EXPERIENCE VERSATILITY.

One polymer. Many solutions.

From controlled release to bioavailability enhancement, tailor your formulation with our portfolio of polyvinyl alcohol excipients.

More Information

We provide information and advice to our customers on application technologies and regulatory matters to the best of our knowledge and ability, but without obligation or liability. Existing laws and regulations are to be observed in all cases by our customers. This also applies in respect to any rights of third parties. Our information and advice do not relieve our customers of their own responsibility for checking the suitability of our products for the envisaged purpose.

For additional information, please visit MerckMillipore.com
To place an order or receive technical assistance, please visit MerckMillipore.com/contactPS

The life science business of Merck operates as MilliporeSigma in the U.S. and Canada.

SAFC®

Pharma & Biopharma Raw Material Solutions

POLYVINYL ALCOHOL

Take your drug to the next level: One polymer. Versatile applications.

Whether you're working on solid, liquid or semi-solid formulations, there are specific issues to consider and challenging hurdles to overcome before you can successfully launch your final drug product.

We are committed to understanding your requirements and enabling you with products and support to help you achieve your goals. Our wide range of pharmaceutical polyvinyl alcohols (PVAs) includes PVA grades of different viscosities, molecular weights and hydrolysis grades as well as PVA-based excipients – so whatever your application, we have just the right product.

PVA-based **Parteck® SRP 80** excipient is specifically designed for solid oral sustained release matrix formulations, while **PVA-based Parteck® MXP** excipient aims to enhance the solubility of poorly water-soluble active pharmaceutical ingredients (APIs) in hot melt extrusion processes. The Parteck® range comprises functional excipients with unique particle structures designed to tackle critical challenges in pharmaceutical formulation and manufacture. Our PVA product range is part of our **EMPROVE®** Program, which is dedicated to helping you satisfy today's ever-increasing risk assessment requirements.

WHICH FUNCTION DO YOU NEED?

LIQUID

SEMI-SOLID

SOLID

Emprove® Program | **Packaging & Ordering** | **PVA Portfolio** | **PVA Safety**

GENERAL FORMULATION WITH PVA

Overview of the different PVA types and their application areas

PVA can be used for a broad range of applications. Depending on the physicochemical properties of the individual PVAs, different grades might be better suited to different applications. The table below is intended as a guideline, highlighting typical application fields.

	LIQUID		SEMI-SOLID		SOLID			
Grade	Thickener / Viscosity enhancer	Solubilizer / Solubility enhancement	Hydrogel-forming	Sustained-release matrix	Granulation binder	Film-forming agent	Solubility enhancement	Controlled release
PVA 4-88	●	●	●		●	●		
PVA 5-88	●	●			●	●		
PVA 8-88	●	●			●	●		
PVA 18-88	●	●	●					
PVA 26-88	●	●	●					
PVA 28-99		●		●				
PVA 40-88	●	●		●				
Parteck® SRP 80 excipient								●
Parteck® MXP excipient							●	

Emprove® Program Packaging & Ordering

LIQUID

In liquid applications, common challenges include viscosity enhancement to stabilize the formulation or to improve contact time, e.g. with the cornea, solubilization of the API or other components of your formulation, and finding raw materials of the right quality for your application – just to name a few.

Our experts can provide raw material solutions in a range of formats and sizes to fit your quality, performance and safety requirements and help you minimize risk. Our PVA complies with the major pharmacopoeias and we have enhanced our product specifications to surpass compendial requirements, for improved patient safety and excellent tolerability. Our **Emprove® Program** supports the compliance of your pharmaceutical products and supports you throughout the different stages of operations.

WHICH PVA GRADE DO YOU NEED?

THICKENER / VISCOSITY ENHANCER

One of the most common applications of PVA is its usage as a viscosity enhancer in liquid formulations.

More Information

SOLUBILIZER / SOLUBILITY ENHANCEMENT

Even small amounts of PVA may have an effect on API solubility.

More Information

How do I bring PVA into solution?

