling sick or being sick.
- Itching (pruritis).
- Pain or a burning feeling along the vein where Ceftriaxone AptaPharma has been given. Pain where the injection was given.
- A high temperature (fever).
- Abnormal kidney function test (blood creatinine increased).

Rare (may affect up to 1 in 1,000 people)

- Inflammation of the large bowel (colon). The signs include diarrhoea, usually with blood and mucus, stomach pain and fever.
- Difficulty in breathing (bronchospasm).
- A lumpy rash (hives) that may cover a lot of the patient's body, feeling itchy and swelling.
- Blood or sugar in the patient's urine.
- Oedema (fluid build-up).
- Shivering.

Not known (frequency cannot be estimated from the available data)

- A secondary infection that may not respond to the antibiotic previously prescribed
- Form of anaemia where red blood cells are destroyed (haemolytic anaemia).
- Severe decrease in white blood cells (agranulocytosis).
- Convulsions.
- Vertigo (spinning sensation).
- Inflammation of the pancreas (pancreatitis). The signs include severe pain in the stomach which spreads to the patient's back.
- Inflammation of the mucus lining of the mouth (stomatitis).
- Inflammation of the tongue (glossitis). The signs include swelling, redness and soreness of the tongue.
- Problems with patient's gallbladder, which may cause pain, feeling sick and being sick.
- A neurological condition that may occur in neonates with severe jaundice (kernicterus).
- Kidney problems caused by deposits of calcium ceftriaxone. There may be pain when passing water (urine) or low output of urine.
- A false positive result in a Coombs' test (a test for some blood problems).
- A false positive result for galactosaemia (an abnormal build up of the sugar galactose).
- Ceftriaxone AptaPharma may interfere with some types of blood glucose tests – patients should check with their doctor.

Reporting of side effects

If the patients get any side effects, they should talk to their doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. Patients can also report side effects

directly via the national reporting system listed in [Appendix V](#). By reporting side effects patients can help provide more information on the safety of this medicine.

How to store Ceftriaxone AptaPharma?

This medicine should be kept out of the sight and reach of children.

This medicinal product does not require any special temperature storage conditions.

Patients should keep the vial in the outer carton in order to protect from light.

Ceftriaxone AptaPharma solutions are colourless to yellow depending on their concentration, which is not related to their activity, efficacy and tolerability.

The reconstituted solution should be administered immediately after preparation.

Patients should not throw away any medicines via wastewater or household waste. Their pharmacist should be asked how to throw away medicines they no longer use. These measures will help protect the environment.

SCIENTIFIC DISCUSSION

This module reflects the scientific discussion for the approval of Ceftriaxone AptaPharma 1 g and 2 g powder for solution for injection/infusion. The procedure was finalised on 20-10-2020. For information on changes after this date please refer to the module 'Update'.

I. INTRODUCTION

Based on the review of the quality, safety and efficacy data, the Member States have granted a marketing authorisation for **Ceftriaxone AptaPharma 1 g and 2 g powder for solution for injection/infusion from Aptapharma.**

The product is indicated for the treatment of the following infections in adults and children including term neonates (from birth):

- *Bacterial meningitis*
- *Community acquired pneumonia*
- *Hospital acquired pneumonia*
- *Acute otitis media*
- *Intra-abdominal infections*
- *Complicated urinary tract infections (including pyelonephritis)*
- *Infections of bones and joints*
- *Complicated skin and soft tissue infections*
- *Gonorrhoea*
- *Syphilis*
- *Bacterial endocarditis*

A comprehensive description of the indications and posology is given in the SmPC.

The marketing authorisation has been granted pursuant to Article 10(1) of Directive 2001/83/EC and therefore contained no new clinical or preclinical data, other than supporting literature where necessary.

The reference medicinal products are:

Rocephin 1 g Powder for solution for injection or infusion, Roche Products Limited, UK., approved on 02-09-1988

and

Rocephin 2 g Powder for solution for injection or infusion, Roche Products Limited, UK., approved on 02-09-1988.

