**Table 1.** Inclusion criteria used in pediatric urinary tract infection clinical trials compared with the FDA and EMA guidance in adults, and with AAP and NICE pediatric guidelines

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| --- | --- | --- | --- | --- | --- |
| **Inclusion criteria** | **FDA 13** | **EMA 14** | **AAP 1999, 16 2011, 17 2016 18** | **NICE 2007 19** | **Number of study that used the criteria (%)n=40** |
| **Clinical**  | Yes | Yes | Yes | Yes | 39 (98) |
|  Temperature | Yes | Yes | Yes | Yes | 31 (78) |
|  ≥ 37.5° |  |  |  |  | 1 (2) |
|  ≥ 38° |  |  | 2011 | Yes | 12 (30) |
|  ≥ 38.3° |  |  |  |  | 2 (5) |
|  ≥ 38.5° |  |  |  |  | 10 (25) |
|  > 39° |  |  | 1999 |  | 0 (0) |
|  Fever (not defined) | Yes | Yes | 2016 |  | 6 (15) |
|  UT-related clinical findings | Yes | Yes | No | Yes | 22 (55) |
|  Dysuria | Yes | Yes |  | Yes | 9 (23) |
|  Loin pain | Yes | Yes |  | Yes | 17 (43) |
|  Clinical signs (not defined) |  |  |  |  | 3 (8) |
|  Non-UT-related clinical findings | Yes | Yes | No | Yes | 17 (43) |
|  Gastro-intestinal signsa | Yes |  |  | Yes | 14 (35) |
|  Sepsis signs | Yes | Yes |  | Yes | 5 (13) |
|  Clinical signs (not defined) |  |  |  |  | 3 (8) |
|  Other clinical conditions |  |  |  |  |  |
|  Sex or weight restricted |  |  |  |  | 4 (10) |
|  Absence of other source of infection |  |  |  |  | 5 (13) |
| **Laboratory** | No | No | No | No | 16 (40) |
|  CRP |  |  |  |  | 13 (33) |
|  >10 mg/l |  |  |  |  | 5 (13) |
|  >25 mg/l |  |  |  |  | 3 (8) |
|  Increased (not defined) |  |  |  |  | 5 (13) |
|  ESR (1st hour) |  |  |  |  | 7 (18) |
|  >25 mm |  |  |  |  | 4 (10) |
|  Increased  |  |  |  |  | 3 (8) |
|  White blood cell counts |  |  |  |  | 8 (20) |
|  Leukocytosis |  |  |  |  | 8 (20) |
|  Otherb |  |  |  |  | 3 (8) |
| **Microbiology** | Yes | Yes | Yes | Yes | 37 (93) |
|  Sample method |  |  |  |  |  |
|  Suprapubic aspiration |  |  | Yes | Possible | 12 (30) |
|  Catheterization |  |  | Yes | Possible | 16 (40) |
|  Clean-catch midstream |  |  | Yes | Yes | 24 (60) |
|  Sterile bag |  |  | No | Possible | 10 (25) |
|  Not mentioned |  |  |  |  | 13 (33) |
|  ≥ 2 samples required if bags or clean-catch |  |  |  |  | 9 (23) |
|  Dipstick | Yes | No | Yes | Yes |  |
|  Positive Leukocyte esterase | Yes | No | Yes | Yes | 4 (10) |
|  Positive nitrite | No | No | Yes | Yes | 2 (5) |
|  Microscopic analysis | Yes | Yes | Yes | Yes | 29 (73) |
|  Pyuria ≥0.2/mm3 |  |  |  |  | 1 (3) |
|  Pyuria ≥5/mm3 |  |  |  |  | 1 (3) |
|  Pyuria ≥10/mm3 | Yes | Yes | Yes | No | 7 (18) |
|  Pyuria ≥25/mm3 |  |  |  |  | 5 (13) |
|  Pyuria ≥50/mm3 |  |  |  |  | 3 (8) |
|  Pyuria ≥100/mm3 |  |  |  |  | 1 (3) |
|  Pyuria ≥125/mm3 |  |  |  |  | 1 (3) |
|  Pyuria (not defined) | No | No | No | Yes | 8 (20) |
|  Gram staining: any bacteria | No | No | Yes | Yes | 11 (28) |
|  Not used |  |  |  |  | 11 (28) |
|  Positive urine culture | Yes | Yes | Yes | Yes | 37 (93) |
|  Minimum bacterial count threshold specified  | Yes | Yes | Yes | No | 32 (80) |
|  Type of pathogen  |  |  |  |  | 19 (48) |
|  Single pathogen | Yes | Yes | Yes | No | 14 (35) |
|  ≥1 pathogen |  |  |  |  | 2 (5) |
|  GNB |  |  |  |  | 1 (3) |
|  *Escherichia coli* |  |  |  |  | 2 (5) |
|  Not specified |  |  |  |  | 21 (53) |
|  Antibiotic susceptibility test |  |  |  |  | 7 (18) |
|  Susceptibility to study drugs |  |  |  |  | 7 (18) |
|  Not specified |  |  |  |  | 33 (83) |
| **Imaging** | No | No | Yes | Variable | 11 (28) |
|  DMSA  |  |  |  | Variable | 8 (20) |
|  US  |  |  | Yes | Variable | 4 (10) |
|  Otherc |  |  |  |  | 2 (5) |

Abbreviations: FDA, Food Drug Administration; EMA, European Medicines Agency; AAP, American Academy of Pediatrics; NICE, National Institute for Health and Care Excellence; UTI, urinary tract infection; UT, urinary tract; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; GNB, Gram negative bacteria; DMSA, Dimercaptosuccinic Acid Scintigraphy; US, ultrasonography

a Abdominal pain or tenderness nausea, vomiting, loss of appetite, diarrhea, dehydration

b One study used blood laboratory findings with no precision, 22 1 used procalcitonin, 28 and 1 used osmolality 49 as inclusion criterion

c Computerized tomography scan 30, 55 or voiding cystourethrogram 55