



Neotame and Sucralose

TWO WAYS TO ACE THE TASTE TEST

Achieve stable formulations
and clean, sugar-like taste
with our high-intensity
sweeteners.

MilliporeSigma is the U.S.
and Canada Life Science
business of Merck KGaA,
Darmstadt, Germany.

SAFC[®]

Pharma & Biopharma Raw
Material Solutions

Mask bitter aftertaste for a sweeter pill to swallow

Bitter medications are an important issue for the pharmaceutical industry, as several APIs have bitter-tasting components. For pediatric and geriatric applications in particular, pleasant taste and palatability are crucial and support patients' compliance and the therapeutic benefit. With our safe high-intensity taste optimizers **neotame** and **sucralose**, you have effective tools at hand which are superior to other sweeteners in many aspects.

Our high-quality products ensure consistent and reliable high-performance at every stage and scale. As part of the Emprove® Program, our neotame and sucralose meet the highest quality standards such as EXCiPACT®. They are complemented by our Emprove® dossiers, which help you with your risk assessments and go above and beyond quality requirements to simplify and speed up your regulatory filings.

Benefits

- Excellent clean, sugar-like taste profiles
- Outstanding sweetness factors, masking bitter aftertaste with ease
- Enhanced stability
- Compatible with other sweeteners, possible synergies when used in combinations
- Non-cariogenic, suitable for patients with phenylketonuria and diabetes (zero glycemic index)

NEOTAME EMPROVE® ESSENTIAL

UNCOVER NEW OPPORTUNITIES.

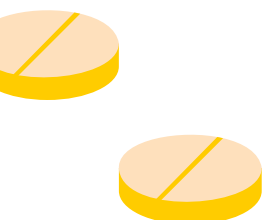
Unlock the next generation of taste optimizers

Discover Neotame EMPROVE® ESSENTIAL. This high performance sweetener is 8,000 – 13,000 times sweeter than sucrose and thus very efficient in use and costs. With a similar taste to that of sucrose, neotame has no unpleasant aftertaste, a good mouthfeel, and enables safe and heat-stable formulations. It is chemically stable at room temperature and supports heat treatment, in contrast to aspartame.

Another benefit: As neotame does not release phenylalanine under normal storage conditions, a phenylketonuria warning is not required.

No specific restrictions for use in pediatric formulations

Neotame, a dipeptide methyl ester derivate of aspartame, is an established excipient for oral applications. This high-intensity sweetener is widely approved as a food additive in the EU and in the USA. The US FDA has conducted a comprehensive safety evaluation for its use as a sweetening agent and flavor enhancer in foods. Its safety has also been evaluated by the Joint FAO/WHO Expert Committee on Food Additives (JECFA). With an entry in the FDA Inactive Ingredient Database, neotame is not considered new and may require a less extensive review when included in a new drug product.



SUCRALOSE EMPROVE® ESSENTIAL

SO MUCH BETTER THAN BITTER.

Ideal solubility and taste masking with sucralose

Our multi-compendial high-intensity sweetener sucralose excels at masking bitterness and medical off-notes with ease. Sucralose is 600 times sweeter than sucrose and widely used as a taste optimizer in various pharmaceutical applications. It is well known for its clean and pleasant taste, is readily soluble and has excellent aqueous heat and pH stability. As an inert compound, it does not interact with other ingredients.

Sucralose, a substituted disaccharide, has long been used in different applications in both food and pharma and is suitable for children, pregnant women and people with diabetes or glucose intolerance who require a sugar substitute.

The right particle size tailored to your application needs

For easy handling at your end, we are offering sucralose in micronized and granular form. Due to its optimal dispersion behavior, our sucralose powder is typically recommended for solid dose formulations, while the fast dissolution behavior of our granular sucralose makes it very well-suited for liquid formulations. Both sucralose types are easily soluble in water and ethanol, even at low temperatures.



Neotame and Sucralose

Dosage forms

The high-intensity sweeteners neotame and sucralose can be widely used in various pharmaceutical applications:

- Orally disintegrating tablets
- Effervescent tablets
- Lozenges
- Liquid formulations
- Oral films

The ideal taste optimizers in your oral solid, liquid and film applications

The taste of an oral formulation can be important for the treatment adherence. From the characteristics of the API to the patient population, there are several factors that must be considered to find the most appropriate taste optimizer. Make your choice tailored to your formulations needs:

	Neotame EMPROVE® ESSENTIAL	Sucralose powder EMPROVE® ESSENTIAL	Sucralose granular EMPROVE® ESSENTIAL
Taste	Clean, sugar-like taste slightly delayed onset and lasting sweetness		
Sweetness Potency vs. Sucrose	8,000 – 13,000	400 – 800	
Pharmacopoeia	NF listed in IID*	Ph Eur, ChP, NF, JPE listed in IID*	Ph Eur, NF, JPE listed in IID*
Safety Profile	Widely approved food additives (FDA, EU, China; safety evaluation by JECFA)		
Recommended Dosage	1 – 750 ppm	0.05 – 2.0 %	
Cost Efficiency	+++	+	
Heat Stability in Solid Formulations	+++	++	+
Solid Applications	✓	✓	-
Liquid Applications	✓	✓	✓
Oral Film Applications	✓	✓	✓

Table 1: Features and recommended applications of neotame and sucralose

* IID: FDA Inactive Ingredient Database

Sweetening strength

In comparison to sucrose and other commonly used sweeteners, neotame and sucralose feature a high sweetness potency. This extraordinary sweetening strength enhances their effectiveness in use.

