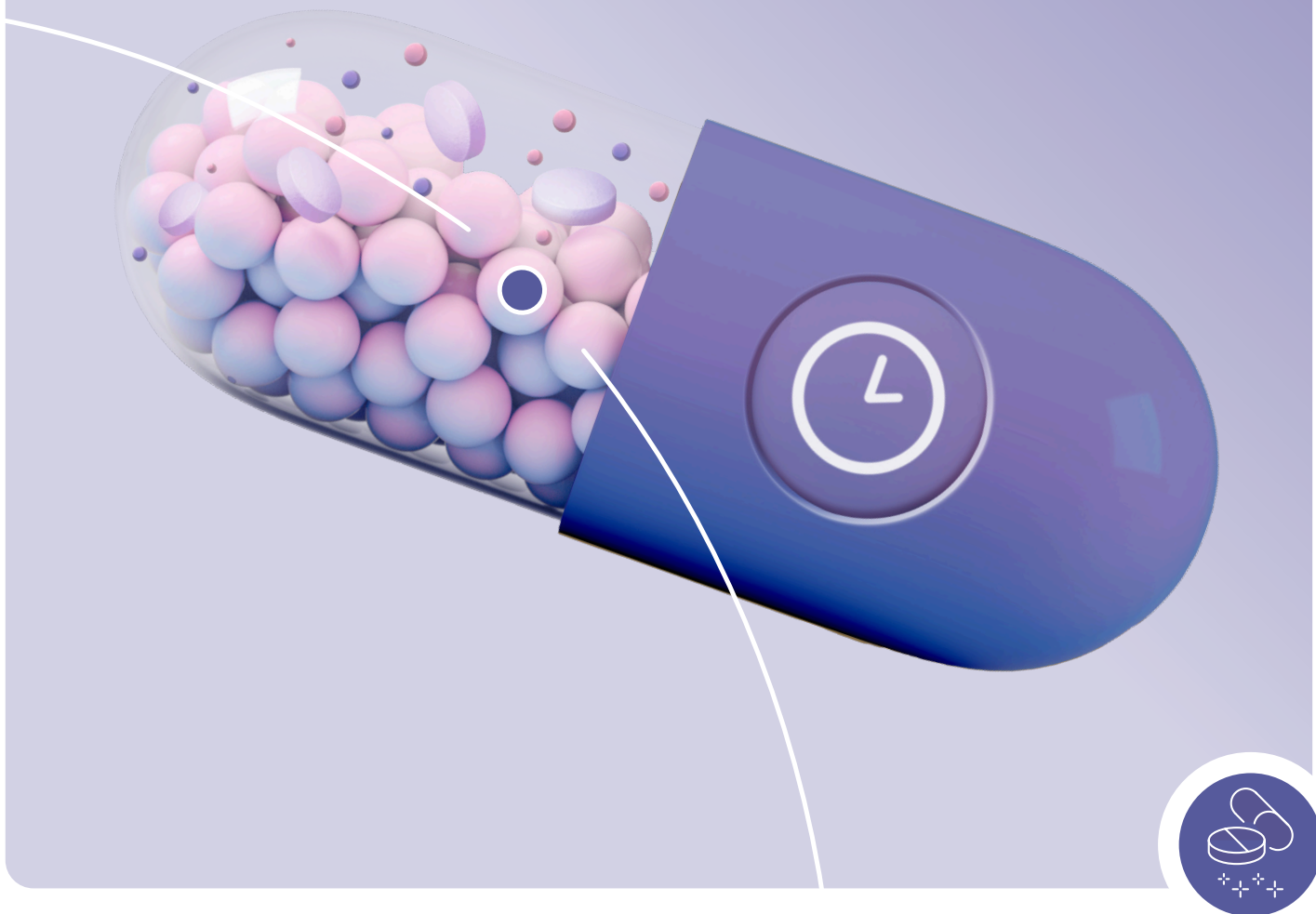


# GATTEFOSSÉ

• PHARMACEUTICALS

**Sustained drug release  
with Compritol® 888 ATO**



# 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

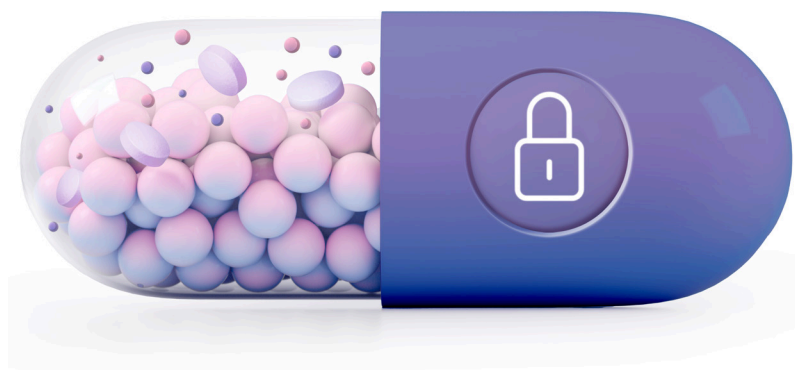
With a high melting point, narrow melting range and rapid recrystallization behavior, Compritol® 888 ATO is suitable for cold processes (direct compression, wet granulation) and hot processes (melt extrusion, 3D printing, melt granulation, solid dispersion...)

