

# **Amoxicillin Dispersible Tablets (DT): Product Profile, Availability and Guidance**

**UNICEF Supply Division**

**July 2013**

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## **Amoxicillin Dispersible Tablets (DT): Product Profile, Availability and Guidance – July 2013**

**A more recent note covering Amoxicillin exists. Please visit [http://www.unicef.org/supply/index\\_54214.html](http://www.unicef.org/supply/index_54214.html)**

### **1. Summary**

- This note provides a product profile for Amoxicillin Dispersible Tablets (DT), describes its availability and summarizes its role with reference to WHO guidance for pneumonia treatment.
- Amoxicillin is an effective broad-spectrum antibiotic for use against bacterial infections and especially for the treatment of children with bacterial pneumonia.
- Its availability and use as first-line treatment for pneumonia in countries with a high burden caseload remains limited, despite higher effectiveness compared to existing alternative treatments.
- UNICEF introduced Amoxicillin DT tablets into its supply catalogue in 2011. The most recent tender resulted in increasing Amoxicillin DT availability and supporting increased supply to critical markets. In order to further increase its accessibility and use, advocacy efforts are required to support changes to national treatment guidelines and inclusion in national Essential Medicine Lists.

### **2. Pneumonia Epidemiology and Amoxicillin**

Pneumonia is the leading cause of under-five child mortality globally, with an estimated 1.2 million deaths annually.<sup>1</sup> 60% occur in just ten countries: Bangladesh, D.R. Congo, Ethiopia, India, Kenya, Niger, Nigeria, Pakistan, Tanzania and Uganda.<sup>2</sup> Despite affordable diagnostics and inexpensive antibiotic availability, only a third of pneumonia cases receive antibiotics as part of their treatment regimens. In addition, product presentations in many developing countries are predominantly for adults, whereby health care workers face difficulty administering appropriate dosages to children. Paediatric formulations are often proxied by breaking adult formulations and/or changing their method of administration. For instance, tablets are often cut, crushed and then mixed into a liquid; concentrated capsules are diluted; or injectables are taken orally. These adaptations compromise effectiveness.

Amoxicillin is a penicillin-class, broad-spectrum antibiotic which is commonly prescribed to children for the treatment of pneumonia and other illnesses, including bacterial infections of the ears, sinuses, throat, urinary tract, skin, abdomen and blood, amongst others. Additionally, it is often used as part of the treatment for Severe Acute Malnutrition (SAM). Studies have demonstrated a greater efficacy in the treatment of children with severe cases of pneumonia with Amoxicillin compared to Co-trimoxazole by 4% to 15%.<sup>3</sup> A five-day course of oral Amoxicillin has also been found to be as safe and clinically similar to treatment with Co-trimoxazole and referral to

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<sup>1</sup> WHO, *Factsheet: Pneumonia*, WHO, Geneva, April 2012 at <http://www.who.int/mediacentre/factsheets/fs331/en/>.

<sup>2</sup> Every Woman Every Child, *Amoxicillin - Product Profile*, United Nations Foundation, Washington, 2012 at <http://www.everywomaneverychild.org/component/content/article/1-about/305-amoxicillin-product-profile->.

<sup>3</sup> Dr. Grant, Gavin B., et al., *Recommendations for Treatment of Childhood Non-Severe Pneumonia*, The Lancet, Volume 9, Issue 3, March 2009, p. 189 at [http://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(09\)70044-1/fulltext#bib66](http://www.thelancet.com/journals/laninf/article/PIIS1473-3099(09)70044-1/fulltext#bib66).

a health facility.<sup>4</sup> Amoxicillin remains a low cost (estimated \$0.21-0.42 per treatment course),<sup>5</sup> highly effective antibiotic treatment which could save the lives of up to 1.56 million children over five years.<sup>6</sup>

In 2011, WHO updated its recommendations for the home treatment of pneumonia in the context of Integrated Management of Childhood Illnesses (IMCI), replacing Co-trimoxazole with Amoxicillin 250mg as the new first-line treatment for childhood pneumonia.<sup>7</sup> The recommendation is to treat at community level pneumonia without danger signs (non chest in-drawing) using a simple protocol for administration of oral amoxicillin 250mg (i.e. 10 or 20 tablets per treatment depending on age). New IMCI guidelines for facility-based treatment of pneumonia are currently under review and a separate protocol based on three weight bands for under-five year olds may be introduced (personal communication from Dr. Qazi Shamim Ahmad, WHO Geneva).

