Amoxicillin, paediatric: Expert opinion on extemporaneous unlicensed formulations

Expert opinion of the European Drug Shortage Formulary (EDSForm) Working Party

Foreword

In view of the difficulties encountered in the supply of paediatric products containing amoxicillin, the EDSForm Working Party (WP) has compiled a list of existing licensed medicines, recommendations and unlicenced pharmaceutical preparations that have been or are being prepared to alleviate the lack of age-appropriate licensed products.

The present document is the result of this compilation effort and should be understood and used as an overview of current practices. Its content has not been formally approved by the European Pharmacopoeia Commission or by the European Committee on Pharmaceuticals and Pharmaceutical Care and represents the opinion of the experts of the EDSForm WP.

It is intended to assist healthcare professionals in decision-making process and is not to be used as a substitute for a proper risk assessment carried out by the healthcare professionals concerned. It is reminded that the quality of the formulations listed has not been verified by the EDSForm WP.

The EDSForm WP and the EDQM emphasise that the use of licensed medicines is always preferable to the use of unlicensed pharmaceutical preparations. However, as stated in the European Pharmacopoeia (Ph. Eur.) general monograph *Pharmaceutical preparations (2619)*, "*when deciding to use an unlicensed preparation all health professionals involved (e.g. the prescribing practitioners and/or the preparing pharmacists) have, within their area of responsibilities, a duty of care to the patient receiving the pharmaceutical preparation*".

The data given in the table below and related appendixes are reproduced from the original sources in part only. Users are advised to refer directly to the source for further information and to check that the data presented in this document or in other documents to which it refers comply with their own local/national requirements.

Although every care has been taken in compiling and checking the information contained in the tables below, neither the EDSForm WP nor the EDQM can be held responsible for any errors or inaccuracies they may contain.

Content of the document

Information on licensed products

Licensed amoxicillin 125 mg/5 mL, 250 mg/5 mL or 500 mg/5 mL powders for oral suspension are appropriate for paediatric patients or patients that are unable to swallow capsules. Despite the large number of generic products licensed, it has been reported that these products are in short supply in several of the member states in which they are authorised. Whenever possible, priority should be given to their use before opting for an unlicensed pharmaceutical preparation.

The products whose composition is given below are provided either as an example or because they are used as a starting material in the unlicensed preparations detailed thereafter.

Numerous brands of **powder for oral suspension** include Amoxicillin Sandoz, Amoxil Almacin, Amitron, Amoksicillin Belupo, Amorion, Amotaks, Amoxapen, Amoxicilina Ardine, Amoxicilina Aurobindo, Amoxicilina Generis, Amoxicilina Labesfal, Amoxicilina Netpharmalab, Amoxicilina Normon, Amoxicillin 1A, Amoxicillin Arrow, Amoxicillin Aurovitas, Amoxicillin Centrient, Amoxicillin EG, Amoxicillin Micro Labs, Amoxicillin ratiopharm, Amoxicillin Teva, Amoxicillin Viatris, Amoxicillin Zentiva Lab, Amoxicillin Zydus, Amoxicillina Cinfa, Amoxicillina Clonmel, Amoxicilline forte suikervrij, AmoxiHEXAL, Amoxilan, Amoxin, Cipamox, Clamoxyl, Hiconcil, Imaxi, InfectoMox, Oraminax, Oramox, Ospamox, Pinamox.

Amoxicillin **dispersible tablets** under several strengths include Ageniprim, Amotaks, Amoxapen, Amoxar, Amoxicillin AB, Amoxicillin Almus, Amoxicillin Arrow, Amoxicillin Aurobindo, Amoxicillin Aurovitas, Amoxicillin Belupo, Amoxicillin Centrient, Amoxicillin Copyfarm, Amoxicillin Cristers, Amoxicillin EG, Amoxicillin Krka, Amoxicillin Sandoz, Amoxicillin Siromed, Amoxicillin Sun, Amoxicillin Teva, Amoxicillin Viatris, Amoxicillin Zentiva Lab, Amoxicillin Zydus, Amoxil, Amoxonor, Clamoxil, Duomox, Hiconcil, Imadrax Novum, Ospamox, Zimox.

Some of the unlicensed pharmaceutical preparations listed below may use licensed products as a starting material; examples of the composition of these licensed products are provided. Other compositions are possible, and the user should always verify that the composition of the licensed product they intend to use is appropriate.