## 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: a unique sustained-release agent

Use the table below to determine your starting-point formulation

Getting started

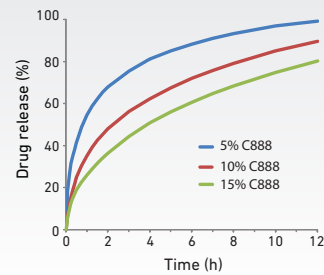
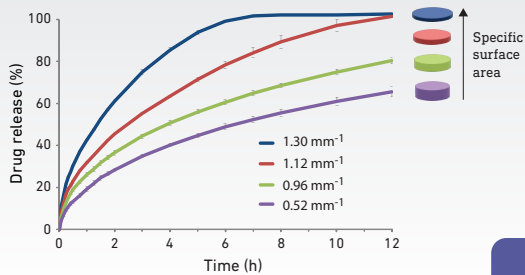
The aqueous solubility of the Active Pharmaceutical Ingredient (API) determines the concentration of Compritol® 888 ATO and the type of diluent to use in your formulation:

- 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

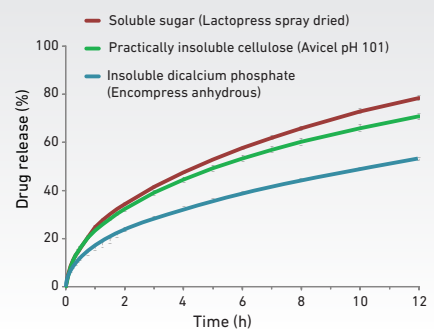
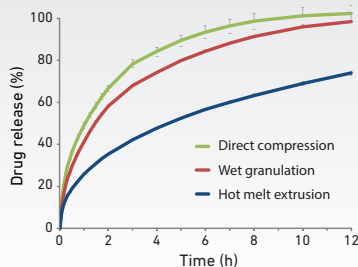


