



Gattefossé Products in Pediatric Dosage Forms



People make our name

Dose Flexibility



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Developing pediatric medicines can be challenging due to physiological changes from birth to adolescents. In addition to differences in pharmaco-kinetics and pharmaco-dynamics, pediatric medicines require different dosage forms, strengths and routes of administration. Until the age of 12, the dosage requires adjustment based on body weight or surface area. Therefore, dosage forms need to be flexible for easy measurement and administration without creating any risk of aspiration or choking for oral administration. Another important consideration for pediatric drug development is taste, which must be masked to ensure compliance and acceptance.

The need for easy, reliable and flexible dosing of pediatric oral formulations can be met with technologies such as powders/granules for reconstitution, liquids or syrups dosed by volume, and conventional solid formulations such as mini-tablets in various dosage strengths.

The choice of excipient is as important as the dosage form. Gattefossé offers a wide range of lipid excipients for the development of various pediatric dosage forms, including powders / granules for reconstitution, mini-tablets, oral solutions, topical creams and gels and suppositories (please refer to summary table on page 8). Suitable dosage forms by age groups have been defined in the [Reflection paper](#), EMEA 2006.

Safety First



Glyceride-based lipid excipients are similar to dietary fats, have GRAS status and therefore offer an advantage for use in pediatric formulations. Glyceryl dibehenate (Compritol® 888 ATO) has a wide history of use in pediatric patients, e.g. in single easy-to-dose antibiotics (Zmax®) and in chronic conditions like attention deficit hyperactivity disorder. Compritol® 888 ATO has been also listed in the STEP (Safety & Toxicity of Excipients for Pediatrics) database which is available: <http://www.eupfi.org/step-database-info/>.

Gattefossé glycerides in oral pediatric dosage forms

TRADE NAME (NF DEFINITION)	PEDIATRIC DOSAGE FORMS (FUNCTIONALITY)	EXAMPLE OF MARKET REFERENCES (AGE)
COMPRITOL® 888 ATO (Glyceryl dibehenate)	Powders, granules for reconstitution, mini-tablets (Lipid matrix for sustained release, lubricant)	Oral worldwide (6 months and older)
PRECIROL® ATO 5 (Glyceryl distearate)	Powders, granules for reconstitution, mini-tablets (Taste masking agent, lubricant)	Oral worldwide (8 years and older)
COMPRITOL® HD 5 ATO (Behenoyl polyoxyglycerides)	Effervescent tablets (Lubricant for effervescent)	Oral worldwide (12 years and older)

Taste Masking



Glycerides like Precirol® ATO 5 (glyceryl distearate) are ideal for coating drug particles, which results in acceptable taste and mouthfeel for bitter drugs. Precirol® ATO 5 is a finely atomized and crystalline powder with a narrow melting range (53°C to 57°C) and rapid recrystallization; it is ideal for hot melt processes.

Molten Precirol® ATO 5 can be sprayed onto solid drug particles in a fluid bed coating device. The lipid excipient produces a thin, homogeneous film coating that delivers improved tablet compaction and resolves drug taste and compatibility problems. The process is quick and solvent-free, and no drying step is required.

Precirol® ATO 5 is also used in an alternative and simpler taste masking process using a high shear mixer. During mixing, the inter-particulate friction caused by high shear rates generates sufficient heat to partially melt the lipid excipient, which then coats individual drug particles. Upon cooling below its melting point, Precirol® ATO 5 recrystallizes instantly, providing a solid film that is neutral in taste and perfectly suitable for taste masking approaches. For more details, please ask your Gattefossé representative for this poster: Efficient taste masking through high shear coating with lipid excipients, Rosiaux et al, **EuPFI 2017**.

The coated API can be used in mini-tablets or multi-particulates in sachets as flexible dosage forms.

Sustained Release Administration



Lipid excipients have a proven history of use as simple sustained release (SR) matrices in pediatric-friendly dosage forms such as mini-tablets and multi-particulates.

Lipophilic matrices are insoluble in aqueous systems, they do not swell, and diffusion is the principle mechanism of drug release. Desired drug release rates can be achieved by simple modifications of basic formulation and process parameters. Compritol® 888 ATO (glyceryl dibehenate), a high melting point, low HLB lipid, can create a lipophilic matrix via numerous standard processing techniques (direct compression, wet/melt granulation, solid dispersion, hot/cold melt extrusion, spray cooling). In addition, its acceptable taste and mouthfeel make for a pediatric-friendly formulation.

Compritol® 888 ATO can be used to create lipid multi-particulates. The lower melting point of Compritol® 888 ATO makes solvent-free processing possible. Compritol® 888 ATO offers many functionalities, such as lubrication, protection and sustained release. The functionality for your product can be tuned by adjusting its concentration in the formula. Compritol® 888 ATO finished products are amenable to pediatric-friendly delivery forms such as sachets, dispersions, capsule fill or mini-tablets. It has precedence of use in pediatric populations for azithromycin (Bo et al: Drug Development and Industrial Pharmacy, Volume 35, 2009 - Issue 12, Pages 1522-1529).

Guanfacine hydrochloride, used to treat ADHD in 6-17 year-olds, is available for sustained release in four strengths: 1, 2, 3 and 4 mg/tablet. A glyceryl dibehenate based matrix can create a sustained release mini-tablet for such low doses.