Licensed medicines - Powder for oral suspension			
Product[1]	**Strength**	**Excipients**	**Ref.**
AMOXIL® 125 mg/1.25 mL Powder for oral suspension	Each 1.25 mL contains 125 mg amoxicillin, 4 mg **aspartame**, 2 mg **sodium benzoate** and **maltodextrin** (glucose)	Carboxymethylcellulose sodium, crospovidone, lemon-peach-strawberry dry flavour, magnesium stearate, **aspartame** (E951), **sodium benzoate** (E211), xanthan gum (E415), silica hydrophobic colloidal	(1–3)
AMOXIL® 125 mg/5 mL 250 mg/5 mL 500 mg/5 mL Powder for oral suspension	Each 5 mL contains 125 mg, 250 mg or 500 mg amoxicillin, 16 mg **aspartame**, 8.5 mg **sodium benzoate** and **maltodextrin** (glucose)		
AMOXIL® 250 mg Powder for oral suspension (sachet)	Each sachet contains 250 mg amoxicillin, 16 mg **aspartame**, 850 mg **lactose monohydrate** and **maltodextrin** (glucose)	Crospovidone, peach-lemon-strawberry dry flavour, magnesium stearate, **aspartame** (E951), **lactose monohydrate**	
AMOXIL® 500 mg Powder for oral suspension (sachet)	Each sachet contains 500 mg amoxicillin, 32 mg **aspartame**, 1.7 g **lactose monohydrate** and **maltodextrin** (glucose)		
AMOXIL® 1000 mg Powder for oral suspension (sachet)	Each sachet contains 1000 mg amoxicillin, 25 mg **aspartame** and **maltodextrin** (glucose)	Crospovidone, peach-lemon-strawberry dry flavour, sodium citrate, **aspartame** (E951), saccharin sodium, xanthan gum (E415), **sorbitol** (E420)	
AMOXIL® 3000 mg Powder for oral suspension (sachet)	Each sachet contains 3000 mg amoxicillin, 4.7 g **sorbitol** and **maltodextrin** (glucose)		
Licensed medicines – Dispersible tablets			
AMOXIL® 750 mg, 1000 mg, dispersible tablets	Each tablet contains 750 mg or 1000 mg amoxicillin and 15 mg or 20 mg **aspartame** (E951)	Crospovidone, peppermint dry flavour, magnesium stearate (E572), **aspartame** (E951)	(1,2)
Licensed medicines – Capsules			
AMOXIL® 250 mg, 500 mg, capsules	Each capsule contains 250 mg or 500 mg amoxicillin	Magnesium stearate (E572)	(1)
Licensed medicines – Coated tablets			
OSPAMOX® 500 mg, 750 mg 1000 mg, Film coated tablets	Each tablet contains 500 mg, 750mg or 1000 mg amoxicillin	Microcrystalline cellulose (E460) (Avicel PH-102), sodium starch glycolate, povidone (E1201), magnesium stearate (E470b), titanium dioxide (E171), hypromellose (hydroxypropyl methylcellulose) (HPMC) (E464), talc (E553b)	(3)

[1]Several pharmaceutical forms and strengths of Amoxil are available in the following member states: Belgium, Cyprus, France, Greece, Ireland, Latvia, Lithuania, Luxembourg, Malta, Portugal, Spain and the United Kingdom. In some countries it is available under the brand names Amoxicilline Biogaran and Clamoxyl (1).

Pharmaceutical preparations containing amoxicillin: general considerations

Regarding amoxicillin:

Amoxicillin doses of up to 875 mg have high water solubility and high bioavailability (BCS class I) (4). It is therefore expected that the handling of the pharmaceutical forms (crushing of tablets, opening of capsules, etc.) during preparation of the formulation will have a minimal impact on bioavailability. In accordance with the literature and other recommendations, and in the absence of a licensed powder for oral suspension, licensed capsules may be opened and the contents emptied and mixed with liquid or soft food for immediate oral administration (5). Amoxicillin is subject to hydrolysis of the β-lactam ring at an alkaline pH. The ideal pH for stability is 5.77(6).

1 g of amoxicillin, anhydrous (CAS: 26787-78-0) = 1.148 g of amoxicillin trihydrate (CAS: 61336-70-7)

Molar mass of amoxicillin trihydrate: 419.4 g/mol (see Ph. Eur. monograph *0260*),

Molar mass of anhydrous amoxicillin: 365.4 g/mol (see PubChem)

Regarding the handling of amoxicillin:

Safety precautions: when opening the capsules or handling the API, healthcare professionals should take appropriate measures to **prevent inhalation of the potentially harmful active ingredient** (e.g. using dedicated or disposable equipment, following appropriate cleaning procedures, and protecting from dust by wetting with suspension vehicle and using careful trituration). **Amoxicillin API should not be handled by personnel presenting a penicillin allergy.**

The following precautions may be taken to prevent cross-contamination:

1.Temporal segregation of the compounding of these preparations from non-β-lactam products.

2. Use of dedicated or disposable equipment, utensils, and personal protective equipment (e.g. gowns, gloves).

3. Segregation and storage in a separate area of any equipment, utensils and personal protective equipment used in the compounding of these preparations (e.g., glassware, mortar and pestle) from equipment, utensils, and personal protective equipment not used in β-lactam compounding.

4. Use of proper cleaning procedures after completing compounding, including use of hydrogen peroxide or bleach solutions to deactivate the β-lactam ring of any drug residue on surfaces. The use of strong oxidisers should be followed by neutralisers and volatile cleaning agents (e.g., purified water, isopropanol) to minimize damage to these surfaces.

