**Supplementary table 1. Antibiotic FDCs in 2015 sorted by SU globally sold**

|  |  |  |
| --- | --- | --- |
| **FDC** | **SU globally sold** | **Number of selling countries** |
| amoxicillin/clavulanic acid | 8.38 x 109 | 75 |
| sulfamethoxazole/trimethoprim | 3.61 x 109 | 75 |
| ampicillin/cloxacillin | 0.95 x 109 | 13 |
| piperacillin/tazobactam | 0.79 x 109 | 66 |
| cefixime/ofloxacin | 0.31 x 109 | 1 |
| metronidazole/spiramycin | 0.24 x 109 | 17 |
| cefpodoxime proxetil/clavulanic acid | 0.23 x 109 | 3 |
| amoxicillin/flucloxacillin | 0.19 x 109 | 7 |
| azithromycin/cefixime | 0.17 x 109 | 2 |
| cefoperazone/sulbactam | 0.16 x 109 | 28 |
| amoxicillin/cloxacillin | 0.16 x 109 | 4 |
| ampicillin/sulbactam | 0.12 x 109 | 49 |
| cefixime/clavulanic acid | 0.12 x 109 | 2 |
| cefalexin/trimethoprim | 0.09 x 109 | 1 |
| cefuroxime axetil/clavulanic acid | 0.08 x 109 | 1 |
| piperacillin/sulbactam | 0.07 x 109 | 4 |
| amoxicillin/dicloxacillin | 0.07 x 109 | 4 |
| mezlocillin/sulbactam | 0.06 x 109 | 1 |
| cefpodoxime proxetil/ofloxacin | 0.05 x 109 | 1 |
| cefixime/dicloxacillin/lactobacillus acidophilus | 0.05 x 109 | 1 |
| ceftriaxone/sulbactam | 0.04 x 109 | 6 |
| ceftriaxone/tazobactam | 0.04 x 109 | 3 |
| azithromycin/cefpodoxime proxetil | 0.04 x 109 | 1 |
| amoxicillin/cloxacillin/lactobacillus acidophilus | 0.04 x 109 | 1 |
| amoxicillin/pivsulbactam | 0.04 x 109 | 15 |
| amoxicillin/dicloxacillin/lactobacillus acidophilus | 0.04 x 109 | 1 |
| cefixime/ornidazole | 0.03 x 109 | 1 |
| cefpodoxime proxetil/levofloxacin | 0.03 x 109 | 1 |
| cefixime/linezolid | 0.03 x 109 | 1 |
| cefdinir/clavulanic acid | 0.03 x 109 | 1 |
| amoxicillin/sulbactam | 0.03 x 109 | 14 |
| azithromycin/levofloxacin | 0.02 x 109 | 1 |
| cefotaxime/sulbactam | 0.02 x 109 | 2 |
| cefadroxil/clavulanic acid | 0.02 x 109 | 2 |
| amoxicillin/clavulanic acid/lactobacillus acidophilus | 0.02 x 109 | 2 |
| ampicillin/dicloxacillin | 0.02 x 109 | 5 |
| ampicillin/flucloxacillin | 0.02 x 109 | 4 |
| ampicillin/cloxacillin/lactobacillus acidophilus | 0.02 x 109 | 1 |
| cefoperazone/tazobactam | 0.02 x 109 | 2 |
| ciprofloxacin/tinidazole | 0.02 x 109 | 5 |
| cefaclor/clavulanic acid | 0.02 x 109 | 1 |
| clavulanic acid/ticarcillin | 0.02 x 109 | 19 |
| cefixime/cloxacillin/lactobacillus acidophilus | 0.01 x 109 | 1 |
| cefixime/cloxacillin | 0.01 x 109 | 1 |
| cefuroxime/clavulanic acid | 0.01 x 109 | 2 |
| amoxicillin/bacillus coagulans/cloxacillin | 0.01 x 109 | 1 |
| azithromycin/ofloxacin | 0.01 x 109 | 1 |
| cefpodoxime proxetil/dicloxacillin/lactobacillus acidophilus | 0.01 x 109 | 1 |
| cefuroxime axetil/linezolid | 0.01 x 109 | 1 |
| ciprofloxacin/metronidazole | 0.01 x 109 | 1 |
| cefadroxil/trimethoprim | \*0.08 x 108 | 1 |
| acetylspiramycin/metronidazole | 0.08 x 108 | 1 |
| sulfadiazine/sulfamethoxazole/trimethoprim | 0.08 x 108 | 1 |
| ampicillin/lidocaine/sulbactam | 0.05 x 108 | 1 |
| ofloxacin/ornidazole | 0.04 x 108 | 6 |
| ampicillin/dicloxacillin/lactobacillus acidophilus | 0.04 x 108 | 1 |
| cefixime/dicloxacillin | 0.04 x 108 | 1 |
| fosfomycin/trimethoprim | 0.04 x 108 | 1 |
| ampicillin/oxacillin | 0.04 x 108 | 2 |
| cefpodoxime proxetil/cloxacillin/lactobacillus acidophilus | 0.03 x 108 | 1 |
