

Pharma Solutions



Liquid API:

Liveo™ Q7-2243
LVA Simethicone

Solid Carrier Excipient:

Budenheim – TRI-CAFOS® 500
Beneo – galenIQ™

**Solid dosage forms
with liquid Simethicone**

Our partners

Biesterfeld Spezialchemie successfully works together with its partners Budenheim and BENEQ.



Budenheim – a deeply rooted tradition as a reliable partner of the pharmaceutical industry

Since the 1950's, we have been dedicated to providing the pharmaceutical market with high quality phosphate based excipients for the manufacturing of liquid and solid dosage forms. Continuous development and improvement of our products, exclusively manufactured in Germany following current Good Manufacturing and current Good Distribution Practices, make us a unique partner.

For cooperation please contact:

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www.budenheim.com



BENEQ-Palatinit is part of the Südzucker Group and member of the International Pharmaceutical Excipient Council (IPEC).

BENEQ-Palatinit produces galenIQ™ (Isomalt Ph.Eur., USP-NF, JP) according to IPEC-PQG cGMP requirements for pharmaceutical excipients. galenIQ™ is a highly functional filler-binder, characterised by its good flavour, ease of use and applicability to a wide range of solid and liquid dosage forms, such as tablets, sachets, lozenges and syrups.

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Biesterfeld Spezialchemie is one of the leading international distributors of products and solutions in the world of specialty chemicals and food ingredients:

Our product portfolio is carefully tailored to the needs of selected industries such as cosmetics, healthcare, paints and coatings, adhesives, polyurethanes, composites, construction, food, electro, electronics and energy.

- Active market development combined with high innovation capacities
- Customer-specific advice from specialists with solution-oriented, technical expertise and know-how in formulations
- Close long-term cooperation with leading global suppliers
- Proximity to customers thanks to branches in Europe and Latin America

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Solid dosage forms with liquid Simethicone

A major advantage of liquid dosage forms is that the API is already dissolved, so the dosage can be taken in as it is.

Solid dosage forms, on the other hand, have the advantage of not requiring preservatives and are generally more stable and easier to handle.

A liquisolid is a tablet or powder with a **liquid API** absorbed into a **solid carrier excipient** which leads to a combination of the advantages of both, liquid and solid dosage forms.*

In the following we are presenting two easy and fast solutions for turning liquid Simethicone into a solid dosage form.

Liveo™ Q7-2243 LVA Simethicone as offered by Biesterfeld Spezialchemie is an anti-foaming agent that is used in pharmaceutical formulations for treatment of certain disorders within the lower gastro intestinal tract.

Composition

- 100% Simethicone USP
- A mixture of polydimethylsiloxane fluid and silicon dioxide

Typical Applications

- Highly effective defoamer at low concentrations
- Active for prescription/ OTC/ medical device antilflatulents
- Foam control in medical and pharmaceutical applications
- Process aid for biofermentation

Regulatory Status

- Tested according to and complies with all United States Pharmacopeia (USP) requirements for Simethicone and European Pharmacopeia (EP) requirements for Simeticone
- Certificate of Suitability (CEP)
- ICH Q7 GMP
- FDA Drug Master File (DMF)



Typical Properties

Parameter	Result	Unit
Silicon Dioxide Content	4-7	%
Volatility	<1.0	w/w %
Heavy Metal Content	<5	ppm
Defoaming Performance	<15 20 ppm	seconds
PDMS Content	90.5-99	%

* [cf. Tablets & Capsules Magazine, „eye on excipients“, Suedzucker/Beneo-Palatinit, April 2018, page 39]

TRI-CAFOS® 500

Tricalcium phosphate

Complies to:
Ph.Eur., NF

FACTS

Tablets to swallow

Direct compression

41 % Simethicone



Tablets to swallow with liquid Simethicone

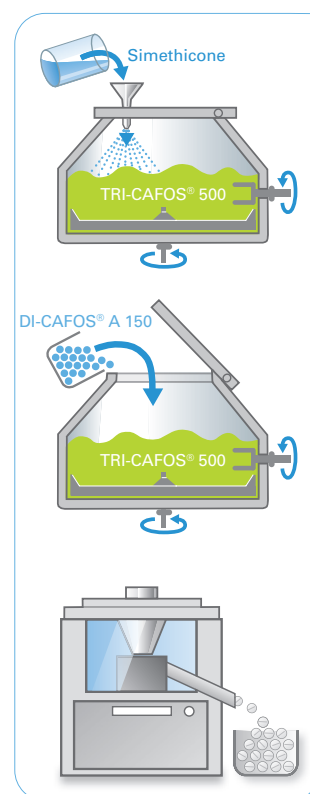
TRI-CAFOS® 500 is a unique tricalcium phosphate of Budenheim, which stands out through its spherical shape and its large surface area of 80 m²/g. This highly elevated surface area of **TRI-CAFOS® 500** enables the sustained binding of Simethicone. Furthermore, the enhanced surface area provides excellent bonding capacity for direct compression processes. Both properties are key to the suitability as carrier material for loading up to 41 % of the **Liveo™ Q7-2243 LVA Simethicone**.