Further information can be found in the FDA guidance on compounding certain β-lactam products in shortage, published in November 2022 (7).

Existing unlicensed pharmaceutical preparations: overview

Formulations listed in national formularies or sanctioned by national pharmacopoeia authorities

Denomination	Pharmaceutical form	Strength	Starting material	Excipients/ vehicle	Stability	Assigned shelf life	Comments	Ref.
Source: French National Agency for the Safety of Medicines and Health Products (ANSM)								
ANSM capsules #1	Capsules	Each capsule contains 125 mg, 250 mg or 500 mg amoxicillin	Amoxicillin trihydrate (API)	Gelatin capsule, no excipient	**Physicochemical stability data available** In-use or microbiological stability data not available	**2 to 3 months** Ambient temperature	Paediatric capsules: can be opened and their contents mixed with food or a beverage before administration. See Appendix 1	(8)
ANSM capsules #2			Amoxicillin 1000 mg dispersible tablets	Gelatin capsule	In-use or microbiological stability data not available	**1 month** Ambient temperature	Paediatric capsules: can be opened and their contents mixed with food or a beverage before administration. See Appendix 2	(9)

Denomination	Pharmaceutical form	Strength	Starting material	Excipients/ vehicle	Stability	Assigned shelf life	Comments	Ref.
Source: Listed in Deutsche Arzneimittel-Codex/Neues Rezeptur Formularium (DAC/NRF) Knowledge section								
DAC/NRF Knowledge section oral suspension #1	Oral suspension	1 mL contains 150 mg amoxicillin	Amoxicillin trihydrate (API)	German Pharmacopoeia (DAB) simple syrup	In-use or microbiological stability data not available	**14 days** 2–8 °C, based on the general specifications for reconstituted solutions	See Appendix 3	(10)
DAC/NRF Knowledge section oral suspension #2			Amoxicillin 750 mg coated tablets	DAB simple syrup			See Appendix 4	
DAC/NRF Knowledge section oral suspension #3			Amoxicillin trihydrate (API)	German Drug Codex (DAC) vehicle for oral suspensions			See Appendix 5	
DAC/NRF Knowledge section oral suspension #4			Amoxicillin 750 mg coated tablets	DAC vehicle for oral suspensions			See Appendix 6	(10,11)
Source: Österreichische Apothekerkammer (ÖAK)								
ÖAK oral suspension #1	Oral suspension	1 mL contains 50 mg amoxicillin	Amoxicillin trihydrate (API)	DAC vehicle for oral suspensions	In-use or microbiological stability data not available	**10 days** 2–8 °C	See Appendix 7	(11)
ÖAK oral suspension #2				SyrSpend® PH4 Liquid		**30 days** 2–8 °C	See Appendix 8	
ÖAK oral suspension #3				SyrSpend® SF PH4 Dry OR SyrSpend®SF PH4 NEO		SyrSpend® SF PH4 Dry: **14 days** 2–8 °C SyrSpend® SF PH4 NEO: **30 days** 2–8 °C	See Appendix 9	
ÖAK oral suspension #4			OSPAMOX 500 mg Coated tablets	SyrSpend® PH4 Liquid		**14 days** 2–8 °C	See Appendix 10	
ÖAK oral suspension #5			OSPAMOX 1000 mg Coated tablets	SyrSpend® SF PH4 Dry		**14 days** 2–8 °C	See Appendix 11	

Source: Società Italiana di Farmacia Ospedaliera e dei Servizi Farmaceutici delle Aziende Sanitarie (SIFO)								
SIFO oral suspension	Oral suspension	1 mL contains 50 mg amoxicillin	Amoxicillin trihydrate (API) Or Amoxicillin 1000 mg capsules	Cherry (or other) flavour, dextrose monohydrate, hypromellose, purified water	In-use or microbiological stability data not available	**14 days** 2–8 °C In appropriate, amber-coloured PET containers	See Appendix 12	(12)
Powder for oral suspension SIFO	Powder for oral suspension	After reconstitution, 1 mL contains 50 mg amoxicillin	Amoxicillin trihydrate (API) Or Amoxicillin 1000 mg capsules	**Sucrose** carmellose sodium Strawberry flavour **Methylparaben sodium**	In-use or microbiological stability data not available	*Powder:* **6 months** Ambient temperature in a dark glass bottle *Reconstituted suspension:* **14 days** 2–8 °C	See Appendix 13	(12,13)

Formulations listed in scientific literature (books or journals)

Denomination	Pharmaceutical form	Strength	Starting material	Excipients/ vehicle	Stability	Assigned shelf life	Comments	Ref.
Source: Handbook of Pharmaceutical Manufacturing Formulations Vol 3 (Niazi, 2004)								
Powder for oral suspension Handbook	Powder for oral suspension	After reconstitution: 1 mL contains 25 mg amoxicillin	Amoxicillin trihydrate (API)	Simethicone, caster sugar, sodium citrate, xanthan gum, blood orange dry flavour, vanilla dry flavour, orange banana dry flavour, Aerosil® 200	Stability data not available	Shelf-life data not available	Suitable for large batches (5 L) See Appendix 14	(13,14)
Source: U.S. Pharmacist, December 2022 issue.								
Allen oral suspension	Oral suspension	1 mL contains 50 mg amoxicillin	Amoxicillin trihydrate (API) Or Commercial capsules or tablets	Ora-Blend® or Ora-Blend® SF	No in-use or microbiological stability data available. Theoretical shelf life assigned as per USP<795>	**14 days** 2-8 °C	See Appendix 15	(6,15)

