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TO: THE CHIEF OF OPERATIONS
ALL CHIEF DIRECTORS/ DIRECTORS/ DISTRICT MANAGERS
HEADS: ALL HOSPITALS, COMMUNITY HEALTH CENTRES, CLINICS
EXECUTIVE DIRECTOR HEALTH: CITY OF CAPE TOWN

N.B. FOR CIRCULATION TO ALL MEDICAL, PHARMACEUTICAL AND NURSING STAFF.

ANTIBIOTIC SELECTION AND DOSING FOR EMPIRIC TREATMENT OF URINARY TRACT INFECTIONS (UTI)

BACKROUND:

Subsequent to the changes made by the South African Health Products Regulatory Authority (SAHPRA) in 2018 to the professional and patient information leaflets of fluoroquinolones, specifically in relation to indications for fluoroquinolones, several changes to the standard treatment guidelines for the treatment of urinary tract infections were made.

This circular seeks to provide clarity with respect to the optimal selection of antibiotics for the empiric treatment of urinary tract infections.

Please refer to the attached recommendations which were made in consultation with the Provincial Antimicrobial Stewardship Committee.

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DIRECTOR: PHARMACY SERVICES
DATE: 8/5/20

ANTIBIOTIC SELECTION AND DOSING FOR EMPIRIC TREATMENT OF URINARY TRACT INFECTION (UTI) IN ADOLESCENTS AND ADULTS.

These recommendations should be read in conjunction with the National Standard Treatment Guidelines and Essential Medicine List (EML), with specific reference to: Description, Features, General Measures and Referral. (No dose adjustments are provided for renal or hepatic failure – please consult the package insert for guidance.)

1. PREGNANT WOMEN: (INCLUDING ASYMPTOMATIC BACTERIURIA)

CYSTITIS

- Nitrofurantoin, oral, 100 mg 4 times daily (with meals and at bedtime) for 7 days as first line[1].

If nitrofurantoin not available or impractical to use

- Fosfomycin, oral, 3 g immediate dose. It is important that the efficacy of fosfomycin be preserved, and therefore should be used judiciously.

ACUTE PYELONEPHRITIS

- Ceftriaxone, intravenously (IV), 1 g, daily until fever subsides. Change antibiotic cover according to culture and sensitivity results. Switch to oral therapy as soon as the patient is able to take oral fluids. If the culture and sensitivity results are not available and switch to oral therapy is indicated:

  For pregnant women with intact membrane:

  - Amoxicillin/clavulanic acid, oral, 875/125 mg 12-hourly to complete 14 days of treatment.

  For pregnant women with preterm premature rupture of the membranes (PPROM)

  - Cefuroxime, oral, 500 mg 12 hourly to complete 14 days of treatment.

Confirmed penicillin allergy:

For patients with mild –moderate allergy and no previous anaphylaxis with penicillins:

- *Ceftriaxone, IV, 1 g, daily until fever subsides. Change antibiotic cover according to culture and sensitivity results.*
  - *Switch to Cefuroxime, oral, 500 mg 12 hourly to complete 14 days of treatment as soon as the patient is able to take oral fluids.*

For patients with severe penicillin allergy or with previous anaphylaxis with penicillin and/or if MSU results show no other oral option[2]

  - *Ciprofloxacin, oral, 500 mg 12-hourly for 7 days OR 400 mg, IV, 12-hourly - switch to oral ciprofloxacin as soon as possible, to complete 7 day course.*

[1] Nordeng H[1], Lupattelli A, Romøren M, Koren G; Neonatal outcomes after gestational exposure to nitrofurantoin; Obstet Gynecol. 2013 Feb;121(2 Pt 1):306-13. doi: http://10.1097/AOG.0b013e31827c5f88.