II. QUALITY ASPECTS

II.1 Introduction

The chemical-pharmaceutical assessment report concerns the application of Ceftriaxone Apta-Pharma 1 g and 2 g powder for solution for injection or infusion via a decentralized procedure according to Article 10.1 of Directive 2001/83/EC (i.e a generic application). The products have been developed by Apta Medica Internacional d.o.o.

The reference products are Rocephin 1 g and 2 g powder and solvent for solution for injection, which were the products of Roche Products Limited.

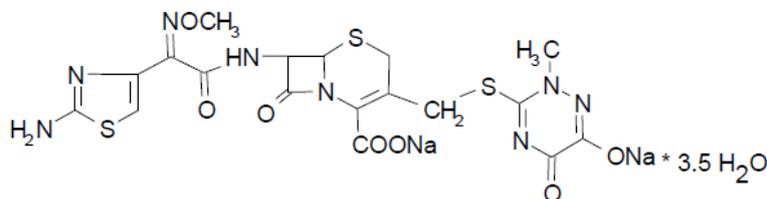
II.2 Drug substance

Data on the quality and manufacture of the active substance were provided in the applicant's submission using CEP procedures with additional data in the marketing authorization dossier. The Quality Overall Summary is adequate.

INN name: Ceftriaxone Sodium

Chemical name: Disodium (6R,7R)-7-[[[(2Z) (2-aminothiazol-4-yl)(methoxyimino)acetyl]amino] -3-[[[(2-methyl-6-oxido-5-oxo-2,5-dihydro-1,2,4-triazin-3-yl)sulfanyl]methyl] -8-oxo -5-thia-1-azabicyclo [4.2.0] oct-2-ene-2-carboxylate, Hemiheptahydrate

Structure:



The active substance is almost white or yellowish crystalline powder, slightly hygroscopic. It is very soluble in water, sparingly soluble in methanol, very slightly soluble in ethanol.

The presented specification is in accordance with the Ph.Eur. general monograph on *Substances for Pharmaceutical Use* and the ICH Q6A guideline. The specifications reflect all relevant quality attributes of the active substance and were found to be adequate to control the quality of the drug substance. The limits set are properly justified.

Testing methods not described in details in the Pharmacopoeia are adequately drawn up and sufficiently validated. Reference materials used by the drug product manufacturer for the control of the substance are adequately characterised.

The substance complies with the requirements of the EMA guideline on genotoxic impurities.

Batch analysis data justify the limits, indicate the good performance of testing methods and demonstrate the batch-to-batch consistency of the production.

Re-test periods and the packaging materials have been mentioned on the CEPs.

Good Manufacturing Practice (GMP) compliance of the API manufacture is demonstrated by the Applicant.

II.3 Medicinal product

The aim was to develop a generic product of Ceftriaxone for injection/infusion (sterile powder corresponding to 1 g or 2 g of Ceftriaxone) essentially similar to the one which has already been marketed in E.C. member states for over 10 years.

A satisfactory package of data on development pharmaceuticals has been presented. The chosen sterilization method of the drug product is justified.

As a result of development studies product with the following appearance was obtained:

- Almost white or yellowish crystalline sterile powder.

The drug product consist of the sterile Ceftriaxone sodium without any excipients.

A description and flow chart of the manufacturing method has been provided. Appropriate in-process controls are included in the manufacturing process. Satisfactory batch formulae were also presented. GMP compliance of the manufacturing site has been demonstrated.

The finished product specification is satisfactory. Acceptance criteria have been justified with respect to conventional pharmaceutical requirements as prescribed in the relevant dosage form monograph of the Ph.Eur. and the ICH Q6A guideline. Appropriate control strategy was selected. The test methods have been described and have been adequately validated, as appropriate. Batch data have been provided and complied with the specification.

The primary packaging material of the product is glass vial type III, closed with bromobutyl stopper, Type I and flip cap. The colour of the plastic disc for dosage 1 g and 2 g is red or purple, respectively.

Specifications and quality certificates for all packaging components are enclosed.

Finished product stability studies have been conducted in accordance with the current guidelines. Based on the results, a shelf-life of 3 years is approved with the following special storage restriction: "Keep in the outer carton in order to protect from light. This medicinal product does not require any special temperature storage conditions."