Formulations listed in other sources

Denomination	Pharmaceutical form	Strength	Starting material	Excipients/ vehicle	Stability	Assigned shelf life	Comments	Ref.
Source: Medisca.com shortage formulary								
MEDISCA oral suspension #1	Oral suspension	1 mL contains 50 mg amoxicillin	Amoxicillin capsules	*Vehicle:* MEDISCA Oral Mix® flavoured suspension *Other excipients:* Strawberry flavour, banana flavour, stevia powder, glycerin, NaOH, HCl	No in-use or microbiological stability data available. Theoretical shelf life assigned as per USP<795>	**14 days** 2–8 °C	See Appendix 16	(13,15)
Source: Pharmacytimes.com								
Ora oral suspension #1	Oral suspension	1 mL contains 80 mg amoxicillin	Amoxicillin capsules	ORA-PLUS®, ORA-SWEET® (1:1 v/v) (pH 4.4)	No in-use or microbiological stability data available. Theoretical shelf life assigned as per USP<795>	**10 days** Room temperature or 2–8 °C in amber-coloured PET containers	See Appendix 17	(16)
Ora oral suspension #2	Oral suspension	1 mL contains 80 mg amoxicillin	Amoxicillin capsules	ORA-PLUS®, ORA-SWEET® (1:1 v/v) alkalinised with sodium hydroxide 20% (w/v) to pH 6		**10 days** Room temperature or 2-8 °C in amber-coloured PET containers	Alkalinised with NaOH to pH 6 See Appendix 18	(16)

Other information and guidance that might be helpful during shortages

Some guidelines (5) state that amoxicillin capsules can be opened and contents mixed with liquids or soft food for immediate oral administration.. .
The capsule contents will taste bitter so it can be helpful to use a strongly flavoured drink (e.g. blackcurrant cordial) or food (e.g. jam, apple sauce, yoghurt) that the child likes:

- Use a small amount of food or drink (e.g. a teaspoonful) to ensure the child eats it all and swallows the whole dose.
- It is recommended to use an oral syringe for liquids.
- After mixing the powder with food or drink, give it straight away.

The capsules should only be opened at the time of administration, not in advance.

Appendices

Appendix 1: ANSM **capsules #1**

Source: Monograph published by the French National Agency for the Safety of Medicines and Health Products (ANSM), in French - 12/2023

Data from the original source only partially reproduced here. Users are advised to refer directly to the source for further information.

1. **Formulation:**

AMOXICILLIN **125 MG** PAEDIATRIC CAPSULES

Composition	For one capsule
Amoxicillin trihydrate (API)	143.47 mg amoxicillin trihydrate (equivalent to 125 mg amoxicillin)
Empty gelatin capsule of suitable size	NA

AMOXICILLIN **250 MG** PAEDIATRIC CAPSULES

Composition	For one capsule
Amoxicillin trihydrate (API)	286.95 mg amoxicillin trihydrate (equivalent to 250 mg amoxicillin)
Empty gelatin capsule of suitable size	NA

AMOXICILLIN **500 MG** PAEDIATRIC CAPSULES

Composition	For one capsule
Amoxicillin trihydrate (API)	573.9 mg amoxicillin trihydrate (equivalent to 500 mg amoxicillin)
Empty gelatin capsule of suitable size	NA

2. **Preparation:**

For one batch of capsules

1. Comply with clothing, hygiene and protection rules in accordance with national requirements.
2. Work under a chemical hood or equivalent, in accordance with national requirements.
3. Check that the equipment is clean and disinfect with a product designed for this purpose.
4. Define the number of capsules to be produced.
5. Install the capsule-filling machine and add the empty capsules.
6. Weigh the amoxicillin trihydrate on appropriate and qualified weighing scales in a suitable container.
7. Triturate until a fine powder is obtained.
8. Pour the powder into a suitable container.
9. Fill the capsules by levelling. The powder must fill the capsules evenly. Close the capsules.
10. Check the number, cleanliness and homogeneity of the capsules.
11. Check the uniformity of mass in accordance with the Ph. Eur.
12. Pack and label

3. Stability data:

On the basis of the stability studies carried out, a shelf life of 2 or 3 months has been set for amoxicillin capsules stored under the strict conditions defined below:

Strength	API manufacturer	Type of capsules Manufacturer	Type of packaging Supplier	Conditions and duration of stability studies	Shelf life
125 mg	Deretil (Spain)	T4 opaque capsule (gelatin) Capsugel	65 mL PET crystal bottle LDPE cap ID labo	25°C/60% RH D90	90 days
250 mg	Deretil (Spain)	T1 opaque capsule (gelatin) Capsugel	65 mL PET crystal bottle LDPE cap ID labo	25°C/60% RH D56 40°C/75% RH D56	56 days
250 mg	Zhuhai United Laboratories (China)	T1 opaque capsule (gelatin) Capsugel	65 mL PET crystal bottle PET cap Fagron	25°C/60% RH D56	56 days
250 mg	The United Laboratories Inner Mongolia (China)	T0 opaque capsule (gelatin) Capsugel	50 mL PET amber bottle LDPE cap ID labo	25°C/60% RH D56	56 days
500 mg	Deretil (Spain)	T00 opaque capsule (gelatin) Capsugel	65 mL PET crystal bottle PET cap ID labo	25°C/60% RH D90	90 days

Appendix 2: ANSM capsules #2

Source: Monograph published by the French National Agency for the Safety of Medicines and Health Products (ANSM), in French - 12/2022

Data from the original source only partially reproduced here. Users are advised to refer directly to the source for further information.

1. **Formulation:**

AMOXICILLIN **125 MG** PAEDIATRIC HARD CAPSULES

Composition	For one capsule
Amoxicillin 1000 mg dispersible tablets	125 mg (equivalent to 143.47 mg of amoxicillin trihydrate)
Empty gelatin capsule size 4	NA

AMOXICILLIN **250 MG** PAEDIATRIC HARD CAPSULES

Composition	For one capsule
Amoxicillin 1000 mg dispersible tablets	250 mg (equivalent to 286.95 mg of amoxicillin trihydrate)
Empty gelatin capsule size 1	NA

1 g of amoxicillin = 1.148 g of amoxicillin trihydrate
Molar mass of amoxicillin trihydrate: 419.4 g/mol (see Ph. Eur. monograph *0260*)
Molar mass of anhydrous amoxicillin: 365.4 g/mol (see PubChem)

2. **Preparation:**

For one batch of capsules

1. Comply with clothing, hygiene and protection rules in accordance with national requirements.
2. Work under a chemical hood or equivalent, in accordance with national requirements.
3. Check that the equipment is clean and disinfect with a product designed for this purpose.
4. Define the number of capsules to be produced.
5. Install the capsule-filling machine and add the empty capsules.
6. Remove the amoxicillin 1000 mg dispersible tablets from their primary packaging and place them in an appropriate container.
7. Crush the tablets and grind to a fine powder using a mortar and pestle.
8. Fill the capsules by levelling. The powder must fill the capsules evenly. Close the capsules.
9. Check the number, cleanliness and homogeneity of the capsules.
10. Check the uniformity of mass in accordance with the Ph. Eur.
11. Pack and label

Appendix 3: DAC/NRF Knowledge section oral suspension #1

Source: Rezepturenfinder, DAC/NRF-Wissen, in German - 09/2023

Data from the original source only partially reproduceRezepturfinder, DAC/NRF wissen, in Germand here. Users are advised to refer directly to the source for further information.

1. Formulation

Composition	Quantity (g) or volume (mL) Per 100 mL of preparation
Amoxicillin trihydrate	17.22 g (equivalent to 15 g of amoxicillin)
DAB simple syrup	q.s. 133.9 g

100 mL of the final preparation corresponds to 133.9 g

2. Other information

DAB simple syrup contains sucrose (64%, w/v) and purified water (36%, w/v).

Appendix 4: DAC/NRF Knowledge section oral suspension #2

Source: Rezepturenfinder, DAC/NRF-Wissen, in German - 10/2023

Data from the original source only partially reproduced here. Users are advised to refer directly to the source for further information.

1. Formulation

Composition	Quantity (g) or volume (mL) Per 100 mL of preparation
Amoxicillin 750 mg coated tablets or uncoated tablets	20 tablets (equivalent to 15 g of amoxicillin)
DAB simple syrup	q.s. 133.2 g

100 mL of the final preparation corresponds to 133.2 g

2. Preparation

The film might dissolve poorly in the vehicle; any remaining fragments should be sieved out before further processing.

3. Other information

The suitability of the formulation was only evaluated with the following licensed products: Amoxicillin 1A 750 mg coated tablets, Amoxicillin AL 750 mg coated tablets, Amoxicillin Aristo 750 mg tablets.

The qualitative and quantitative composition of licensed products can vary from one brand to another; users are therefore advised to check the suitability of the starting material they intend to use.

Appendix 5: DAC/NRF Knowledge section oral suspension #3

Source: Rezepturenfinder, DAC/NRF-Wissen, in German - 06/2023

Data from the original source only partially reproduced here. Users are advised to refer directly to the source for further information.