PREPARATION OF PVA SOLUTIONS

Many applications require the preparation of a PVA solution. We recommend using elevated temperatures during the preparation process, as this increases the dissolution speed of the PVA. The dissolution time varies depending on the molecular weight and/or hydrolysis grade as well as the amount of PVA to be dissolved, and it may even require stirring overnight.

We recommend preparing the solution directly before use.

add PVA to **cold** water while **stirring**

heat up to **90 – 95 °C** while **continuously stirring**, keep at temperature until dissolved

add water if necessary, **cool** to desired temperature while **stirring**

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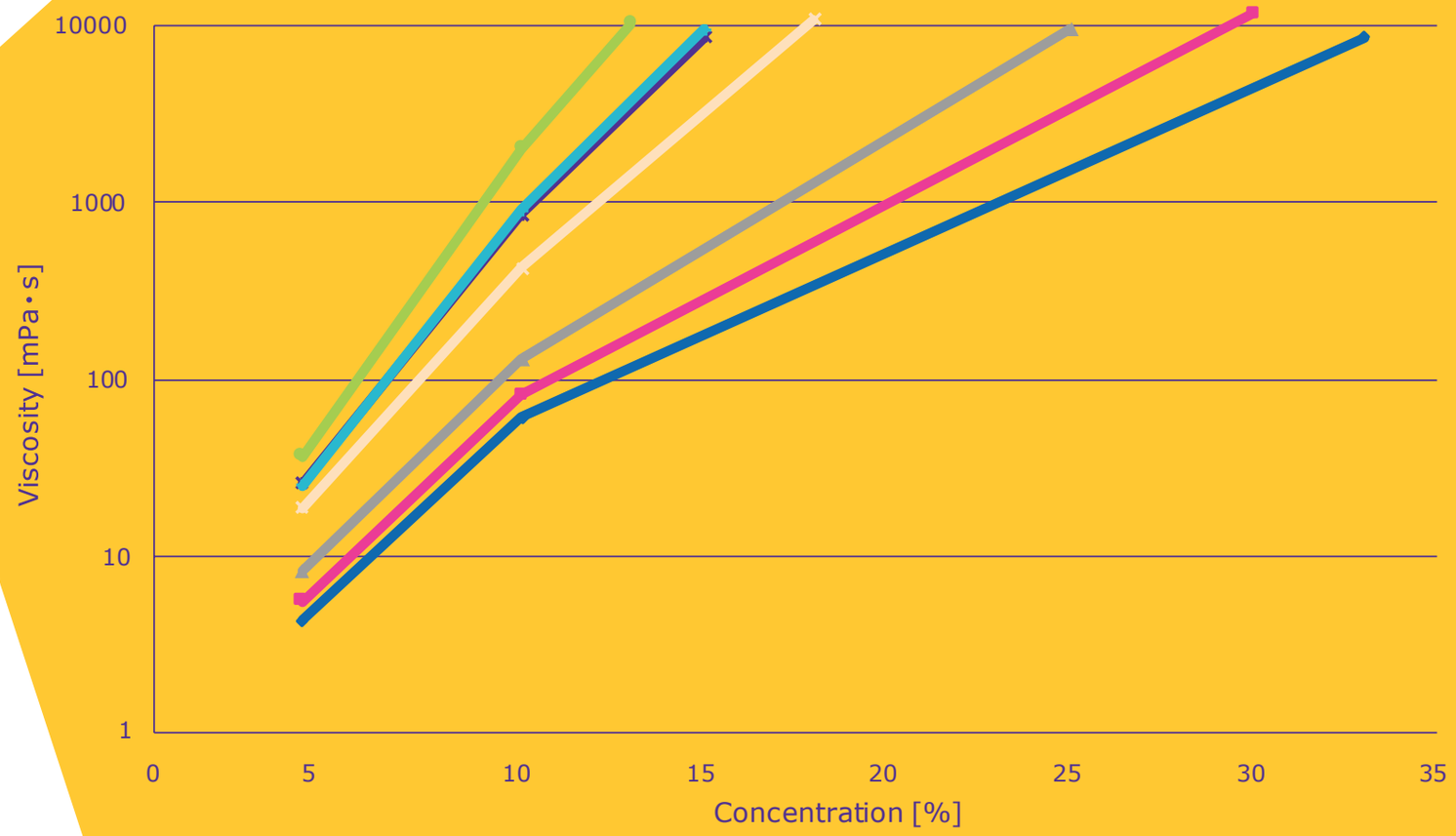
THICKENER / VISCOSITY ENHANCER