Topicals, Gels and Ointments



Emulsion-based soft creams are preferred over other topical formulations to treat eczema, dermatitis and rash due to their easy applications over large areas. Tefose® 63 and Tefose® 1500 are emulsifiers known to be non-irritating and gentle on the skin. Therefore, they are ideal for use in pediatric creams.

Gels are also used to treat bumps and bruises, and for anti-acne and anti-inflammatory actives. Transcutol® and Labrasol® can be used as solubilizers in such gels. Recently, Labrasol® has also been used to create foams for an anti-inflammatory medicine.

Gattefossé products in topical pediatric dosage forms

TRADE NAME (NF DEFINITION)	PEDIATRIC DOSAGE FORMS (FUNCTIONALITY)	EXAMPLE OF MARKET REFERENCES (AGE)
LABRASOL® (Caprylocaproyl polyoxyl-8 glycerides)	Topical gels, foams (Solubilizer; permeation enhancer)	Topical in EU (6 years and older)
GELEOL™ MONO AND DIG- LYCERIDES NF (Mono and diglycerides)	Topical creams (Thickener)	Topical in EU and North America (2 years and older)
TEFOSE® 1500 (PEG-6 stearate & PEG-32 stearate)	Topical creams (Emulsifier)	Topical in North America (12 years and older)

Administering to Infants and Toddlers



Rectal Dosage Forms

The rectal route can be considered a good alternative for the pediatric population because these dosage forms need neither to be swallowed nor to be taste-masked. Rectal forms can also be administered in an emergency to unconscious or vomiting children. Their manufacturing cost is low with excipients generally regarded as safe.

Suppositories are used in infants and children especially for antipyretics. Suppocires® composed of hard fat have been used in acetaminophen suppositories at various dosage levels: 50, 80, 100, 125, 150, 200, 250 and 300 mg/unit.

Gattefossé products in rectal pediatric dosage forms

TRADE NAME (NF DEFINITION)	PEDIATRIC DOSAGE FORM (FUNCTIONALITY)	EXAMPLE OF MARKET REFERENCES (AGE)
SUPPOCIRE® SERIES (Hard Fat)	Suppositories (Lipid based vehicle)	Rectal worldwide (1 month and older)

Gattefossé Products in Pediatric Dosage Forms - Summary Table

TRADE NAME (NF DEFINITION)	PEDIATRIC DOSAGE FORMS * (FUNCTIONALITY)	EXAMPLE OF MARKET REFERENCES (AGE)
COMPRITOL® 888 ATO (Glyceryl dibehenate)	Powders, granules for reconstitution, mini-tablets (Lipid matrix for sustained release, lubricant)	Oral worldwide (6 months and older)
PRECIROL® ATO 5 (Glyceryl distearate)	Powders, granules for reconstitution, mini-tablets (Taste masking agent, lubricant)	Oral worldwide (8 years and older)
COMPRITOL® HD 5 ATO (Behenoyl polyoxyglycerides)	Effervescent tablets (Lubricant for effervescent)	Oral worldwide (12 years and older)
LABRASOL® (Caprylocaproyl polyoxyl-8 glycerides)	Topical gels, foams (Solubilizer; permeation enhancer)	Topical in EU (6 years and older)
GELUCIRE® 44/14 (Lauroyl polyoxyglycerides)	Hard-gelatin capsules (Solubilizer; Bioavailability enhancer)	Oral worldwide (12 years and older)
GELUCIRE® 50/13 (Stearoyl polyoxyglycerides)	Hard-gelatin capsules (Solubilizer; Bioavailability enhancer)	Oral worldwide (12 years and older)
LABRAFIL® M1944 CS (Oleoyl polyoxyl-6 glycerides)	Oral solutions, Topical creams (Solubilizer; Bioavailability enhancer)	Oral and Topical worldwide (6 months and older)
TRANSCUTOL® P & HP (Diethylene glycol monoethyl ether)	Oral syrups, Topical gels (Solubilizer; Penetration enhancer)	Oral in EU (6 months and older)
LABRAFAC® WL 1349 (Medium chain triglycerides)	Liquids (Oily vehicle; Solubilizer)	Oral in EU (3 months and older)
GELEOL™ MONO AND DIGLYCERIDES NF (Mono and diglycerides)	Topical creams (Thickener)	Topical in EU and North America (2 years and older)
TEFOSE® 1500 (PEG-6 stearate & PEG-32 stearate)	Topical creams (Emulsifier)	Topical in North America (12 years and older)
SUPPOCIRE® SERIES (Hard Fat)	Suppositories (Lipid based vehicle)	Rectal worldwide (1 month and older)

* Suitable dosage forms by age groups have been defined in "Formulations of choice for the pediatric population, Reflection paper, EMEA, 2006"

This document focuses on Gattefossé products with precedence of use. To learn about other potential products suitable for pediatric dosage forms please contact your local Gattefossé representative.



USA Regional Office

GATTEFOSSÉ Corporation
Plaza I, 115 West Century Road, Suite 340
Paramus, New Jersey 07652
Tel: +1 201 265 4800 - Fax: +1 201 265 4853
info@gattefossecorp.com



Canada Regional Office

GATTEFOSSÉ Canada, Inc.
170 Atwell Drive, Suite 580
Toronto, Ontario M9W 5Z5
Tel: +1 416 243 5019 - Fax: +1 416 243 8628
service@gattefosse.ca

www.gattefosse.com



Corporate Headquarters

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