1. Formulation

Composition		Quantity (g) or volume (mL) Per 110.4 g of preparation
Amoxicillin trihydrate		17.22 g (equivalent to 15 g of amoxicillin)
DAC base for oral suspension	Hydroxyethylcellulose 1000	0.51 g
	Glucose monohydrate	11.4 g
	Potassium sorbate	0.14 g
	Citric acid	0.077 g
	Purified water	q.s. 109.3 g

100 mL of the final preparation corresponds to 109.3 g

2. Other information

The base for oral suspensions (Grundlage für Suspensionen zum Einnehmen DAC) is available as a commercial, ready-to-use vehicle (e.g. Caelo) or can be prepared according to the instructions below (1.–6.). The base for oral suspension can be stored for 6 months. Physicochemical and microbiological stability data for the vehicle was evaluated by DAC/NRF.

1. Weigh separately the potassium sorbate and citric acid.
2. Weigh hydroxyethyl cellulose and glucose monohydrate into a beaker, add the separately-weighed potassium sorbate and mix the solids in the dry state.
3. Add the purified water to the powder and immediately stir the mixture.
4. Add the citric acid while stirring.
5. Cover the batch and allow it to stand, with occasional stirring (up to 2 hours for batches of 1-2 litres, shorter if necessary for smaller batches).
6. Replace evaporation losses with purified water and stir the batch again.

Appendix 6: DAC/NRF Knowledge section oral suspension #4

Source: Rezepturenfinder, DAC/NRF-Wissen, in German - 10/2023

Data from the original source only partially reproduced here. Users are advised to refer directly to the source for further information.

1. Formulation

Composition		Quantity (g) or volume (mL) Per 110.4 g of preparation
Amoxicillin 750 mg coated tablets or uncoated tablets		20 tablets (equivalent to 15 g of amoxicillin)
DAC base for oral suspension	Hydroxyethylcellulose 1000	0.51 g
	Glucose monohydrate	11.4 g
	Potassium sorbate	0.14 g
	Citric acid	0.077 g
	Purified water	q.s. 110.4 g

100 mL of the final preparation corresponds to 110.4 g

2. Other information

For more information on the preparation of the base for oral suspensions, see *Appendix 5*.

Appendix 7: ÖAK oral suspension #1

Source: Magistrale pädiatrische Notfallrezepturen bei Lieferengpässen, published by the pharmacy department and the pharmacists' laboratory of the Austrian Chamber of Pharmacists, in German - 09/2023

Data from the original source only partially reproduced here. Users are advised to refer directly to the source for further information.

1. Formulation

The composition given below was calculated according to data from the original source.

Composition		Quantity (g) or volume (mL) Per 100.4 g of preparation
Amoxicillin trihydrate		5.75 g (equivalent to 5 g of amoxicillin)
DAC base for oral suspension	Hydroxyethylcellulose 1000	0.47 g
	Glucose monohydrate	10.4 g
	Potassium sorbate	0.13 g
	Citric acid	0.07 g
	Purified water	q.s. 100.4 g

100 mL of the final preparation corresponds to 100.4 g

2. Other information

3. For more information on the preparation of the base for oral suspensions, see *Appendix 5*.

Appendix 8: ÖAK oral suspension #2

Source: *Magistrale pädiatrische Notfallrezepturen bei Lieferengpässen*, published by the pharmaceutical department and the pharmacists' laboratory of the Austrian Chamber of Pharmacists, in German - 09/2023

Data from the original source only partially reproduced here. Users are advised to refer directly to the source for further information.

1. Formulation

Composition	Quantity (g) or volume (mL) Per 100 mL of preparation
Amoxicillin trihydrate	5.75 g (equivalent to 5 g of amoxicillin)
SyrSpend® SF PH4 Liquid	q.s. 100 mL

2. Other information

SyrSpend® SF PH4 Liquid contains purified water, modified food starch, sodium citrate, citric acid, malic acid, sodium benzoate (<0.1%, preservative), sucralose, simethicone, cherry flavour.

Appendix 9: ÖAK oral suspension #3

Source: Magistrale pädiatrische Notfallrezepturen bei Lieferengpässen, published by the pharmacy department and the pharmacists' laboratory of the Austrian Chamber of Pharmacists, in German - 09/2023

Data from the original source only partially reproduced here. Users are advised to refer directly to the source for further information.

1. **Formulation**

Composition	Quantity (g) or volume (mL) Per 100 mL of preparation
Amoxicillin trihydrate	5.75 g (equivalent to 5 g of amoxicillin)
SyrSpend® SF PH4 Dry or SyrSpend® SF PH4 NEO	6.5 g
Purified water	q.s. 100 mL

2. **Other information**

SyrSpend® SF PH4 Dry contains modified food starch, calcium carbonate and sucralose.
SyrSpend® SF PH4 NEO contains potassium sorbate, citric acid and sodium citrate.

Appendix 10: ÖAK oral suspension #4

Source: *Magistrale pädiatrische Notfallrezepturen bei Lieferengpässen*, published by the pharmaceutical department and the pharmacists' laboratory of the Austrian Chamber of Pharmacists, in German - 09/2023

Data from the original source only partially reproduced here. Users are advised to refer directly to the source for further information.

