**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

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **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