The Summary of Product Characteristics, patient Information Leaflet and label texts are pharmaceutically acceptable.

II.4 Discussion on chemical, pharmaceutical and biological aspects

Conclusion: The product has been shown to meet the current regulatory requirements with regards to its quality and content of the active substance as well as dosage-form characteristics until the end of the approved shelf-life consistently. The manufacture and the quality standards applied adequately support the safe use and efficacy of the product.

III. NON-CLINICAL ASPECTS

III.1 Introduction

Pharmacodynamic, pharmacokinetic and toxicological properties of Ceftriaxone are well known. As Ceftriaxone is a widely used, well-known active substance, no further studies are required and the Applicant provides none.

The non-clinical overview is therefore based on a review of data available in several scientific databases or published in relation to the active ingredient.

III.2 Pharmacology

Ceftriaxone inhibits bacterial cell wall synthesis following attachment to penicillin binding proteins (PBPs). This results in the interruption of cell wall (peptidoglycan) biosynthesis, which leads to bacterial cell lysis and death.

III.3 Pharmacokinetics

No new non-clinical pharmacokinetic studies were conducted by the Applicant.

III.4 Toxicology

Published information on toxicological studies with Ceftriaxone was the basis for the evaluation. No new toxicity studies were submitted by the Applicant for the product, which is acceptable for this type of application.

There is evidence from animal studies that high doses of Ceftriaxone calcium salt led to formation of concrements and precipitates in the gallbladder of dogs and monkeys, which proved to be reversible. Animal studies produced no evidence of toxicity to reproduction and genotoxicity. Carcinogenicity studies on ceftriaxone were not conducted.

III.5 Ecotoxicology/environmental risk assessment (ERA)

Since *Ceftriaxone AptaPharma 1 g and 2 g powder for solution for injection/infusion* is intended for generic substitution, this will not lead to an increased exposure to the environment. An environmental risk assessment is therefore not deemed necessary.

III.6 Discussion on the non-clinical aspects

Pharmacodynamics, pharmacokinetics and toxicology of Ceftriaxone are well-known. As *Ceftriaxone AptaPharma 1 g and 2 g powder for solution for injection/infusion* is a generic product there is no need for further excessive non-clinical studies. The non-clinical part of the application is acceptable.

IV. CLINICAL ASPECTS

IV.1 Introduction

The clinical pharmacology of ceftriaxone is well known.
The application contains an adequate review of published clinical data.

IV.2 Pharmacokinetics

The medicinal product *Ceftriaxon AptaPharma 1 g and 2 g powder for solution for injection/infusion* is a generic medicinal product, it contains the same drug substance, Ceftriaxon, in the same pharmaceutical form, a sterile powder for injection, and the same strength, as the originator products.

In compliance with Appendix II of the Guideline on the Investigation of Bioavailability and Bioequivalence – *CPMP/EWP/QWP/1401/98 Rev. 1, Corr *** of 20th January 2010, bioequivalence studies were not required.

IV.3 Pharmacodynamics

There were no clinical pharmacology studies performed to evaluate the pharmacodynamics of Ceftriaxone Aptapharma and none are required for applications of this type.

IV.4 Clinical efficacy

No new efficacy data have been submitted and none are required. The applicant has provided an adequate review of clinical trials published in the literature, describing the efficacy and safety profile of ceftriaxon.

IV.5 Clinical safety

No new safety data have been submitted and none are required. The applicant has provided an adequate review of clinical trials published in the literature, describing the efficacy and safety profile of Ceftriaxon.

IV.6 Pharmacovigilance

IV.6.1 Summary of the Pharmacovigilance System

The Applicant has submitted a signed Summary of the Applicant's Pharmacovigilance System. Provided that the Pharmacovigilance System Master File fully complies with the new legal requirements as set out in the Commission Implementing Regulation 520/2012 and as detailed in the relevant GVP module, the Summary is considered acceptable.

