GATTEFOSSÉ

Compritol® 888 ATO

The lubricant for challenging pharmaceutical tablets

People make our name

Inertness

Compritol 888 ATO is inert

Compritol 888 ATO - glyceryl dibehenate - does not react with active pharmaceutical ingredients (API) or other excipients.

Its inertness is explained by its chemical nature and Gattefossé's robust production process:

- It is a lipid excipient with less than 1% of water
- It does not have reactive groups
- It has very low level of impurity: low peroxide value, low iodine value

Test	Glyceryl dibehenate specification
Appearance	Fine powder
Odor	Faint
Color (Gardner Scale)	≤ 5
Acid value	≤ 4.00 mg KOH/g
Saponification value	145 to 165 mg KOH/g
Iodine value	≤ 3.0 g I_2/100 g
Peroxide value	≤ 6.0 meq O_2/kg
Total ashes content	≤ 0.10%
Water content	≤ 1.0%
Heavy metals content (Pb)	< 10 ppm
Arsenic content (expressed in As_2O_3)	< 2 ppm
Residue on ignition	≤ 0.1%
Nickel content	< 1 ppm

Precedence of use

More than 50 years of use around the world in tablets is proof that Compritol 888 ATO is a high performance lubricant.

Glyceryl dibehenate has been successfully used with the following APIs:

Aceclofenac, Acetaminophen, Acetylsalicylic Acid, Adefovir Dipivoxil, Alfuzosin Hydrochloride, Allyl Isopropyl Acetyl, Amlodipine Maleate, Ascorbic Acid, Atovastatin, Bosentan, Bromelain, Bupropion Hydrochloride, Calcium Mineral, Cefprozil, Chlorpheniramine Maleate, Chondroitin Sulfate, Cimethicon, Clarithromycin, Clemastine Fumarate, Clopidogrel, Colecalciferol, Dehydrocholic Acid, Dexibuprofen, Dextromethorphan Hbr, Diclofenac Sodium, Diphenhydramine Citrate, Domperidone Maleate, Ecabet Sodium, Emodepside, Enalapril, Entacapone, Felodipine, Fesoterodine Fumarate, Fosinopril*, Gabapentin, Gliclazide, Glucosamine Hydrochloride, Herbal Extracts, Hydrochlorothiazide, Ibuprofen*, Ivy Leaf Extract, Lansoprazole, Levofloxacin, L-Theanine, Lysozyme Chloride, Magnesium Aluminum Trisilicate, Mazindol, Meloxicam, Metformin Hydrochloride, Methyl-Sulfonyl-Methane, Mosapride Citrate Hydrate, Naftidrofuryl, Nicotinic Acid, Omeprazole, Orlistat, Pancreatin, Pantoprazole Sodium, Phenylephrine Hydrochloride, Polycarbophil Calcium, Potassium Cresolsulfonate, Prasugrel Hydrochloride, Pseudoephedrine Hydrochloride, Pyridoxin, Ranitidine, Riboflavin, Rilmenidine, S-Adenosylmethionine, Sennosid, Simethicone, Tegaserod Maleate, Thiamine Nitrate, Thioctic Acid, Ticlopidine Hydrochloride, Toltrazuril, Trimebutine Maleate, Tropicamide, Urea, Vitamin K, Yeast (non exhaustive list).*

*API incompatible with magnesium stearate

No incompatibility reported between Compritol 888 ATO and active pharmaceutical ingredients

Robustness

Compritol 888 ATO is insensitive to mixing conditions

Mixing time and speed do not impact Compritol 888 ATO lubricant efficiency nor tablet hardness, irrespective of its concentration.