1. **Formulation**

Composition	Quantity (g) or volume (mL) Per 100 mL of preparation
OSPAMOX® 500mg coated tablets	10 tablets (equivalent to 5 g of amoxicillin)
SyrSpend® SF PH4 Liquid	q.s. 102 g

2. **Other information**

SyrSpend® SF PH4 Liquid contains purified water, modified food starch, sodium citrate, citric acid, malic acid, sodium benzoate (<0.1%, preservative), sucralose, simethicone and cherry flavour.

Appendix 11: ÖAK oral suspension #5

Source: Magistrale pädiatrische Notfallrezepturen bei Lieferengpässen, published by the pharmaceutical department and the pharmacists' laboratory of the Austrian Chamber of Pharmacists, in German - 09/2023

Data from the original source only partially reproduced here. Users are advised to refer directly to the source for further information.

1. Formulation

Composition	Quantity (g) or volume (mL) Per 100 mL of preparation
OSPAMOX® 1000 mg coated tablets	5 tablets (equivalent to 5 g of amoxicillin)
SYSRPEND® SF PH4 Dry	5.5 g
Purified water	q.s. 101 g

2. Other information

SYRSPEND® SF PH4 Dry contains modified food starch, calcium carbonate and sucralose

Appendix 12: SIFO oral suspension

Source: *Istruzione Operativa per l'allestimento di Amoxicillina sospensione orale*, published by the Italian Society of Hospital Pharmacy (SIFO), in Italian – 06/2023 (link)

Data from the original source only partially reproduced here. Users are advised to refer directly to the source for further information.

1. Formulation

Composition	Quantity (g) or volume (mL) Per 100 mL of preparation
Amoxicillin trihydrate	5.75 g (equivalent to 5 g of amoxicillin)
Cherry flavour (or other)	0.2 g
Dextrose monohydrate	30 g
Hypromellose	0.6 g
Purified water	q.s. 100 mL

or

Composition	Quantity (g) or volume (mL) Per 100 mL of preparation
Amoxicillin 1000 mg tablets	5 tablets (equivalent to 5 g of amoxicillin)
Cherry flavour (or other)	0.2 g
Dextrose monohydrate	30 g
Hypromellose	0.6 g
Purified water	q.s. 100 mL

2. Other information

pH specifications: 4.0–7.0 (optimal pH 5.7–5.8).

Appendix 13: SIFO powder for oral suspension #2

Source: *Istruzione Operativa per l'allestimento di amoxicillina sospensione orale*, published by the Italian Society of Hospital Pharmacy (SIFO), in Italian – 06/2023 (link)

Data from the original source only partially reproduced here. Users are advised to refer directly to the source for further information.

1. **Formulation**

Composition	Quantity (g) or volume (mL) Per 250 mL of preparation
Amoxicillin trihydrate	5.75 g (equivalent to 5 g of amoxicillin)
Sucrose	30 g
Strawberry flavour	0.2 g
Methylparaben sodium	0.1 g
Carboxymethyl cellulose (CMC) sodium	0.48 g CMC sodium (390 mPa.s) **OR** 0.72 g CMC sodium (495 mPa.s)

Or

Composition	Quantity (g) or volume (mL) Per 250 mL of preparation
Amoxicillin 1000 mg tablets	5 tablets (equivalent to 5 g of amoxicillin)
Sucrose	30 g
Strawberry flavour	0.2 g
Methylparaben sodium	0.1 g
Carboxymethyl cellulose (CMC) sodium	0.48 g CMC sodium (390 mPa.s) **OR** 0.72 g CMC sodium (495 mPa.s)

Appendix 14: Handbook powder for oral suspension

Source: *Handbook of Pharmaceutical Manufacturing Formulations, Vol 3*. (Niazi, 2004)

Data from the original source only partially reproduced here. Users are advised to refer directly to the source for further information.

1. **Formulation**

Bill of Materials	Quantity (g) or volume (mL) Per 5L of preparation
Amoxicillin trihydrate	143.50 g
Simethicone A	1.04 g
Caster sugar	3035.41 g
Sodium citrate	0.468 g
Xanthan gum	0.034 g
Blood orange dry flavour	0.268 g
Vanilla dry flavour	0.015 g
Orange, banana dry flavour	0.089 g
Aerosil® 200	0.290 g

2. **Other information**

Bill of material given for a 5 L batch. Preparation of the formulation requires an hammer mill.

Appendix 15: Allen oral suspension

Data from the original source only partially reproduced here. Users are advised to refer directly to the source for further information.