[2] Benjamin Bar-Oz et.al.; The safety of quinolones – A meta-analysis of pregnancy outcomes; European Journal of Obstetrics & Gynaecology and Reproductive Biology 143 (2019) 75-78 as well as: Stéphanie Padberg et.al; Observational Cohort Study of Pregnancy Outcomes after First Trimester Exposure to Fluoroquinolones; Antimicrobial Agents and Chemotherapy; August 2014 Volume 58 Number 8 p 4392-4398

2. <u>NON-PREGNANT ADOLESCENTS AND ADULTS</u>

UNCOMPLICATED CYSTITIS

- Gentamicin, 5 mg/kg intramuscular injection (IM), as a single dose.

OR

- Nitrofurantoin, oral, 100 mg 4 times daily (with meals and at bedtime) for 5 days.

<u>If nitrofurantoin or gentamicin not available or impractical to use</u>

- Fosfomycin, oral, 3 g immediate dose. It is important that the efficacy of fosfomycin be preserved, and therefore should be used judiciously.

COMPLICATED CYSTITIS

For adults:

- Ciprofloxacin, oral, 500 mg 12-hourly for 7 days.

For adolescents:

- Nitrofurantoin, oral, 100mg 4 times a day (with meals and at bedtime) for 7 days

ACUTE PYELONEPHRITIS

Outpatient therapy is only indicated for women of reproductive age, who do not have any manifestations required for referral. All other patients should be referred.

- Ciprofloxacin, oral, 500 mg 12 hourly for 7-10 days (at least 7 days).

Empiric therapy, Adult Hospital Level

- Gentamycin, IV, 6 mg/kg / day (ensure normal renal function; therapeutic drug monitoring of trough levels is required).

  Change antibiotic cover according to culture and sensitivity results. If the culture and sensitivity results are not available and switch to oral therapy is indicated:

  - Amoxicillin/clavulanic acid, oral, 875/125 mg 12-hourly to complete **10-14 days** of treatment.

OR,

- Ceftriaxone, IV, 1 g, daily for 48 hours or until fever subsides

  Change antibiotic cover according to culture and sensitivity results. If the culture and sensitivity results are not available and switch to oral therapy is indicated:

  - Amoxicillin/clavulanic acid, oral, 875/125 mg 12-hourly to complete **10-14 days** of treatment.

Confirmed penicillin allergy:

- *Ciprofloxacin, oral, 500 mg 12-hourly for 7 days OR 400 mg, IV, 12-hourly - switch to oral ciprofloxacin as soon as possible, to complete 7 day course.*

ANTIBIOTIC SELECTION AND DOSING FOR EMPIRIC TREATMENT OF URINARY TRACT INFECTION (UTI) IN CHILDREN (<10 YEARS OF AGE).

1. NEONATES AND ACUTELY ILL INFANTS (<12 MONTHS OF AGE) WITH SUSPECTED OR CONFIRMED UTI

Treat as presumed pyelonephritis with parenteral (intravenous) therapy initially:

- If <28 days of age: cefotaxime 50 mg/kg/dose:
  - 1st week of life: 12 hourly
  - ≥1 - <3 weeks: 8 hourly
  - ≥3 weeks: 6 hourly
- If ≥28 days of age: ceftriaxone 80-100 mg/kg/dose once daily or 40-50 mg/kg/dose 12 hourly.
- Change antibiotic treatment according to culture and sensitivity results if needed.
- If there has been a good clinical response to treatment, consider switching to oral therapy guided by culture and sensitivity results or if not available or cultures are negative: amoxicillin/clavulanic acid, oral, 15 mg/kg (of amoxicillin dose) 12 hourly or cefuroxime 10-15 mg/kg/dose 12 hourly to complete **10-14 days** of treatment.