Figure 1 WHO’s New Pneumonia Treatment Guidelines for Community Case Management<sup>8</sup>

Age	Pneumonia in <u>low</u> HIV prevalence areas	Pneumonia in <u>high</u> HIV prevalence areas	Severe pneumonia	Severe pneumonia with danger signs
>2 months	1 <sup>st</sup> dose antibiotic, referral to health facility for supportive therapy			
2-12 months 4-10kg	1 Amoxicillin 250mg tablet / twice a day/ 3 days	1 Amoxicillin 250mg tablet / twice a day/ 5 days	1 Amoxicillin 250mg tablet / twice a day/ 5 days	1 <sup>st</sup> dose antibiotic, referral to health facility for supportive therapy
12-59 months 10-19kg	2 Amoxicillin 250mg tablets / twice a day / 3 days	2 Amoxicillin 250mg tablet / twice a day/ 5 days	2 Amoxicillin 250mg tablets / twice a day/ 5 days	1 <sup>st</sup> dose antibiotic, referral to health facility for supportive therapy

Amoxicillin is formulated into conventional capsules (“Amoxicillin Caps”), tablets (“Amoxicillin Tab.”), powder for oral suspension (“Amoxicillin OS”), and dispersible tablets (“Amoxicillin DT”). Other forms available include syrups, sachets and oral drops.

<sup>4</sup> Soofi, Sajid, et al., *Effectiveness of Community Case Management of Severe Pneumonia with Oral Amoxicillin in Children Aged 2—59 Months in Matiari District, Rural Pakistan: A Cluster-Randomised Controlled Trial*, The Lancet, Volume 379, Issue 9817, p. 734 at [http://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(11\)61714-5/fulltext](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(11)61714-5/fulltext).

<sup>5</sup> Every Woman Every Child, *Amoxicillin - Product Profile*, United Nations Foundation, Washington, 2012 at <http://www.everywomaneverychild.org/component/content/article/1-about/305-amoxicillin-product-profile->.

<sup>6</sup> UNICEF, *UN Commission On Life-Saving Commodities for Women and Children: Commissioners’ Report*, New Every Woman Every Child, New York, September 2012, p. 17 at [http://www.unicef.org/media/files/UN\\_Commission\\_Report\\_September\\_2012\\_Final.pdf](http://www.unicef.org/media/files/UN_Commission_Report_September_2012_Final.pdf).

<sup>7</sup> WHO, *Integrated Management of Childhood Illness: Caring for New-borns and Children in the Community. Manual for the Community Health Worker: Caring for the Sick Child in the Community, Treat Diarrhoea, Confirmed Malaria and Fast Breathing*, WHO, Geneva, 2011, p. 87 at [http://whqlibdoc.who.int/publications/2011/9789241548045\\_Manual\\_eng.pdf](http://whqlibdoc.who.int/publications/2011/9789241548045_Manual_eng.pdf).

<sup>8</sup> Qazi, Shamim, *Management for Pneumonia in Developing Countries*, WHO, Geneva, June 2013.

**Figure 3 Different Amoxicillin Product Formulations**

Amoxicillin Products	Purpose
Amoxicillin Caps	<ul style="list-style-type: none"> <li>• Amoxicillin capsules are the most widely available pharmaceutical form, available in strengths of 125mg to 1,000mg.</li> <li>• It is the preferred formulation for adults and can be taken without water if necessary.</li> </ul>
Amoxicillin Tabs	<ul style="list-style-type: none"> <li>• Amoxicillin tablets are another conventional form, often available with scoring.</li> <li>• Scored tablets allow pharmaceutical tablets to be broken and dosing adjusted according to prescription.</li> <li>• They are not as extensively used as capsules and often need to be taken with water.</li> </ul>
Amoxicillin OS	<ul style="list-style-type: none"> <li>• Amoxicillin powder for oral suspension is at present the most commonly used paediatric formulation.</li> <li>• It is available in strengths of 125 mg/5mL and 250 mg/5mL.</li> <li>• It is administered as a liquid which facilitates the treatment of children and those with difficulties swallowing solid dosage forms like tablets or capsules.</li> </ul>
Amoxicillin DT	<ul style="list-style-type: none"> <li>• Amoxicillin dispersible tablets are the equivalent of Amoxicillin OS, with each dose compacted into a tablet, dispersible in 5-10 ml of water.</li> <li>• Amoxicillin DT is cheaper than its equivalent OS.</li> <li>• It offers logistical and supply chain advantages in term of volume and weight.</li> <li>• It is also designed to accommodate patients with difficulties in swallowing.</li> <li>• Amoxicillin DT facilitates and simplifies Community Case Management (CCM) and greater dosage accuracy compared to OS which has to be manually measured and mixed.</li> <li>• DT does not need refrigeration.</li> <li>• The new protocols combined with clear and easy instructions for prescribing and administering Amoxicillin DT provides the most effective method of treatment for pneumonia.</li> </ul>