Compritol 888 ATO facilitates scale-up

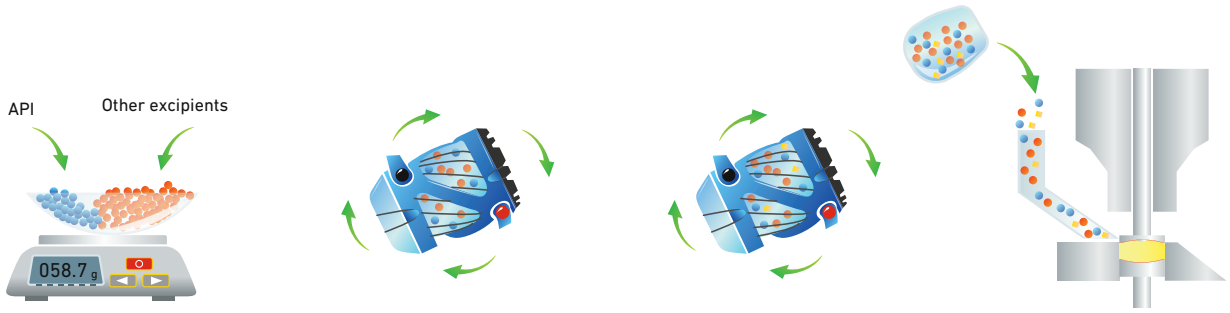
Case studies showed that with Compritol

- Excellent batch reproducibility is obtained
- Press speed has no impact on tablet properties
- No difference observed between lab and pilot scale

Conditions of use

Level of use: 1 to 3%.

Recommended process for an R&D batch:



1. **Weigh API and excipients, except lubricant.**
2. **Blend for 10 min at 60 rpm in a Turbula.**
3. **Weigh Compritol 888 ATO and add it to the previous blend.**
4. **Mix for 5 min at 60 rpm.**
5. **Fill the hopper and compress the tablets.**

Quality by Design

Quality by Design aims to understand the variation of excipient properties related to Critical Process Parameters (CPP) and Critical Quality Attributes (CQA), to ensure more robustness and flexibility in the manufacturing process and enhance drug product quality.

Gattefossé supports customer's QbD programs by providing data on Compritol to facilitate the establishment of the final product Critical Quality Attributes (CQA).

Compritol 888 ATO brings flexibility in formulation development and production

Efficiency

Compritol 888 ATO: an efficient lubricant for tablets

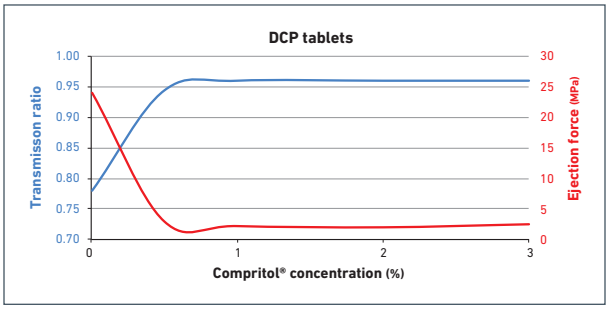
Frictions are efficiently reduced

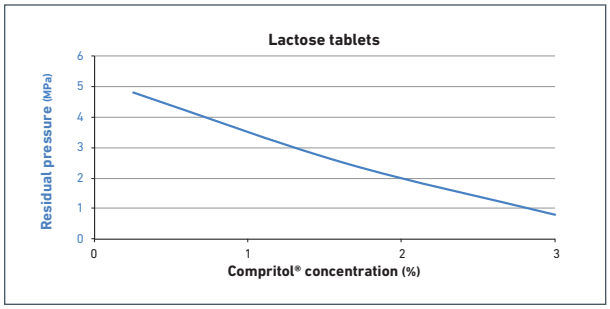
Transmission ratio R is the ratio between upper punch and lower punch forces. If friction is high, ratio R decreases. A good lubricant will give an R value near 1.

Ejection force is the force necessary for the lower punch to eject the tablet from the die. The lower the ejection force, the better the anti-friction effect of the lubricant.

Sticking is effectively avoided

Residual pressure on the upper punch of the tableting machine is measured. If the tablet sticks to the upper punch, residual pressure will be high.

