21.06.2021 TEK BAŞINA SEFIKSIM ETKIN MADDESINI İÇEREN ÜRÜNLER HK_ENG_

MINISTRY OF HEALTH OF THE REPUBLIC OF TURKEY Medicines and Medical Devices Agency of Turkey

Number : E-24931227-000-465772 Subject : Products Containing the Active Substance Cefixime Alone NORMAL 21.06.2021

DOSSIER

a) Association announcement dated 27.04.2018, with No. E.79750 b) Association announcement dated 05.12.2018, with No. E.210290 c) Association announcement dated 31.07.2019, with No. E.120042

As a result of the re-assessment made by the "Clinical Evaluation Commission of Medicinal Products for Human Use" regarding products containing the active substance cefixime alone, the 5- tablet package size has been deemed suitable and the referred Association announcements (a), (b) and (c) have been revoked.

It is necessary to make the following amendments in the Summary of Product Characteristics of the registered products and products for which registration application will be submitted:

4.1. In the therapeutic indications section:

For All Formulations:

1. Acute otitis media: In the treatment of acute otitis media caused by Streptococcus pneumonia, Hemophilus influenzae and Moraxella catarrhalis,

2. Acute sinusitis: In the treatment of acute sinusitis caused by Streptococcus pneumonia, Hemophilus influenzae and Moraxella catarrhalis,

3. Acute tonsillopharyngitis or pharyngitis: Antimicrobial treatment in acute tonsillopharyngitis or pharyngitis is necessary only for Streptococcus pyogenes.

4. Acute bacterial exacerbation of chronic bronchitis (caused by Streptococcus pneumoniae and Hemophilus influenzae),

5. In non-complicated urinary system infections,

6. In the treatment of non-complicated gonococcal infections.

4.2 In the posology and mode of administration section: a) For oral liquid forms containing 100 mg/5 ml and 200 mg/5 ml cefixime (suspension, solution, syrup, etc.):

Dose for children aged 12 years and below:

Total daily recommended dose is 8 mg/kg/day. A daily dose of 8 mg/kg is recommended for clinical use to be used as a single daily dose of 8 mg/day/kg or two separated doses of 4 mg/kg each.

Body weight (kg) Daily dose (mg) Daily dose (mL) 5 – 7.5 50 2.5 7.6 – 10 80 4 10.1 – 12.5 100 5 12.6 – 20.5 150 7.5 20.6 – 28 200 10 28.1 – 33 250 12.5 33.1 – 40 300 15 40.1 – 45 350 17.5 45.1 and above 400 20

*It is necessary to use a measurement device (e.g., injector) marked at each ml for ensuring recommended dosage.

Dosage for adults and children aged above 12 years: Daily recommended dose is 400 mg. A single daily dose of 400 mg/kg or 200 mg in two equally divided doses is recommended for clinical use. <NAME OF MEDICINE> may be taken at empty or full stomach.

A single dose of 400 mg should be used in non-complicated gonococcal infections.

The treatment of streptococcal tonsillopharyngitis should last 10 days.

The use of doses and pharmaceutical dosage forms suitable for adults is recommended. Patients with difficulty in swallowing solid food may use the oral suspension and sachet forms.

Supplementary information on special populations:

Pediatric population: The efficacy and safety of cefixime has not been proven in infants younger than 6 months.

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Renal Failure: The dose should be reduced in patients with significant renal dysfunction.

The dose of cefixime should be 1x200 mg for adults with a creatinine clearance of <20 ml/min/1.73 m 2

or who receive continuous peritoneal dialysis and children aged above 12 years. Hemodialysis or peritoneal dialysis does not guarantee significant clearance of the medicine from the body.

Liver Failure: Dose adjustment is not required.

Geriatric population: No special warning is needed. Cefixime may be used in the elderly in the same way as with adults.

b) For oral tablets, capsules and similar forms containing 200 mg and 400 mg cefixime:

Dosage for adults and children aged above 12 years:

Daily recommended dose is 400 mg. A single daily dose of 400 mg/kg or 200 mg in two equally divided doses is recommended for clinical use. <NAME OF MEDICINE> may be taken at empty or full stomach.