| amoxicillin/bacillus coagulans/dicloxacillin | 0.03 x 108 | 1 |
| cefpodoxime proxetil/dicloxacillin | 0.03 x 108 | 1 |
| amoxicillin/metronidazole | 0.02 x 108 | 3 |
| phenazopyridine/sulfamethoxazole/trimethoprim | 0.02 x 108 | 1 |
| ceftazidime/tazobactam | 0.02 x 108 | 2 |
| cefixime/moxifloxacin | 0.02 x 108 | 1 |
| ciprofloxacin/ornidazole | 0.02 x 108 | 3 |
| cefepime/tazobactam | 0.02 x 108 | 1 |
| metronidazole/norfloxacin | 0.02 x 108 | 1 |
| sulfadiazine/trimethoprim | 0.01 x 108 | 3 |
| erythromycin/trimethoprim | 0.01 x 108 | 1 |
| erythromycin/sulfamethoxazole/trimethoprim | 0.01 x 108 | 1 |
| amoxicillin/cloxacillin/dl/lactic acid | 0.01 x 108 | 1 |
| sulfametrole/trimethoprim | 0.01 x 108 | 4 |
| amoxicillin/clavulanic acid/nimesulide | 0.01 x 108 | 1 |
| cefixime/levofloxacin | \*0.07 x 107 | 1 |
| azithromycin/cefixime/lactobacillus acidophilus | 0.07 x 107 | 1 |
| ascorbic acid/metamizole sodium/penicillin g /streptomycin | 0.06 x 107 | 1 |
| azithromycin/fluconazole/secnidazole | 0.06 x 107 | 3 |
| cefpodoxime proxetil/sulbactam | 0.04 x 107 | 2 |
| cefixime/lactobacillus acidophilus/ofloxacin | 0.04 x 107 | 1 |
| oleandomycin/tetracycline | 0.03 x 107 | 1 |
| meropenem/sulbactam | 0.03 x 107 | 1 |
| cefuroxime/sulbactam | 0.03 x 107 | 1 |
| penicillin g/streptomycin | 0.02 x 107 | 3 |
| amoxicillin/dicloxacillin/saccharomyces boulardii | 0.02 x 107 | 1 |
| levofloxacin/metronidazole | 0.02 x 107 | 1 |
| ceftolozane/tazobactam | 0.01 x 107 | 9 |
| meropenem/sodium/sulbactam | 0.01 x 107 | 1 |
| kanamycin/penicillin g | 0.01 x 107 | 1 |
| rifampicin/trimethoprim | 0.01 x 107 | 2 |
| levofloxacin/ornidazole | 0.01 x 107 | 2 |
| sulfamethizole/trimethoprim | \*0.09 x 106 | 2 |
| cefixime/cefpodoxime proxetil | 0.09 x 106 | 1 |
| ceftazidime/sulbactam | 0.08 x 106 | 4 |
| amoxicillin/cloxacillin/lactobacillus lactis | 0.07 x 106 | 1 |
| avibactam/ceftazidime | 0.07 x 106 | 2 |
| bromelains/doxycycline/lactobacillus reuteri/lactobacillus rhamnosus/ornidazole | 0.06 x 106 | 1 |
| chloramphenicol/tetracycline | 0.07 x 106 | 1 |
| gatifloxacin/ornidazole | 0.04 x 106 | 1 |
| amikacin/cefepime | 0.04 x 106 | 1 |
| doxycycline/tinidazole | 0.04 x 106 | 1 |
| ampicillin/cloxacillin/saccharomyces boulardii | 0.04 x 106 | 1 |
| ceftriaxone/vancomycin | 0.03 x 106 | 1 |
| ampicillin/bacillus coagulans/cloxacillin | 0.03 x 106 | 1 |
| dalfopristin/quinupristin | 0.02 x 106 | 3 |
| amoxicillin/clavulanic acid/lactic ferments | 0.01 x 106 | 1 |
| cefepime/sulbactam | 0.01 x 106 | 1 |
| sulfamoxole/trimethoprim | 0.01 x 106 | 1 |
| cefixime/clavulanic acid/lactobacillus acidophilus | \*0.08 x 105 | 1 |
| bromhexine/sulfamethoxazole/trimethoprim | 0.07 x 105 | 1 |
| amoxicillin/flucloxacillin/lactobacillus acidophilus | 0.06 x 105 | 1 |
| ceftazidime/tobramicin | 0.05 x 105 | 1 |
| cefuroxime axetil/sulbactam | 0.04 x 105 | 1 |
| amoxicillin/cloxacillin/serrapeptase | 0.01 x 105 | 1 |
| ampicillin/sultamicillin | 0.01 x 105 | 1 |
| ceftibuten/clavulanic acid | \*0.09 x 104 | 1 |
| amoxicillin/cloxacillin/lactobacillus acidophilus/serrapeptase | 0.01 x 104 | 1 |
| metronidazole/tetracycline | 0.01 x 104 | 1 |