Decreasing the matrix specific surface area decreases the drug release

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



# 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).



# Compritol® 888 ATO at a glance

|                                   |  |
|-----------------------------------|--|
| <b>Definition</b>                 | Glycerol dibehenate EP<br>Glyceryl dibehenate NF<br>Glyceryl behenate Ch.P.  |
| <b>Regulatory</b>                 | US DMF (Type IV – Excipient): N°4663<br>Compliant to European, US and Chinese pharmacopoeias<br>Registered under Chinese bundling review procedure<br>GRAS status ( <i>Generally Recognized As Safe</i> )  |
| <b>Production</b>                 | Obtained by esterification of glycerol with behenic acid, followed by atomization.<br>Reaction process does not involve any catalyst or solvent, ensuring low impurities.  |
| <b>Composition</b>                | Well-defined excipient composed of mono-, di- and triglycerides of behenic acid (C <sub>22</sub> ), the diester fraction being predominant (40-60%).   |
| <b>Physicochemical properties</b> | Fine white powder, mean particle diameter 50 µm<br>Melting point 71 °C and rapid recrystallization   |
| <b>Precedence of use</b>          | Glyceryl dibehenate (UNII: R8WTH25YS2) is listed in the FDA Inactive Ingredient Database for sustained, delayed and controlled release tablets and capsules.<br><br>Glyceryl dibehenate is used in sustained-release tablets with the following APIs: <i>acamprosate calcium, acetylsalicylic acid, dipyrindamole, 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.</i> |

## 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

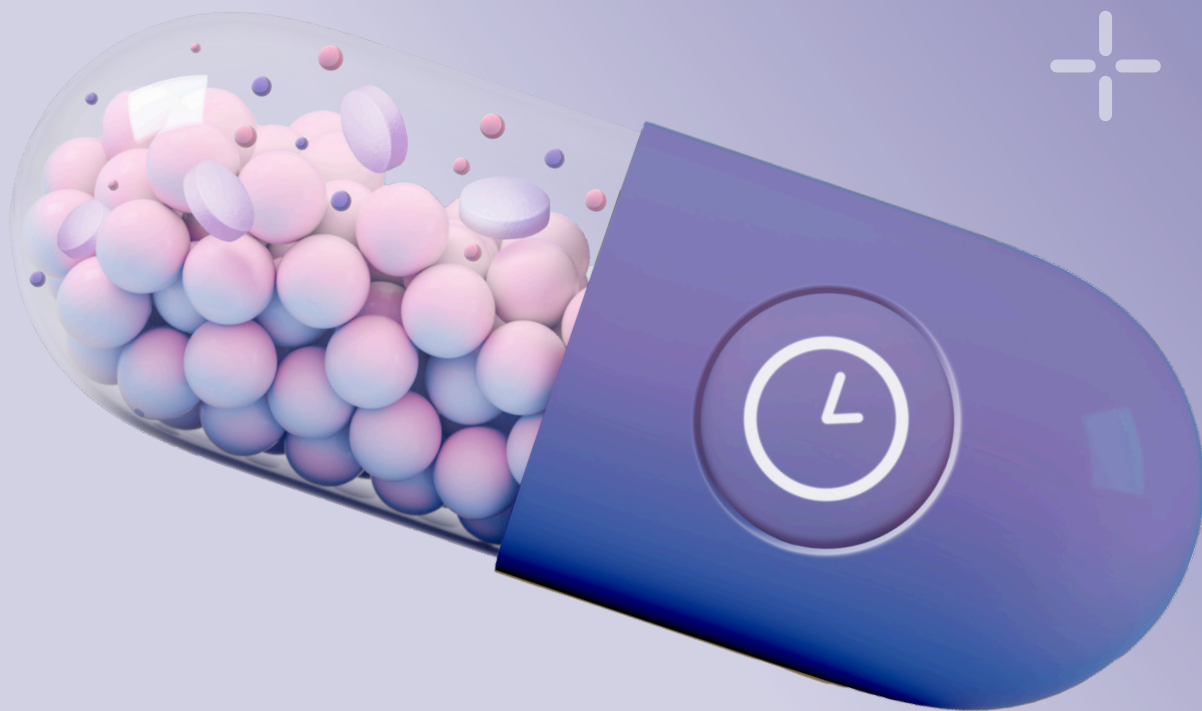
Gattefossé's state of the art production process ensures high product reproducibility.

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](#)

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SUSTAINED DRUG RELEASE WITH COMPRITOL® 888 ATO-SD860Q (3123B5R) 2025

**GATTEFOSSÉ** ● CORPORATE HEADQUARTERS

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

[www.gattefosse.com](http://www.gattefosse.com)



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