Synthetic high-intensity sweeteners	Relative sweetness ranges in relation to Sucrose = 1
Acesulfame K	130 – 200
Aspartame	120 – 220
Cyclamate	20 – 40
Neotame	8,000 – 13,000
Saccharin	200 – 700
Sucralose	400 – 800

Table 2: Overview of synthetic high-intensity sweeteners and their sweetness potency

Outstanding taste-masking performance with no bitter aftertaste

In sensory studies conducted with a panel of professional taste-testers, sucralose and neotame achieved the best scores, confirming that these two sweeteners are effective and potent alternatives to aspartame.

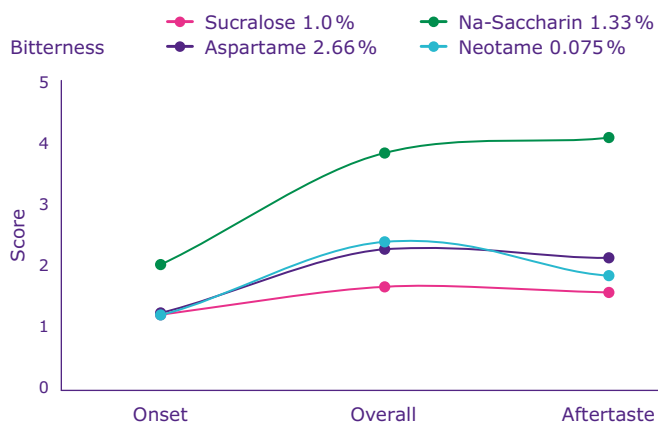


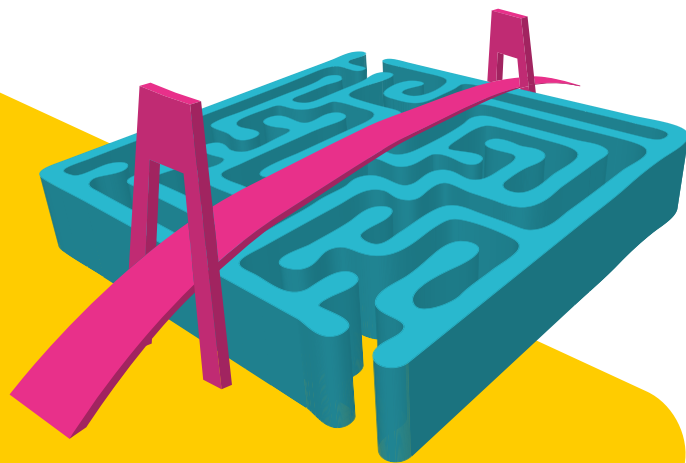
Figure 1: Taste panel evaluation (5-point scale, lower scores indicate better performance)

Bitterness surrogate: 0.06% quinine
NOTE: The usage level of the sweeteners in the formulations considers the different individual sweetness factors.



Neotame and Sucralose taste best when paired with your formulations.

As Emprove® Essential products, both products are designated for moderate-risk applications, offering compliance to IPEC-PQG GMP Guide and EXCIPACT® Certification Standard, as well as regulatory support to assist your risk assessments.



The Emprove® Program

Your fast track through regulatory challenges.

Ensuring the compliance of your pharma and biopharma products involves the compilation of a vast amount of data, which can be time and resource intensive. Our Emprove® Program helps you meet the latest regulatory requirements for risk assessment and offers assistance in developing more robust processes.

To help you optimize your process, our Emprove® Program provides comprehensive and thorough documentation for approximately 400 raw and starting materials as well as a selection of filters, single-use devices and components. It not only covers the latest regulatory requirements, but also anticipates

industry expectations not yet covered by regulation. The Emprove® Program is organized into three different types of dossiers. Every dossier supports you throughout different stages of your operations: qualification, risk assessment, and optimization – so you can speed your way through the regulatory maze.

Find out more at:
SigmaAldrich.com/emprove

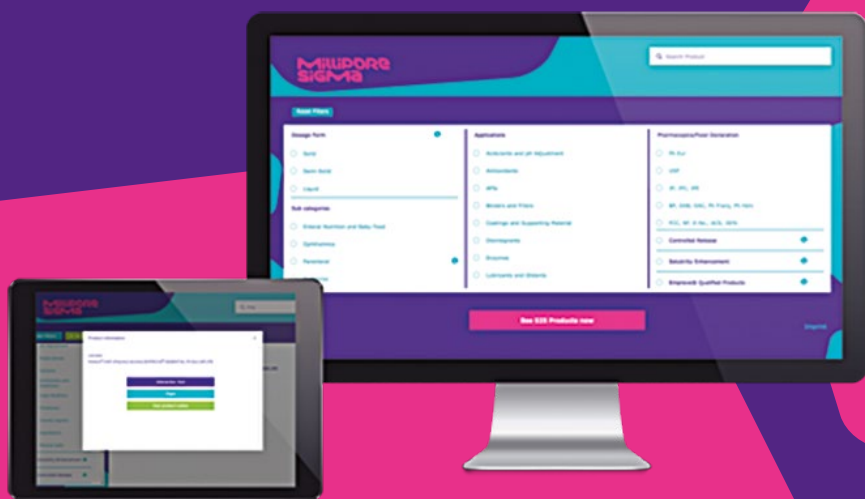


ordering information

Cat. No.	Product	Pack size
1.00894.1000	Sucralose powder EMPROVE® ESSENTIAL Ph Eur, ChP, NF, JPE	1 kg
1.00894.9010		10 kg
1.00895.1000	Sucralose granular EMPROVE® ESSENTIAL Ph Eur, NF, JPE	1 kg
1.00895.9010		10 kg

Cat. No.	Product	Pack size
1.07071.0250	Neotame EMPROVE® ESSENTIAL NF	250 g
1.07071.1000		1 kg

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