One of the most common applications of PVA is its use as a **viscosity enhancer in liquid formulations.** In ophthalmic formulations, it supports a prolonged contact time of the medication, helping to improve corneal drug absorption and reduce precorneal drug loss.

Especially in artificial tears, the **moisturizing effect** of PVA is also important. For suspension formulations, PVA serves as a stabilizer, as it reduces particle sedimentation by enhancing the viscosity of the continuous liquid phase.

INFLUENCE OF CONCENTRATION ON THE VISCOSITY OF A PVA SOLUTION



The viscosity of PVA solutions increases with increasing PVA concentration (measured using a spindle viscometer at concentrations of 4%, 10% and at the respective maximum solubility concentration*; all w/w)

* Maximum solubility was defined as the concentration at which the mixture exceeded a viscosity of 10,000 mPa·s due to limited processability at this and higher viscosities.

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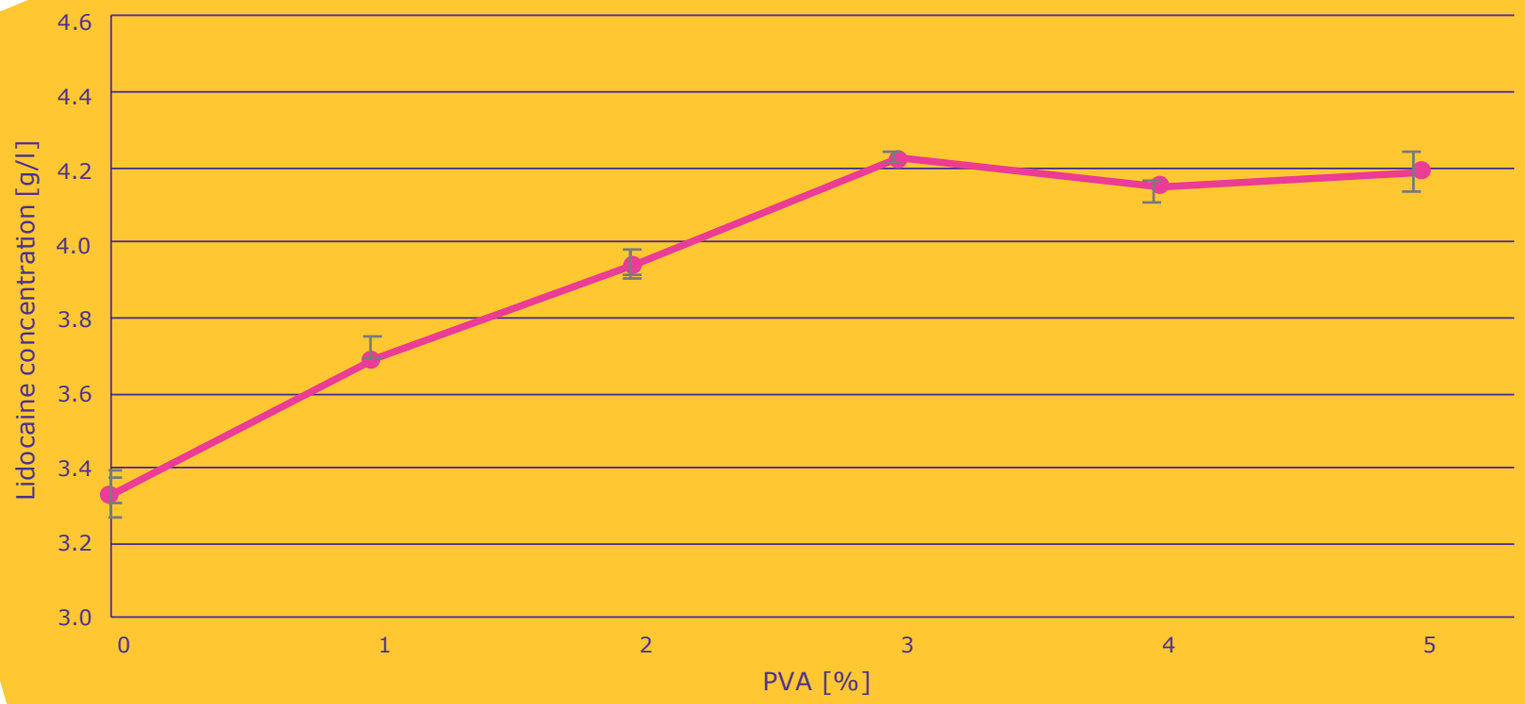
SOLUBILIZER / SOLUBILITY ENHANCEMENT