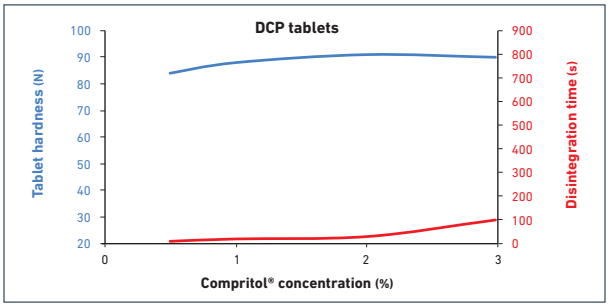


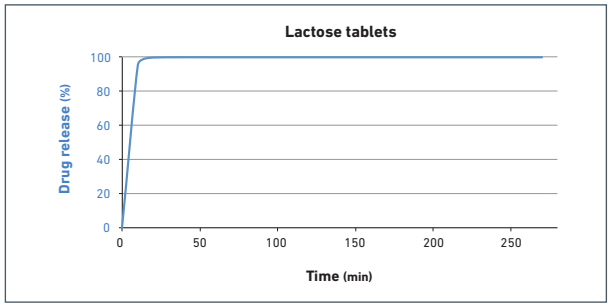


Compritol 888 ATO maintains tablets properties

During mixing, the lubricant particles form a hydrophobic film at the tablet surface. With common lubricants this can sometimes adversely impact tablet hardness, disintegration time or drug release.

With Compritol 888 ATO the tablet properties (hardness, disintegration time or drug release) are maintained.





For further information

A complete technical file is available from your local representative or contact via *www.gattefosse.com*.

This document compiles latest data available on Compritol 888 ATO as a lubricant for pharmaceutical tablets, based on main scientific publications and Gattefossé's case studies.

Compritol 888 ATO provides effective lubrication without compromising tablet properties

Two grades for pharmaceutical tablets

	Compritol 888 ATO	Compritol HD 5 ATO
Description	Glycerol dibehenate EP Glyceryl dibehenate NF Glyceryl behenate Ch.P. CAS: 91052-55-0 (or 30233-64-8) EINECS: 293-216-1 (or 250-097-0)	Behenoyl polyoxyl-8 glycerides NF CAS: 68552-95-4 (or 165658-60-6 or 116810-39-0)
Regulatory	US DMF (Type IV – Excipient): N°4663 Conformity to pharmacopoeias: - European Pharmacopoeia - USP/ NF - Chinese Pharmacopoeia	US DMF (Type IV – Excipient): N°8605 Conformity to pharmacopoeia: - USP/ NF
Production	Obtained by esterification of glycerol with behenic acid (C_{22} fatty acids), followed by atomization. Reaction process does not involve any catalyst or solvent ensuring low impurities. Gattefossé's state of the art production process ensures high product consistency.	Obtained through an esterification reaction between PEG-8, glycerol and behenic acid followed by atomization. No solvent or catalyst is used during the manufacturing process ensuring low impurities. Gattefossé's state of the art production process ensures high product consistency.
Composition	Well defined excipient composed of mono-, di- and triglycerides of behenic acid (C_{22}), the diester fraction being predominant (40-60%).	Well defined excipient composed of mono-, di- and triglycerides and mono- and di-PEG-8 esters of behenic acid.
Physical properties	Presentation: fine white powder Particle shape: spherical Mean particle size: 50 µm Specific surface area: 0.19 m^2/g Melting point: 70°C (drop point method) HLB = 2	Presentation: fine white powder Particle shape: spherical Mean particle size: 50 µm Melting point: 63°C (drop point method) HLB = 5
Uses	Compritol 888 ATO is a non-water soluble, non-dispersible lubricant. It is recommended for use in tablets intended to be swallowed. Use level: 1 to 3%	Compritol HD 5 ATO is a water-dispersible lubricant. It is recommended for use in tablets intended to be dissolved. Use level: 1 to 3%

Other lubricants available from Gattefossé:

- for nutraceutical tablets: Compritol E ATO
- for pharmaceutical capsules: Precirol ATO 5

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COMPRITOL® 888 ATO-GB-2649DD-12 (3123BE)

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