\*Different power

**Supplementary table 2. Antibiotic FDC categories not approved by FDA**

|  |  |  |
| --- | --- | --- |
| **Not FDA approved FDC categories** | **FDCs** | **SU** |
| Aminopenicillin / β-lactamase resistant penicillin +/- other agents | 19 | 1.54 x 109 |
| 3rd-4-5th gen. cephalosporins / β-lactamase inhibitor +/- other agents | 13 | 0.55 x 109 |
| Cephalosporins / Fluoroquinolones | 6 | 0.40 x 109 |
| 1st-2nd gen. cephalosporins / β-lactamase inhibitor +/- other agents | 8 | 0.26 x 109 |
| Macrolide/ 5-nitroimidazole | 3 | 0.25 x 109 |
| Macrolide/cephalosporin +/- other agents | 3 | 0.21 x 109 |
| Antipseudomonal penicillin /β-lactamase inhibitor | 2 | 0.14 x 109 |
| Cephalosporin/ β-lactamase resistant penicillin +/- other agents | 7 | 0.10 x 109 |
| Cephalosporin/trimethoprim | 2 | 0.10 x 109 |
| Aminopenicillin /β-lactamase inhibitor +/- other agents | 8 | 0.09 x 109 |
| Cephalosporin/oxazolidinone | 2 | 0.04 x 109 |
| Fluoroquinolone/ 5-nitroimidazole | 8 | 0.04 x 109 |
| Macrolide / fluoroquinolone +/- other agents | 2 | 0.04 x 109 |
| Cephalosporin/5-nitroimidazole | 1 | 0.03 x 109 |
| Sulphonamides/trimethoprim +/- other agents | 9 | 0.01 x 109 |
| Other combinations | 19 | 0.01 x 109 |

**Supplementary table 3. Total antibiotic sales and FDCs not approved by the US FDA as a percentage of total sales and of total antibiotic FDC sales per each country selling at least one antibiotic FDC not approved by US FDA, sorted by the highest not approved FDCs/ antibiotics.**

|  |  |  |  |
| --- | --- | --- | --- |
| **Country** | **Antibiotic sales (Standard Unite)** | **FDCs not approved by US FDA / Total antibiotic sales (%)** | **FDCs not approved by US FDA / Total antibiotic FDC sales (%)** |
| India | 14.74 x 109 | 16.6% | 50.4% |
| Egypt | 1.72 x 109 | 13.0% | 27.0% |
| Lebanon | 0.09 x 109 | 8.0% | 20.1% |
| Pakistan | 3.55 x 109 | 5.8% | 19.3% |
| Honk Kong | 0.12 x 109 | 5.6% | 18.5% |
| Tunisia | 0.35 x 109 | 4.8% | 19.7% |
| Morocco | 0.36 x 109 | 4.7% | 13.7% |
| Vietnam | 1.69 x 109 | 4.7% | 26.8% |
| France | 1.45 x 109 | 3.7% | 13.5% |
| Bangladesh | 1.53 x 109 | 3.6% | 46.0% |
| China | 13.19 x 109 | 3.4% | 39.8% |
| Jordan | 0.09 x 109 | 3.3% | 9.7% |
| Bulgaria | 0.10 x 109 | 3.3% | 12.1% |
| Korea | 1.39 x 109 | 3.2% | 11.5% |
| Turkey | 2.05 x 109 | 3.0% | 7.1% |
| UAE | 0.17 x 109 | 2.9% | 8.8% |
| Uruguay | 0.04 x 109 | 2.8% | 12.2% |
| Spain | 1.04 x 109 | 2.7% | 7.4% |
| Fr. West Africa | 0.69 x 109 | 2.1% | 7.6% |
| Algeria | 1.02 x 109 | 1.8% | 6.5% |
| Ecuador | 0.20 x 109 | 1.6% | 5.9% |
| Taiwan | 0.50 x 109 | 1.2% | 11.5% |
| Russia | 1.67 x 109 | 1.0% | 5.6% |
| Ukraine | 0.67 x 109 | 1.0% | 11.8% |
| S. Africa | 1.16 x 109 | 0.9% | 2.5% |
| Finland | 0.15 x 109 | 0.9% | 18.4% |
| Mexico | 0.51 x 109 | 0.8% | 3.5% |
| Austria | 0.09 x 109 | 0.8% | 2.6% |
| Argentina | 0.44 x 109 | 0.6% | 2.9% |
| Kazakhstan | 0.50 x 109 | 0.6% | 5.1% |
| Japan | 2.22 x 109 | 0.4% | 6.4% |
| C. America | 0.15 x 109 | 0.3% | 1.6% |
| Kuwait | 0.02 x 109 | 0.3% | 0.9% |
| Dominican Rep | 0.04 x 109 | 0.3% | 2.9% |
| Brazil | 1.48 x 109 | 0.2% | 1.1% |
| Latvia | 0.02 x 109 | 0.1% | 0.5% |
| Greece | 0.23 x 109 | 0.1% | 0.5% |
| Peru | 0.27 x 109 | 0.1% | 1.4% |
| UK | 1.39 x 109 | 0.1% | 1.1% |
| Colombia | 0.34 x 109 | 0.1% | 1.2% |
| Romania | 0.47 x 109 | 0.1% | 0.3% |
| Malaysia | 0.39 x 109 | 0.1% | 0.7% |
| Slovakia | 0.08 x 109 | 0.1% | 0.3% |
| Indonesia | 2.03 x 109 | 0.1% | 0.9% |
| Germany | 0.80 x 109 | 0.0% | 0.3% |
| Czech Republic | 0.12 x 109 | 0.0% | 0.1% |
| Lithuania | 0.03 x 109 | 0.0% | 0.1% |
| Poland | 0.48 x 109 | 0.0% | 0.0% |
| Venezuela | 0.42 x 109 | 0.0% | 0.0% |
| Thailand | 1.17 x 109 | 0.0% | 0.0% |
| Philippines | 0.55 x 109 | 0.0% | 0.0% |
| Sri Lanka | 0.21 x 109 | 0.0% | 0.0% |
| Saudi Arabia | 0.60 x 109 | 0.0% | 0.0% |

