GATTEFOSSÉ

Sustained drug release

with Compritol® 888 ATO

People make our name

Compritol® 888 ATO: one excipient benefits all, from formulator to end-user

Straightforward formulation development

- With a drug release governed by pure diffusion and a first order release kinetic, predictability and reproducibility of drug release is easily obtained with Compritol® 888 ATO sustained-release matrices.
- Being non-ionic and chemically inert, Compritol® 888 ATO is compatible with drugs and excipients of the formulation.

Robustness in physiological conditions

- With water insoluble, non-digestible Compritol® 888 ATO, obtain sustained-release matrices that will not dissolve or erode, irrespective of the media (water, 0.1N HCl, pH 4.5 buffer and 40% ethanol solution) and will not be affected by enzymes and bile salts, offering exceptional robustness in physiological conditions.

Suitable for cold and hot processes

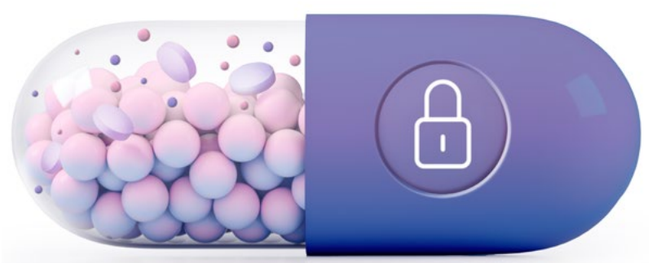
- With a high melting point, narrow melting range and rapid recrystallization behavior, Compritol® 888 ATO is suitable for cold processes (direct compression, wet granulation) and hot processes (melt extrusion, 3D printing, melt granulation, solid dispersion...)

Unlimited dosage forms

- Compritol® 888 ATO is being used to produce sustained-release tablets, mini-tablets, capsules, granules and multi-particulates.

Reduced risk of misuses

- Being insoluble in hydro-alcoholic media and solvents, Compritol® 888 ATO provides abuse-deterrent properties and reduces the risk of alcohol dose dumping.



Compritol® 888 ATO at a glance

Definition	Glycerol dibehenate EP Glyceryl dibehenate NF Glyceryl behenate Ch.P.
Regulatory	US DMF (Type IV – Excipient): N°4663 Compliant to European, US and Chinese pharmacopoeias Registered under Chinese bundling review procedure GRAS status *(Generally Recognized As Safe)*
Production	Obtained by esterification of glycerol with behenic acid, followed by atomization. Reaction process does not involve any catalyst or solvent, ensuring low impurities.
Composition	Well-defined excipient composed of mono-, di- and triglycerides of behenic acid (C_{22}), the diester fraction being predominant (40-60%).
Physicochemical properties	Fine white powder, mean particle diameter 50 µm Melting point 71°C and rapid recrystallization
Precedence of use	Glyceryl dibehenate (UNII: R8WTH25YS2) is listed in the FDA Inactive Ingredient Database for sustained, delayed and controlled release tablets and capsules. Glyceryl dibehenate is used in sustained-release tablets with the following APIs: *acamprosate calcium, acetylsalicylic acid, dipyridamole, azithromycin dihydrate, bupropion hydrobromide, bupropion hydrochloride, clarithromycin, divalproex sodium, fesoterodine fumarate, fluvastatin sodium, gabapentin enacarbil, guanfacine hydrochloride, metformin hydrochloride, rosuvastatin calcium, molsidomine, niacin, nisoldipine, omeprazole, pantoprazole sodium sesquihydrate, paroxetine hydrochloride hydrate, tamsulosin hydrochloride, theophylline, tramadol hydrochloride, tranexamic acid, zileuton.*

Develop sustained-release formulations faster with technical support from Gattefossé

To help you develop sustained-release formulations with Compritol® 888 ATO, Gattefossé provides:

- Formulations with model drugs
- Complete formulation guidelines
- Case studies
- Generic drug dossiers

The experts of our Technical Centers of Excellence in France, India, China and the USA are at your service to provide technical support and formulation feasibility assessment.

Quality-by-Design

Gattefossé's state of the art production process ensures high product reproducibility.

Critical Material Attributes such as product composition, particle size and melting point and their impact on tablet properties have been evaluated.