Source: *Amoxicillin 50 mg/mL Oral Suspension*, Loyd V. Allen, US Pharm. 2022;47(12):59-60. Link

1. **Formulation:**

Composition	Quantity (g) or volume (mL) Per 50 mL of preparation
Amoxicillin trihydrate	5.75 g (equivalent to 5 g of amoxicillin)
ORA-BLEND® or ORA-BLEND® SF	q.s. 100 mL

OR

Composition	Quantity (g) or volume (mL) Per 120 mL of preparation
Amoxicillin tablets	A quantity of tablets equivalent to 5 g of amoxicillin
ORA-BLEND® or ORA-BLEND® SF	q.s. 100 mL

2. **Other information**

ORA-BLEND® contains purified water, sucrose, glycerin, sorbitol, berry citrus flavour (contains FD&C Red #40), microcrystalline cellulose, carboxymethylcellulose sodium, xanthan gum, carrageenan, calcium sulfate, trisodium phosphate, citric acid and sodium phosphate as buffers, dimethicone, methylparaben and potassium sorbate. It is buffered to a pH of approximately 4.2, has a viscosity of approximately 700 cps at 25 °C, and an osmolality of 2107 mosm/kg.

ORA-BLEND® SF contains purified water, sorbitol, glycerin, berry citrus flavour (contains FD&C Red #40), microcrystalline cellulose, carboxymethylcellulose sodium, xanthan gum, carrageenan, calcium sulfate, trisodium phosphate and sodium saccharin, sodium phosphate, citric acid and sodium citrate as buffers, dimethicone, methylparaben, propylparaben and potassium sorbate. It is buffered to a pH of approximately 4.2, has a viscosity of approximately 1,000 cps at 25°C, and has an osmolality of 1073 mosm/kg.

Appendix 16: MEDISCA oral suspension

Data from the original source only partially reproduced here. Users are advised to refer directly to the source for further information.

Source: *Amoxicillin 250 mg/5mL Oral Liquid*, MEDISCA® Shortage formula 10/2022. Link

1. **Formulation:**

Composition	Quantity (g) or volume (mL) Per 150 mL of preparation
Amoxicillin 250 mg capsules	30 capsules (equivalent to 7.5 g of amoxicillin)
Strawberry flavour	0.3 mL
Banana flavour	0.3 mL
Stevia	0.75 g
Glycerin, USP	10 mL
MEDISCA ORAL MIX® (flavoured suspension)	q.s 150 mL
Sodium hydroxide 10% solution (w/v)	As required
Hydrochloric acid 10% solution (w/v)	As required

2. **Other information:**

MEDISCA ORAL MIX® contains cherry flavour, cellulose, glycerine, sucrose and water.

Appendix 17: ORA oral suspension

Data from the original source only partially reproduced here. Users are advised to refer directly to the source for further information.

Source: *Extemporaneous Compounding of Amoxicillin Suspensions During National Shortage*, pharmacytimes.com. Article published 02/2023. Link

1. Formulation

Composition	Quantity (g) or volume (mL) Per 50 mL of preparation
Amoxicillin 500 mg capsules	8 capsules (equivalent to 4.61 g of amoxicillin trihydrate or 4 g of amoxicillin)
ORA-PLUS®	25 mL
ORA-SWEET®	q.s. 50 mL

2. Preparation

1. Measure equal quantities of Ora-Plus® and Ora-Sweet® syrups. Mix until homogeneous. Prepare excess vehicle to ensure the desired quantity can be prepared. The non-alkaline vehicle was used as is without any further pH adjustment.
2. Unlock and pour the contents of amoxicillin 500 mg capsules into a glass mortar. Triturate to reduce particle size.
3. Add a small amount of the prepared vehicle to the powder to wet. Triturate to form a uniform paste.
4. Geometrically add small amounts of the vehicle to the wetted mass until pourable.
5. Transfer the liquid to a calibrated amber bottle.
6. Rinse mortar and pestle with the vehicle until drug residue is adequately transferred to the calibrated amber bottle.
7. QS to final volume with the vehicle. Cap the bottle and shake well. Label and store for stability testing.

3. Other information

ORA-PLUS® contains purified water, microcrystalline cellulose, carboxymethylcellulose sodium, xanthan gum, carrageenan, calcium sulfate, trisodium phosphate, citric acid, sodium phosphate, dimethicone antifoam emulsion, methylparaben, potassium sorbate. It has a final pH of 4.0 to 4.5.
ORA-SWEET® contains purified water, sucrose, glycerin, sorbitol, and berry citrus flavour (contains FD&C Red #40), citric acid and sodium phosphate. It has a final pH of 4.3.

Appendix 18: ORA oral suspension

Data from the original source only partially reproduced here. Users are advised to refer directly to the source for further information.

Source: *Extemporaneous Compounding of Amoxicillin Suspensions During National Shortage*, pharmacytimes.com. Article published 02/2023. Link

1. Formulation

Composition	Quantity (g) or volume (mL) Per 50 mL of preparation
Amoxicillin 500 mg capsules	8 capsules (equivalent to 4.61 g of amoxicillin trihydrate or 4 g of amoxicillin)
ORA-PLUS®	25 mL
ORA-SWEET®	q.s. 50 mL
Sodium hydroxide 20% solution (w/v)	As required to reach pH 6

2. Preparation

See Appendix 17 with the following modification: after mixing the vehicles (step 1), add dropwise sodium hydroxide 20% (w/v) to yield a pH of 6.

3. Other information

See Appendix 16

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