Using **TRI-CAFOS® 500** offers an easy way to turn liquid **Liveo™ Q7-2243 Simethicone** into a solid dosage form with only a few processing steps required. **TRI-CAFOS® 500** is loaded with the desired amount of Simethicone of up to 41 % in a high shear granulator using appropriate process conditions. Afterwards the remaining excipients **DI-CAFOS® A 150**, MCC and Croscarmellose Sodium are blended with the loaded **TRI-CAFOS® 500** mixture for 10 minutes. After lubrication the mixture is compressed into tablets by using a 12 mm biplane, bevelled punch. Tablets of sufficient hardness and fast release are obtained easily, offering quick relief for the patient.

The defoaming activity is the most important parameter to test the efficacy of the final dosage form. This parameter can be measured by observing the collapse of a well-defined foam. To obtain such foam the detergent octoxynol-9 is mixed with water at a concentration 1 % (w/v) and shaken vigorously. Rapid collapse of the created foam was observed. Within **45 seconds** the foam was destroyed completely.

Summary:

- The high porosity of **TRI-CAFOS® 500** ensures that the **Liveo™ Q7-2243 LVA Simethicone** is kept within the tablet during all processing steps.
- Additionally, **DI-CAFOS® A 150** improves the tableting properties of formulations containing **Liveo™ Q7-2243 LVA Simethicone** loaded onto **TRI-CAFOS® 500**.
- The Simethicone tablet formulation with Budenheim **TRI-CAFOS® 500** and **DI-CAFOS® A 150** is simple, fast, reliable and shortens processing time.



Formulation

Item	Component	%	Function
1	TRI-CAFOS® 500 (tricalcium phosphate)	36.6	Carrier
2	Simethicone (Liveo™ Q7-2243)	25.4	Atypical Active
3	DI-CAFOS® A 150 (dicalcium phosphate anhydrous)	30	Filler
4	Microcrystalline cellulose 102	6	Filler
5	Croscarmellose sodium	1	Disintegrant
6	Magnesium stearate	1	Lubricant

Tablet Properties

Property	Method	Unit	Result
Weight	Ph.Eur.	Mg	490
Tensile Strength	at 15 kN	N/mm ²	0.874
Disintegration time in H ₂ O	USP/NF	s	146
Friability	Ph.Eur.	%	0.0



galenIQ™

Isomalt

Complies to:
Ph.Eur., USP/NF,
BP, JP

FACTS

Chewable tablets

Direct compression

7 % Simethicone



Chewable tablets with liquid Simethicone

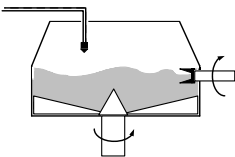
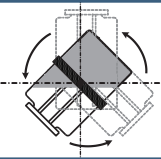
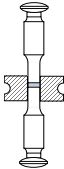
galenIQ™ 721 is an agglomerated Isomalt preferably used as carrier for liquid APIs in the manufacture of direct compression chewable tablets. In comparison to other polyols, isomalt offers a remarkable sensorial profile, including a sugar-like sweet taste and a pleasant mouth feel. It is non-cariogenic and has a low glycemic index.

galenIQ™ 721 acts like a sponge which can absorb up to 7 % of **Liveo™ Q7-2243 LVA Simethicone**.

The loaded isomalt showed suitable flow properties for tableting in an industrial-scale rotary tablet press equipped with a force feeder. The tablet hardness yield was excellent. Both tablet mass uniformity and friability complied well with pharmacopoeial standards.

Summary

- Due to the presence of Corn starch no sticking to the punches occurs
- Self-lubricating: Due to the presence of Simethicone oil no further lubricants are necessary
- Excellent flowability of the mixture
- Very good compressibility, no capping

Workflow	Illustration	Process Parameter		
1. Blending I Blend Items 1, 2 and 3 until a uniform mix is achieved. Pour in the oil carefully.		Rev. of Mixer	[rpm]	250
		Rev. of Chopper	[rpm]	0
		Time	[min]	3
2. Alternative Blending II Blend Items 1, 2 and 3 until a uniform mix is achieved.		Revolutions	[rpm]	20
		Time	[min]	60
3. Compression Compress the blend into 600 mg round convex tablets .		Compression force	[kN]	7,9
		Punch diameter	[mm]	12

Formulation

Item	Component	%	Function
1	Simethicone (Liveo™ Q7-2243)	7	Atypical Active
2	Isomalt (galenIQ™ 721)	88	Filler/Binder
3	Native Corn starch	5	Disintegrant

Tablet Properties

Property	Method	Unit	Result
Weight	Ph.Eur.	Mg	603
Hardness	Ph.Eur.	N	60
Disintegration time	USP/NF	s	320
Friability	Ph.Eur.	%	0.4



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