Even small amounts of PVA can affect API solubility, helping to improve formulation stability and potentially enhancing the bioavailability of the API in the body.

EFFECT OF PVA CONCENTRATION ON API SOLUBILITY



An experiment carried out with lidocaine as the model API under sink conditions using water as a solvent demonstrated the above effect. Concentrations of equal to or greater than 3% PVA 18-88 enhanced the solubility of the model API by a factor of 1.2, confirming that PVA may indeed be used to solubilize APIs.

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SEMI-SOLID

Finding the right excipient that matches your needs as well as regulatory demands can be a complicated challenge in semi-solid formulation. This is why we offer a broad **range of PVAs with different viscosities, molecular weights and hydrolysis grades.** PVA is a very versatile excipient that may be used for a variety of semi-solid applications. It is typically used to improve API solubility or as a viscosity enhancer. Current applications include topical creams and gels as well as transdermal patches. To support improved patient safety and good tolerability, we have also included additional specifications that surpass compendial requirements.

Our Emprove® Program helps you to simplify regulatory processes and ensures the compliance of your pharmaceutical products.

WHICH PVA GRADE DO YOU NEED?

SUSTAINED-RELEASE MATRIX

PVA may be utilized for controlled drug delivery, e.g. in transdermal formulations such as patches.

More Information

HYDROGEL FORMING

PVA is well suited for usage in topical creams and gels.

More Information

HYDROGEL FORMING

PVA is well suited for use in topical formulations such as **creams and gels**. While other polymers are known for their incompatibilities with multiple APIs or other formulation ingredients, PVA shows high inertness and may thus be broadly applied.

We offer a **broad range of PVAs** from which you can choose the ideal PVA grade for your application. You can even combine it with other polymers, allowing you to tailor your formulation to your needs.

Emprove® Program **Packaging & Ordering**

SUSTAINED-RELEASE MATRIX

Transdermal patches offer an excellent opportunity for the controlled delivery of an API through the skin over time periods of several days up to one week. Especially in long-term applications, this may help improve patient convenience and compliance. PVA has the potential to be a major component and matrix material of transdermal formulations such as patches. You can use its solubilizing effect to improve the API's solubility in the patch matrix, making higher drug loads possible.

SOLID

One of the most common applications of PVA today is in coatings for solid oral formulations, typically single-dose tablets. However, its potential application areas extend well beyond that. Whether you are formulating a sustained release solid oral formulation, in need of solubility enhancement or looking for the right product for your granulation or coating method, using PVA might help you formulate a successful drug product. Our broad portfolio of PVAs with a wide range of viscosities, molecular weights and hydrolysis grades offers you the possibility to choose just the right product for your application. Additionally, we have developed the PVA-based **Parteck® SRP 80** excipient for solid oral sustained release formulations and the **Parteck® MXP** excipient for solubility enhancement via hot melt extrusion processes.

Our high-quality products are supported by our regulatory expertise and the **Emprove® Program**, helping you simplify your supplier qualification and accelerate processes, thereby reducing the total costs of ownership.