UNICEF, independently and through partnership with the UN Commission on Life-Saving Commodities for Women and Children, is supporting the scale-up of heretofore limited access and use of Amoxicillin DT. The UN Commission is specifically looking to shape global and local delivery markets, quality, regulatory efficiency, supply, demand, awareness and the use of innovative financing to improve the access and availability of Amoxicillin DT to resource poor communities.

The new protocol and the availability of Amoxicillin in DT form simplify the administration and dosage of treatment. The use of DT versus OS is beneficial as it reduces risk of dosing errors observed when administering OS. Amoxicillin 250mg DT can also easily replace other forms of Amoxicillin for treatment of infections as demand and its inclusion in Essential Medicine Lists by national Ministries of Health (MoH) increases.

### 3. Current Market Situation

#### 3.1 Demand

The Amoxicillin 250mg DT market is steadily increasing as more countries change their treatment protocols accordingly. Amoxicillin DT use is currently more established in Asia than other regions for the paediatric dosages (125mg and 250mg). In Africa, the market is more established for OS and capsules than in dispersible tablet form.<sup>9</sup>

<sup>9</sup> Every Woman Every Child, *Amoxicillin - Product Profile*, United Nations Foundation, Washington, 2012 at <http://www.everywomaneverychild.org/component/content/article/1-about/305-amoxicillin-product-profile->.

Figure 4 Amoxicillin Suppliers to UNICEF SD since 2004

Manufacturers	OS 125mg/5ml	OS 250mg/5ml	Caps 250mg	Caps 500mg	Tabs 250mg	Tabs 500mg	DT 125mg	DT 250mg
Alkem Labs Ltd	•	•						
Durbin Plc		•						
GlaxoSmithKline		•						
Gulf Pharm. Ind.	•							
Ipcal Laboratories	•	•	•	•				
Medopharm	•		•	•			•	•
Medreich Plc			•					•
Milan Laboratories Ltd	•							
Micro Labs Ltd	•		•		•			•
Remedica Ltd		•	•	•		•		

Source: UNICEF Supply Division.

Pilot programs using Amoxicillin 250mg DT have demonstrated the safe, effective and quality treatment of pneumonia through community case management.<sup>10</sup> In these pilots, disease classification was correct in 100% of episodes and supply management was excellent with over 98% of Amoxicillin 250mg DT properly accounted for. The programmes were implemented in locations that benefited from limited national focus and action in addressing pneumonia as a main cause of child mortality.

### 3.2 Supply

In 2012, UNICEF launched a Request for Proposal (RFP) to supply Amoxicillin 250mg DT in order to increase supply to countries in accordance with the new WHO protocol. Four manufacturers were awarded Long Term Arrangements (LTAs).

Figure 5 UNICEF LTA Awards for the 2012 Amoxicillin Tender

Supplier	LTA Duration	Start	End	Product
Medreich Plc	1 year	22-Oct-12	21-Oct-13	Amoxicillin 250mg DT / Pac-10
				Amoxicillin 250mg DT / Pac-20
				Amoxicillin 250mg DT / Pac-100
Micro Labs Ltd	1 year	22-Oct-12	21-Oct-13	Amoxicillin 250mg DT / Pac-100
Medopharm	1 year	22-Oct-12	21-Oct-13	Amoxicillin 250mg DT / Pac-10
				Amoxicillin 250mg DT / Pac-20
				Amoxicillin 250mg DT / Pac-100
Remedica Ltd	1 year	22-Oct-12	21-Oct-13	Amoxicillin 250mg DT / Pac-100

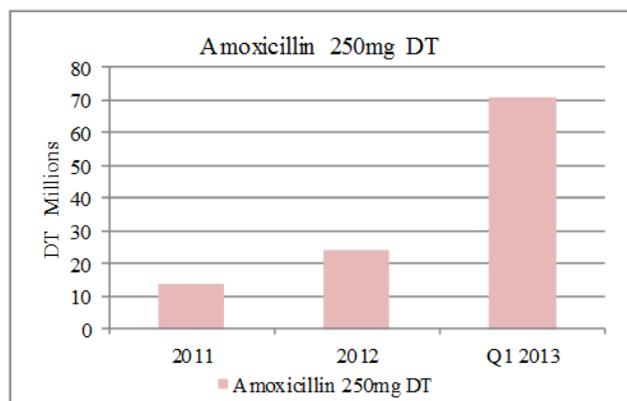
Source: UNICEF Supply Division.