IV.6.2 Risk Management Plan

<i>Summary of safety concerns</i>	
Important identified risks	<ul style="list-style-type: none"> • Hypersensitivity and allergy • Immune mediated hemolytic anemia • Clostridium difficile associated diarrhea (CDAD) • Ceftriaxone calcium precipitation in the neonate population • Hyperbilirubinemia with potential for encephalopathy in the neonate population • Renal lithiasis • Biliary lithiasis • Severe cutaneous adverse reactions (including Erythema multiforme, Stevens Johnson Syndrome, Toxic epidermal necrolysis and Acute generalised exanthematous pustulosis) • Risk of bleeding due to increased anticoagulant effect in patients on oral anticoagulants
Important potential risks	<ul style="list-style-type: none"> • Pancreatitis • Agranulocytosis • Systemic adverse reactions related to incorrect administration of ceftriaxone in combination with lidocaine
Missing information	<ul style="list-style-type: none"> • Use in patients with both severe renal and hepatic impairment • Use in pregnancy and during breastfeeding

Safety concerns of the product is in line with the safety specification of the reference product (version 2.1 - 11 May 2018) - Rocephin 1 g and 2 g powder for solution for injection or infusion - available on the CMDh website (<https://www.hma.eu/464.html>)

Pharmacovigilance plan: Routine pharmacovigilance activities are considered sufficient to manage all of the safety concerns connected to Ceftriaxone AptaPharma 1g and 2 g powder for solution for injection/infusion.

No additional activities are proposed.

Risk Minimisation Measures: Routine risk minimisation measures (i.e. wording in SmPC, PL and classification as a prescription only medicine) are considered sufficient to manage all of the safety concerns connected to Ceftriaxone AptaPharma 1g and 2 g powder for solution for injection/infusion.

No additional activities are proposed. For any further information on risk minimisation, please refer to the product information.

IV.6.3 Periodic Safety Update Reports

The requirements for submission of periodic safety update reports for these medicinal products are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

IV.7 Discussion on the clinical aspects

The application concerns a generic product.

Ceftriaxone AptaPharma Powder for solution for injection/infusion is indicated for the treatment of the following infections in adults and children including term neonates (from birth):

- Bacterial meningitis
- Community acquired pneumonia
- Hospital acquired pneumonia
- Acute otitis media
- Intra-abdominal infections
- Complicated urinary tract infections (including pyelonephritis)
- Infections of bones and joints
- Complicated skin and soft tissue infections
- Gonorrhoea
- Syphilis
- Bacterial endocarditis

There were no objection against granting the marketing authorization from a clinical point of view.

V. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

V.1 Summary

The estimated benefit/risk is positive.

There are no objections to approval of Ceftriaxon AptaPharma 1g and 2g powder for solution for injection/infusion from non-clinical and clinical point of view.

Based on the review of the data on safety and efficacy, the RMS considers that the application for Ceftriaxon AptaPharma 1g and 2g powder for solution for injection/infusion, **is approvable.**

V.2 Classification

Prescription-only medicine.

V.3 Package Leaflet and user consultation

The package leaflet has been evaluated via a user consultation study in accordance with the requirements of Articles 59(3) and 61(1) of Directive 2001/83/EC. The language used for the purpose of user testing the PIL was English.

The results show that the package leaflet meets the criteria for readability as set out in the Guideline on the readability of the label and package leaflet of medicinal products for human use.

The test consisted of the initial pilot study with three professionals and then two phases of testing with ten subjects'. The questions covered the following areas sufficiently: traceability, comprehensibility and applicability.

VI. UPGRADE: STEPS TAKEN AFTER THE INITIAL PROCEDURE WITH AN INFLUENCE ON THE PUBLIC ASSESSMENT REPORT

This module reflects the procedural steps and scientific information after the finalisation of the initial procedure.

Scope	Procedure number	Product information affected	Date of start of the procedure	Date of end of procedure	Approval or non approval
C.I. z) Other variation EMA/PRAC/570590/2020	HU/H/0590/001/IA/001	Yes	2021.01.22	2021.02.21	Positive
C.I. z) Other variation EMA/PRAC/570590/2020	HU/H/0590/002/IA/001	Yes	2021.01.22	2021.02.21	Positive

*Only procedure qualifier, chronological number and grouping qualifier (when applicable)