2. INFANTS >3 MONTHS OF AGE AND CHILDREN WEIGHING <25 KG

a. UNCOMPLICATED (LOWER) UTI

- Amoxicillin/clavulanic acid, oral, 400/57.5 mg/5 ml, administered **12 hourly for 7-10 days.**

Weight band (kg)	Dose (mg)	Dose (ml)	Dose range of amoxicillin in weight band (mg/kg/dose)	Dose range of clavulanic acid in weight band (mg/kg/day)
3 - <5	160/23	2	32.7 – 53.3	4.7 – 7.7
5 - <7	240/34.5	3	34.8 - 48	5 – 6.9
7 - <9	320/46	4	36 – 45.7	5.2 – 6.6
9 - <11	400/57.5	5	36.7 – 44.4	5.3 – 6.4
11 - <13	480/69	6	37.2 – 43.6	5.3 – 6.3
13 – <15	560/80.5	7	37.6 – 43.1	5.4 – 6.2
15 - <17	640/92	8	37.9 – 42.7	5.4 – 6.1
17 - <19	720/103.5	9	38.1 – 42.4	5.5 – 6.1
19 - <21	800/115	10	38.3 – 42.1	5.5 – 6.1
21 - <23	880/126.5	11	38.4 – 41.9	5.5 – 6
23 - <25	960/138	12	38.6 – 41.7	5.5 - 6

- Change antibiotic treatment according to culture and sensitivity results if needed.

b. COMPLICATED UTI OR ACUTE PYELONEPHRITIS

- Amoxicillin/clavulanic acid, IV, 25-30 mg/kg/dose of amoxicillin component (maximum dose of amoxicillin/clavulanic acid: 1.2 g) 8 hourly

OR

- Ceftriaxone, IV, 80-100 mg/kg/dose once daily or 40-50 mg/kg/dose 12 hourly (maximum daily dose: 1g).
- Change antibiotic treatment according to culture and sensitivity results if needed.
    - If there has been a good clinical response to treatment, consider switching to oral therapy guided by culture and sensitivity results or if not available or cultures are negative:
        - amoxicillin/clavulanic acid, oral, dosed according to the Table above to complete **10-14 days** of treatment.

3. CHILDREN WEIGHING ≥25 KG

a. UNCOMPLICATED (LOWER) UTI

- Amoxicillin/clavulanic acid, oral, 875/125 mg tablets: 1 tablet 12 hourly **for 7-10 days**.
- Change antibiotic treatment according to culture and sensitivity results if needed.

b. COMPLICATED UTI OR ACUTE PYELONEPHRITIS

- Amoxicillin/clavulanic acid, IV, 25-30 mg/kg/dose of amoxicillin component (maximum dose of amoxicillin/clavulanic acid: 1.2 g) 8 hourly

OR

- Ceftriaxone, IV, 80-100 mg/kg/dose once daily or 40-50 mg/kg/dose 12 hourly (maximum daily dose: 1g).
- Change antibiotic treatment according to culture and sensitivity results if needed.
    - If there has been a good clinical response to treatment, consider switching to oral therapy guided by culture and sensitivity results or if not available or cultures are negative:
        - amoxicillin/clavulanic acid, oral, 875/125 mg tablets: 1 tablet 12 hourly to complete **10-14 days** of treatment.

4. CONFIRMED PENICILLIN ALLERGY (OR HISTORY OF ANAPHYLAXIS TO PENICILLIN)

a. UNCOMPLICATED (LOWER) UTI

- **Children weighing <25 kg**
  - Ciprofloxacin, oral, 10-15 mg/kg/dose (maximum dose: 500 mg) 12 hourly for **7 days**.
  - Change antibiotic treatment according to culture and sensitivity results if needed.

- **Children weighing ≥25 kg**
  - Nitrofurantoin, oral; 100 mg 4 times daily (with meals and at bedtime) for **5 days** (provided eGFR >60 ml/min/1.73 m^2).
  - Change antibiotic treatment according to culture and sensitivity results if needed.

b. COMPLICATED UTI OR ACUTE PYELONEPHRITIS (CHILDREN <25 KG OR >25 KG)

- Ciprofloxacin, IV, 10 mg/kg/dose (maximum dose: 400 mg) 12 hourly then oral, 10-15 mg/kg/dose (maximum dose: 500 mg) 12 hourly to complete **7-10 days** of treatment.
- Change antibiotic treatment according to culture and sensitivity results if needed.