FILM-FORMING AGENT

PVA may be used as the film-forming component of coatings. It is also very well suited as a basic polymer for orodispersible films (ODFs).

More Information

CONTROLLED RELEASE

Controlled release kinetics make it possible to tailor a formulation to specific therapeutical needs.

More Information

WHICH PVA GRADE DO YOU NEED?

SOLUBILITY ENHANCEMENT

The key factors for absorption are solubility and permeability. Improving the solubility of an API may help to achieve an enhanced bioavailability in the body.

More Information

GRANULATION BINDER

PVA can be used as a binder during the granulation process.

More Information

Emprove® Program **Packaging & Ordering** **PVA Safety**

GRANULATION BINDER

Granulation is a process of particle enlargement by agglomeration. While the granules may also be used directly, e.g. as orally disintegrating or water dispersible granules, granulation typically serves as an intermediate step, improving undesirable powder characteristics and achieving the properties required for subsequent processes such as tablet compression.

PVA can be **used as a binder in wet granulation processes**. Within these processes, it helps to convert fine powders into free-flowing, dust-free agglomerates effectively, thus improving handling properties, compressibility and API content uniformity.

Emprove® Program **Packaging & Ordering**

FILM-FORMING AGENT

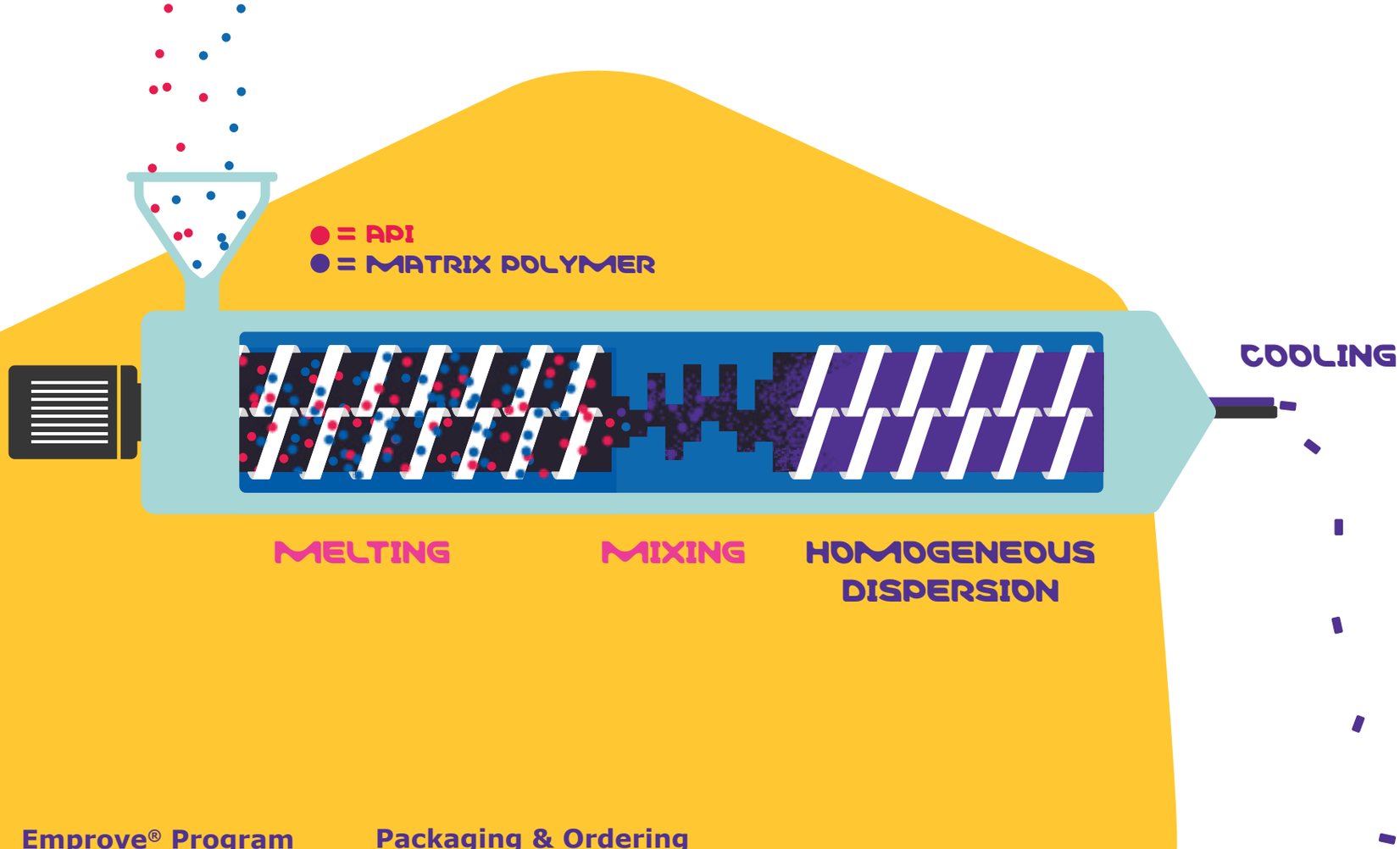
PVA is a film-forming, polymeric material with good moisture vapor barrier and oxygen barrier properties. This makes PVA well suited for the coating of solid oral formulations which contain moisture- and/or oxidation-sensitive APIs. PVA is also well suited for coating **orally dispersible tablets (ODTs)** manufactured using **Parteck® ODT** excipient.