A single dose of 400 mg should be used in non-complicated gonococcal infections.

The treatment of streptococcal tonsillopharyngitis should last 10 days.

The use of doses and pharmaceutical dosage forms suitable for adults is recommended. Patients with difficulty in swallowing solid food may use the oral suspension and sachet forms.

Additional information on special populations: Pediatric population: The efficacy and safety of cefixime has not been proven in infants younger than 6 months.

Renal Failure: The dose should be reduced in patients with significant renal dysfunction.

The dose of cefixime should be 1x200 mg for adults with a creatinine clearance of <20 ml/min/1.73 m 2

or who receive continuous peritoneal dialysis and children aged above 12 years. Hemodialysis or peritoneal dialysis does not guarantee significant clearance of the medicine from the body.

Liver Failure: Dose adjustment is not required.

Geriatric population: No special warning is needed. Cefixime may be used in the elderly in the same way as with adults.

c) For oral sachets, effervescent and similar forms containing 100 mg and 200 mg cefixime:

Dosage for adults and children aged above 12 years:

Daily recommended dose is 200-400 mg. This dose may be administered at once or in two equal doses to be taken at an interval of 12 hours.

Additional information on special populations: Pediatric population: The efficacy and safety of cefixime has not been proven in infants younger than 6 months.

4.4 In the special warnings and precautions for use section: For All Formulations: The following warning should be included: “As absorption is higher in the oral suspension formulation compared to the tablet formulation, tablet formulations should not be used instead of oral suspension formulations in the treatment of acute otitis media due to the deficiency that may occur in the bioequivalence of the tablet.”

The referred corrections should be made in the Package Leaflets as well.

Package sizes should be aligned with the treatment period.

The SPC/PL applications of the products relating to the products in which abovementioned changes are made should be submitted to the Pharmacological Evaluation Unit within 1 month as of the date of publication of this association decision, the applications relating to the products with ongoing registration process should be submitted to the Registration Unit and this announcement should be taken into account for the products with ongoing registration process. I hereby submit for your information and kindly request for the adoption of relevant action so that the applications for the referred applications are not made to the Clinical Evaluation Unit.

Assoc. Prof. Dr. Tolga KARAKAN President of the Agency

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RESTRICTED Revoked MINISTRY OF HEALTH OF THE REPUBLIC OF TURKEY Medicines and Medical Devices Agency of Turkey

NORMAL Number : 77893119-000-E.79750 Subject : Medicines containing Cefixime

27.04.2018 DOSSIER

It is necessary to make the following amendments in the Summary of Product Characteristics of the registered products containing cefixime and products containing cefixime for which registration application will be submitted:

4.1. In the therapeutic indications section:

1. Acute otitis media: In the treatment of acute otitis media caused by Streptococcus pneumonia, Hemophilus influenzae and Moraxella catarrhalis,

2. Acute sinusitis: In the treatment of acute sinusitis caused by Streptococcus pneumonia, Hemophilus influenzae and Moraxella catarrhalis,

3. Acute tonsillopharyngitis or pharyngitis: Antimicrobial treatment in acute tonsillopharyngitis or pharyngitis is necessary only for Streptococcus pyogenes.

4. Acute bacterial exacerbation of chronic bronchitis (caused by Streptococcus pneumoniae and Hemophilus influenzae),

5. In non-complicated urinary system infections,

6. In the treatment of non-complicated gonococcal infections.

4.2 In the posology and mode of administration section:

1. The total daily recommended dose for children is 8 mg/kg/day. A daily dose of 8 mg/kg is recommended for clinical use to be used as a single daily dose of 8 mg/day/kg or two separated doses of 4 mg/kg each. A table should be prepared according to the weight of children also for 100 mg/5ml for suspension formulations and for 200 mg/5 ml for adequate products:

Body weight (kg) Daily dose (mg) Daily dose (mL) 5 – 7.5 50 2.5 7.6 – 10 80 4 10.1 – 12.5 100 5 12.6 – 20.5 150 7.5 20.6 – 28 200 10 28.1 – 33 250 12.5 33.1 – 40 300 15 40.1 – 45 350 17.5 45.1 and above 400 20

2. Daily recommended dose for adults is 400 mg. A single daily dose of 400 mg/kg or 200 mg in two equally divided doses is recommended for clinical use. <NAME OF MEDICINE> may be taken at empty or full stomach.

a. A single dose of 400 mg should be used in non-complicated gonococcal infections.

b. The treatment of streptococcal tonsillopharyngitis should last 10 days.

The following sentences should be added to the SPC and PL texts of oral suspension forms: “The use of adequate dose and pharmaceutical dosage forms is recommended for adults. Oral suspension and sachet forms may be used in patients with swallowing difficulties”, while the following sentence should be added to the SPC and PL of tablet, capsule and sachet forms: “The use of adequate dose and pharmaceutical dosage forms is recommended for children aged between 6 months-12 years.”

Supplementary Information on special populations:

Renal Failure: The dose should be reduced in patients with significant renal dysfunction. The dose of cefixime should be 1x200 mg for adults with a creatinine clearance of <20 ml/min/1.73 m 2

or who receive continuous peritoneal dialysis and children aged above 12 years. Hemodialysis or peritoneal dialysis does not guarantee significant clearance of the medicine from the body.

Liver Failure: Dose adjustment is not required.

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Geriatric population: No special warning is needed. Cefixime may be used in the elderly in the same way as with adults.

Pediatric population: Its efficacy and safety have not been proven in infants younger than 6 months.

The referred corrections should be made also in the Package Leaflet.

As the blood levels achieved in suspension formulations compared to the tablet formulations in the treatment of acute otitis media, clinical success is higher. Therefore, tablet formulations should not be used in place of suspension formulations in the treatment of acute otitis. This information should be included in the warning and precautions section.

As the clinical use specified in the indications of the 5-tablet formulations available on the market is not sufficient for day treatments, the package should be modified accordingly.

I hereby submit for your information and kindly request for the conduct of relevant action so that the SPC/PL applications related to the products in which the referred changes are made are sent to the Clinical Evaluation Unit by 01.06.2018 for review.

Dr. Hakkı GÜRSÖZ President of the Agency Distribution: Association of Research-Based Pharmaceutical Companies Pharmaceutical Manufacturers Association of Turkey Turkish Pharmaceutical Industry Association Association of Innovator Pharmaceutical Companies Self-Care Products Association

RESTRICTED

MINISTRY OF HEALTH OF THE REPUBLIC OF TURKEY Medicines and Medical Devices Agency of Turkey

Number : 77893119-000-E.210290 Subject : Medicines containing Cefixime Revoked NORMAL

05.12.2018

DOSSIER

Ref: a) Circular dated 05.01.2018, with No. E.3072 b) Circular dated 27.04.2018, with No. E.79750

The circular indicated in reference a), published in relation with the medicines containing cefixime which are registered or for which registration application is made is no longer valid and it has been deemed suitable to make the following amendment stated in the circular indicated in reference b):

The statement under the title Renal Impairment in the section 4.2. Posology and mode of administration, Additional Information on Special populations, reading, “Hemodialysis or peritoneal dialysis enables the medicine to be cleared at a significant level from the body.”, shall be amended as “Hemodialysis or peritoneal dialysis does not enable the medicine to be cleared at a significant level from the body.”

The statement indicated in the “warnings and precautions” section in the circular indicated in reference (b), reading “In the treatment of acute otitis, clinical success rate is higher due to high blood levels achieved with the suspension formulations compared to those achieved with tablet formulations. Therefore, tablet formulations should not be used in place of suspension formulations in the treatment of acute otitis media.” should be replaced with the warning reading “Due to the deficiency that may develop in the bioequivalence of the tablet as absorption increases more significantly compared to the tablet formulation in the oral suspension formulation, tablet formulations should not be used in place of oral suspension formulations in the treatment of acute otitis media.” in the section 4.4. Special warnings and precautions for use.