**Supplementary table 4. Antibiotic FDCs compatible with WHO EML and AWaRe classes**

|  |  |  |
| --- | --- | --- |
| **FDCs 2015** | **SU globally sold 2015** | **2017 WHO EML** |
| amoxicillin/clavulanic acid | 8.38 x 109 | Access |
| sulfamethoxazole/trimethoprim | 3.61x 109 | Access |
| piperacillin/tazobactam | 0.79 x 109 | Watch |
| cefpodoxime proxetil/clavulanic acid | 0.23 x 109 | Watch |
| cefoperazone/sulbactam | 0.16 x 109 | Watch |
| cefixime/clavulanic acid | 0.12 x 109 | Watch |
| mezlocillin/sulbactam | 0.06 x 109 | Watch |
| ceftriaxone/sulbactam | 0.04 x 109 | Watch |
| ceftriaxone/tazobactam | 0.04 x 109 | Watch |
| cefdinir/clavulanic acid | 0.03 x 109 | Watch |
| cefotaxime/sulbactam | 0.02 x 109 | Watch |
| cefoperazone/tazobactam | 0.02 x 109 | Watch |
| clavulanic acid/ticarcillin | 0.02 x 109 | Watch |
| ceftazidime/tazobactam | 0.02 x 108 | Watch |
| cefepime/tazobactam | 0.02 x 108 | Reserve |
| cefpodoxime proxetil/sulbactam | 0.04 x 107 | Watch |
| ceftolozane/tazobactam | 0.01 x 107 | Reserve |
| ceftazidime/sulbactam | 0.07 x 106 | Watch |
| avibactam/ceftazidime | 0.07 x 106 | Watch |
| cefepime/sulbactam | 0.01 x 106 | Reserve |
| ceftibuten/clavulanic acid | 0.09 x 105 | Watch |

**Supplementary table 5. Antibiotic FDCs combinations including two highest critically important antibiotics**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **FDC** | **SU sold in 2015** | **US FDA approval** | **EML listed** | **Countries** |
| cefixime/ofloxacin | 0.31 x 109 | not | not | India |
| azithromycin/cefixime | 0.17 x 109 | not | not | India, Indonesia |
| azithromycin/levofloxacin | 0.02 x 109 | not | not | India |
| azithromycin/ofloxacin | 0.01 x 109 | not | not | India |
| cefixime/moxifloxacin | 0.02 x 108 | not | not | India |
| cefixime/levofloxacin | 0.07 x 107 | not | not | India |
| azithromycin/cefixime/*L. acidophilus* | 0.07 x 107 | not | not | India |
| cefixime//ofloxacin/ *L. acidophilus* | 0.04 x 107 | not | not | India |
| cefixime/cefpodoxime proxetil | 0.09 x 106 | not | not | India |
| ceftriaxone/vancomycin | 0.03 x 106 | not | not | India |