In addition to its broad application in coatings, PVA is frequently used as a basic polymer for the production of pharmaceutical films – such as for transdermal drug delivery applications or orodispersible films (ODFs) – on account of its high tensile strength. ODFs are defined as thin sheets based on polymers, which are placed into the oral cavity and disperse rapidly to achieve a faster release of the drug. They can be produced using a continuous film casting process or by hot melt extrusion – a process of heating and mixing that does not require the use of a solvent.

Emprove® Program **Packaging & Ordering**

SOLUBILITY ENHANCEMENT

The solubility and permeability of an API for its absorption from the gastrointestinal tract into the body and its availability at the site of action. Overcoming solubility limitations of APIs is critical, especially since approximately 60% of drugs in the pharmaceutical pipeline have been reported to have solubility issues. There are numerous ways to overcome poor solubility, but not every approach is suitable for each API and formulation. Due to its functionality as a solubilizer, PVA may be used to enhance the solubility of poorly water-soluble APIs. To support you in solving these challenges, we have developed a new, PVA-based excipient for hot melt extrusion processes that is applicable for a broad range of APIs: **Parteck® MXP**. As a matrix polymer in amorphous solid dispersions, for instance, it allows for high, stable drug loads.



PARTECK® MXP EXCIPIENT

More Information

CONTROLLED RELEASE

Controlled release formulations offer the option of tailoring the API's release profile to therapeutic needs in order to optimize the dosing scheme and improve patient compliance.

Sustained release formulations play a major role in the pharmaceutical segment and are most suitable for long-term therapies. PVA-based **Parteck® SRP 80** excipient was developed specifically for solid oral sustained release matrix formulations and provides consistent, sustained drug delivery over long release periods. It is optimized for continuous release behavior over a broad range of compression forces and tablet hardnesses, showing good reproducibility both with respect to its release profile and its manufacturability by direct compression. It is also not susceptible to pH- or alcohol-induced dose dumping, a critical factor when it comes to high-dose API reservoir formulations.

PARTECK® SRP 80 EXCIPIENT

More Information

Emprove® Program **Packaging & Ordering**

MIX. MELT. PERFORM.

Enhancing API solubility with Parteck® MXP excipient

Our **Parteck® MXP** excipient is a new, PVA-based excipient specifically developed for hot melt extrusion processes. It is suitable for a broad range of APIs, and allows for stable and high drug loads.