I hereby submit for your information and kindly request for the relevant action so that the SPC/PL applications relating to the products in which abovementioned changes are made are sent to the Pharmacological Evaluation Unit until 04.01.2019 for review.

Assoc. Prof. Dr. İsmail Mert VURAL Deputy President of the Agency

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RESTRICTED

MINISTRY OF HEALTH OF THE REPUBLIC OF TURKEY Medicines and Medical Devices Agency of Turkey Revoked

Number: 62820468-000-E.120042 Subject: Medicines containing Cefixime NORMAL

31.07.2019 DOSSIER

Ref: Our Association announcement dated 05.12.2018, with No. E.210290

In addition to our announcement to Associations regarding the medicines containing the active substance Cefixime, which are registered or for which a registration application will be made:

It is necessary to make the following arrangements in the Summary of Product Characteristics (SPC) and Package Leaflet (PL) of 100 mg/200 mg sachet and 100 mg/200 mg effervescent forms:

Summary of Product Characteristics:

4.2. Posology and mode of administration

Children: The use of the adequate dose and pharmaceutical dosage forms is recommended for children aged between 6 months-12 years.

The daily total recommended dose is 8 mg/kg. The daily recommended dose in clinical use is 8 mg/kg to be used as a single daily dose of 8m/kg or to be divided into 2 doses of 4 mg/kg each.

Children aged 2 years and above may use the following doses (of the form containing Cefixime): • Between 2-4 years: A daily single dose of 100 mg • Between 5-8 years: A daily single dose of 200 mg or twice daily dose of 100 mg each • Between 9-12 years: A daily single dose of 300 mg • Adult dose should be used in children older than 12 years or at a weight higher than 50 kg.

Supplementary information on special populations: Pediatric population: The efficacy and safety of cefixime has not been proven in infants younger than 6 months. The sachet (or effervescent) forms of cefixime should be used in children older than 2 years due to their dose.

Package Leaflet: 3. How to use X

Children:

The use of the adequate dose and pharmaceutical dosage forms is recommended for children aged between 6 months-12 years.

The daily recommended dose for children is 8 mg per kilogram cefixime. This dose may be given as once daily or may be divided into two equal doses.

Children aged 2 years and above may use the following doses (of the form containing Cefixime): • Between 2-4 years: A daily single dose of 100 mg • Between 5-8 years: A daily single dose of 200 mg or twice daily dose of 100 mg each • Between 9-12 years: A daily single dose of 300 mg • Adult dose should be used in children older than 12 years or at a weight higher than 50 kg.

Various age groups: Use in children: The efficacy and safety of cefixime has not been proven in infants younger than 6 months. The sachet (or effervescent) forms of cefixime should be used in children older than 2 years due to their dose.

The following arrangements should be made in the Summary of Product Characteristics (SPC) and Package Leaflet (PL) of 400 mg sachet and 400 mg effervescent forms:

Summary of Product Characteristics:

4.2. Posology and mode of administration

Children: The daily total recommended dose is 8 mg/kg. The daily recommended dose in clinical use is 8 mg/kg to be used as a single daily dose of 8m/kg or to be divided into 2 doses of 4 mg/kg each.

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Dose in adults and children older than 12 years: The standard daily dose is 200-400 mg. This dose may be taken as once daily or in two equal doses at an interval of 12 hours.

Package Leaflet Children: The daily recommended dose is 8 mg/kg. This dose may be given at once or upon being divided into two equal doses to be given at an interval of 12 hours.

Dose for adults and children older than 12 years: The standard daily dose is 200-400 mg. This dose may be taken at once or upon being divided into two equal doses to be taken at an interval of 12 hours.

I hereby submit for your information and kindly request for the conduct of relevant action so that the SPC/PL applications relating to the products in which abovementioned amendments are made are sent to the Pharmacological Evaluation Unit by 29.08.2019 for review.

Dr. Hakkı GÜRSÖZ President of the Agency

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