Ask for our QbD dossier

Compritol® 888 ATO: a unique sustained-release agent

Getting started

Use the table below to determine your starting-point formulation

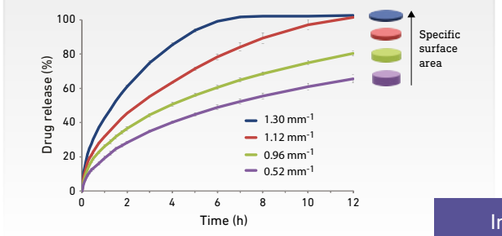
The aqueous solubility of the Active Pharmaceutical Ingredient (API) determines the concentration of Compritol® 888 ATO and the type of diluent to use in your formulation:

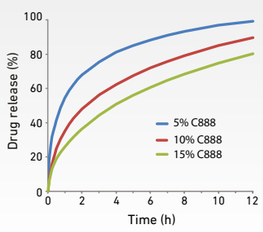
- The higher the drug aqueous solubility, the higher the Compritol® 888 ATO concentration
- Water soluble diluents speed-up drug release

API solubility in release medium	<1 mg/mL	1-50 mg/mL	>50 mg/mL
Compritol® 888 ATO concentration	<15%	10-25%	>20%
Diluents type	Water soluble	Soluble and / or insoluble	Water insoluble

Adjusting the drug release profile

Use one or more of the following tips to fine-tune the drug release profile until you reach your target



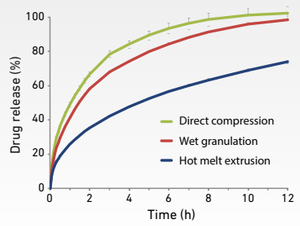


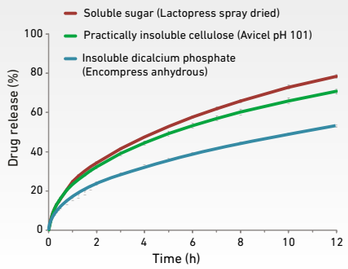
Increasing the concentration of Compritol® 888 ATO decreases the drug release

Decreasing diluent solubility decreases the drug release

Switching from a cold to a hot process decreases the drug release

Decreasing the matrix specific surface area decreases the drug release





Dual sustained-release matrices with Compritol® 888 ATO and HPMC

Reduce the global sustained-release agent concentration

- In a single matrix, HPMC is frequently used at 30% to achieve sustained release.
- In a dual matrix, the ideal ratio is about 10% Compritol® 888 ATO and 15% HPMC.

Reduce the alcohol quantity used in wet granulation

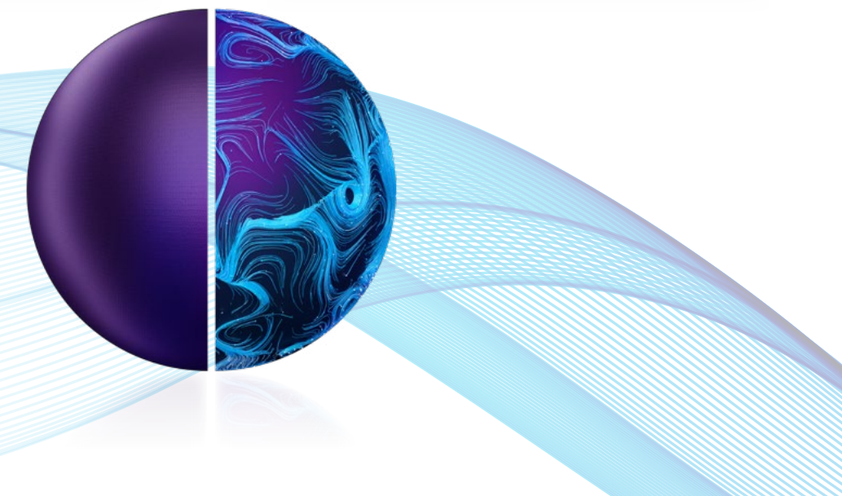
- In a single HPMC matrix, 50% alcohol solution is necessary in wet granulation to prevent sticking.
- In a dual matrix, 20% alcohol is sufficient.

Reduce drug release variability

- Addition of Compritol® 888 ATO reduces the inter-batch variability which can be observed with HPMC

Achieve high drug dose tablet by direct compression

- High drug loading can be achieved with a dual matrix Compritol® 888 ATO/ HPMC in a direct compression process. The dissolution profile was comparable to a market reference (single HPMC matrix, wet granulation + direct compression).



GATTEFOSSÉ

SUSTAINED DRUG RELEASE WITH COMPRITOL® 888 ATO-RC850P- (3123BSR) 2023

www.gattefosse.com

Corporate Headquarters
36 chemin de Genas - CS 70070 - 69804 Saint-Priest Cedex - **France**
+(33) 4 72 22 98 00

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