Since 2011, UNICEF has directly supplied only small quantities of Amoxicillin 250mg DT from three of the four awarded manufacturers (Figure 6). However, following a 70% increase in procurement in 2012 from 2011, Q1 2013 represents an increase of 300% over 2012 procurement, signalling increased awareness and interest in Amoxicillin DT. In addition, an increased number of

<sup>10</sup> Dr Hamer, Davidson H., et al., *Quality and Safety of Integrated Community Case Management of Malaria Using Rapid Diagnostic Tests and Pneumonia by Community Health Workers*, Pathogens and Global Health, vol. 106, no 1, Boston, 2012, p. 32 at <http://www.bu.edu/cghd/files/2012/04/Hamer-DH-et-al-Pathogens-Global-Health-2012-copy.pdf>.

Amoxicillin DT manufacturers are becoming compliant with WHO’s Good Manufacturing Practices (GMP). There are currently seven manufacturers known to be compliant with WHO’s GMP standards.

**Figure 6 UNICEF Procurement Trends of Amoxicillin DT**



Source: UNICEF Supply Division.

With the exception of very small quantities, all procurement has so far been of Amoxicillin scored dispersible tablets in multi-dispensing blister strips of 10x10. Blister strips are also available and packed in the form of patient packs as 1x10 and 2x10. Different packaging options carry different cost implications, depending on the option chosen, which would be subject to the context of the end user environment (Figure 7).

**Figure 7 Amoxicillin 250mg DT Packaging Options and Comparison**

250mg Amoxicillin DT	Cost / Treatment (US\$)	Logistics	Dispensing	Compliance
10x10 Multi-dispensing blister pack	0.21 – 0.78	Less expensive	Re-packing	More challenging
1x10 or 2x10 Patient packs	0.32 – 0.80	More expensive	Easier	Better

Source: UNICEF Supply Division.

#### 4. Issues and Challenges

- Registration.** Many countries still list Co-trimoxazole as their first-line treatment for pneumonia in children under-five years of age. Amoxicillin 250mg DT use adoption is, in part, conditioned on national MoH policy revision and national registration, particularly in Sub-Saharan Africa. Ethiopia and Nigeria are examples of large countries currently in the process of revising their MoH policy. In this region, Amoxicillin registration is limited principally to Amoxicillin OS and Amoxicillin Cap. Formulations. The lack of registered and marketed products is an important barrier for introduction, even if policies are in place (e.g. Tanzania and DRC).
- Treatment Guidelines.** Treatment guidelines for pneumonia are included in national health systems, often in the context of IMCI guidelines. However, even though IMCI guidelines have been revised prescribing the use of Amoxicillin 250mg, most countries have yet to update their own national guidelines after the latest recommendations, for which Amoxicillin 250 mg DT is more relevant.
- Delivery Channel.** The use of antibiotics is usually limited to a certain trained cadre of health professionals. However, there is evidence to support the safety and efficacy of community-level administration of Amoxicillin 250mg DT through Health Care Workers.<sup>11</sup>

<sup>11</sup> Dr Hamer, Davidson H., et al., p. 32 at <http://www.bu.edu/cghd/files/2012/04/Hamer-DH-et-al-Pathogens-Global-Health-2012-copy.pdf>.

## 5. Steps forward

- UNICEF convenes the UN Commission working group dedicated to implementing the global recommendations for Amoxicillin DT. Some of the activities encompassed in the workplan include raising awareness on evidence for adoption of Amoxicillin DT for use by countries, estimating demand, increased availability of quality products and establishing what tools can help facilitate distribution, administration and increased adherence to treatment.
- UNICEF is engaging approved manufacturers to ensure consistent manufacturing capacity and availability of Amoxicillin 250mg DT in order to assess the gap between demand and supply.
- UNICEF anticipates issuing a new tender during Q3 2013 to follow the expiry of current LTAs for the supply of Amoxicillin DT.
- UNICEF is supporting innovation in appropriate pneumonia diagnostic aid devices in resource-poor settings to improve accurate diagnosis and delivery of appropriate treatment.

For further questions or additional information, please contact:

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