MAIN BENEFITS

- **Enhanced solubility**
  100% (nine of nine) model APIs assessed for Parteck® MXP show significant solubility increases.
- **Stable, high drug load**
  78% (seven of nine) assessed model APIs achieve a 30% minimum drug load that is stable under various conditions.
- **High thermostability and broad API range**
  Maintains stability at temperatures above 200°C, making it well suited to broaden the API application range for hot melt extrusion.
- **Flexible release kinetics**
  A variety of final oral dosage forms demonstrating immediate or sustained release, formulated using the same extrudates.
- **Ease of use**
  For all APIs assessed, physical blends and extrudates of the API and polymer were homogeneous.

SOLUBILITY ENHANCEMENT AND DRUG LOADS OF SELECTED APIS AFTER EXTRUSION WITH PARTECK® MXP EXCIPIENT

API	T_m of API [°C]	API Load Achieved* [%]	Solubility Enhancement (max.)
Ibuprofen**	78	30	2 x
Cinnarizine	118 – 122	< 20	10 x
Indomethacin	151	50	3 x
Ketoconazole	146	35	17 x
Naproxen	152	30	4 x
Atorvastatin	159 – 160	55	154 x
Itraconazole	166.5	30	80 x
Carbamazepine	204	30	2 x
Telmisartan**	260	15	35 x

* Maximum API load is defined as the maximum amount of API present in an amorphous state in the extrudate observed for experimental data.
**Plasticizer is required to make the extrusion feasible or easier.

TAKE CONTROL OF SUSTAINED DRUG RELEASE.

Solid oral formulations with Parteck® SRP 80 excipient

Our PVA-based **Parteck® SRP 80** excipient is optimized for solid oral sustained release formulations. It features highly functional particle properties, making it suitable for efficient development and manufacture using direct compression.

MAIN BENEFITS

- **Consistent API release over several hours**
  Allows constant release behavior over a broad range of compression forces and tablet hardnesses.
- **Convenient, cost-efficient manufacturing**
  Suitable for direct compression processes, featuring both high compressibility and low ejection forces.
- **Reliable product performance**
  Fully synthetic origin means decreased variability in quality and performance, facilitating QbD and validation processes.
- **Reduced risk of dose dumping**
  Due to reliable alcohol resistance and constant API release over a broad pH range, dose dumping potential is significantly reduced.

GENERAL FORMULATION WITH PARTECK® SRP 80 EXCIPIENT

Suitable for direct compression

	Amount [%; w/w]
Active ingredient	5 – 50
Parteck® SRP 80 excipient	20 – 70*
Binder, e.g. Parteck® M excipient or MCC	0 – 60
Silicon dioxide, highly dispersed	0.25 – 1.50
Parteck® LUB MST excipient (magnesium stearate)	0.25 – 0.75
TOTAL	100

* The Parteck® SRP 80 excipient content of the formulation should not be less than 20% (w/w), otherwise gel forming will be inhomogeneous.

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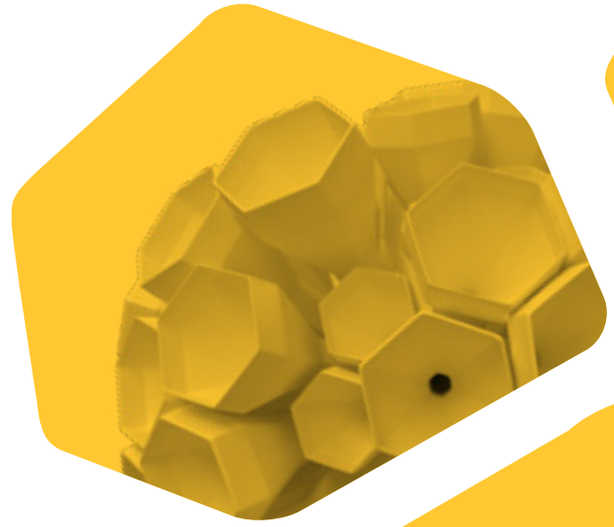
YOUR FAST TRACK THROUGH REGULATORY CHALLENGES.

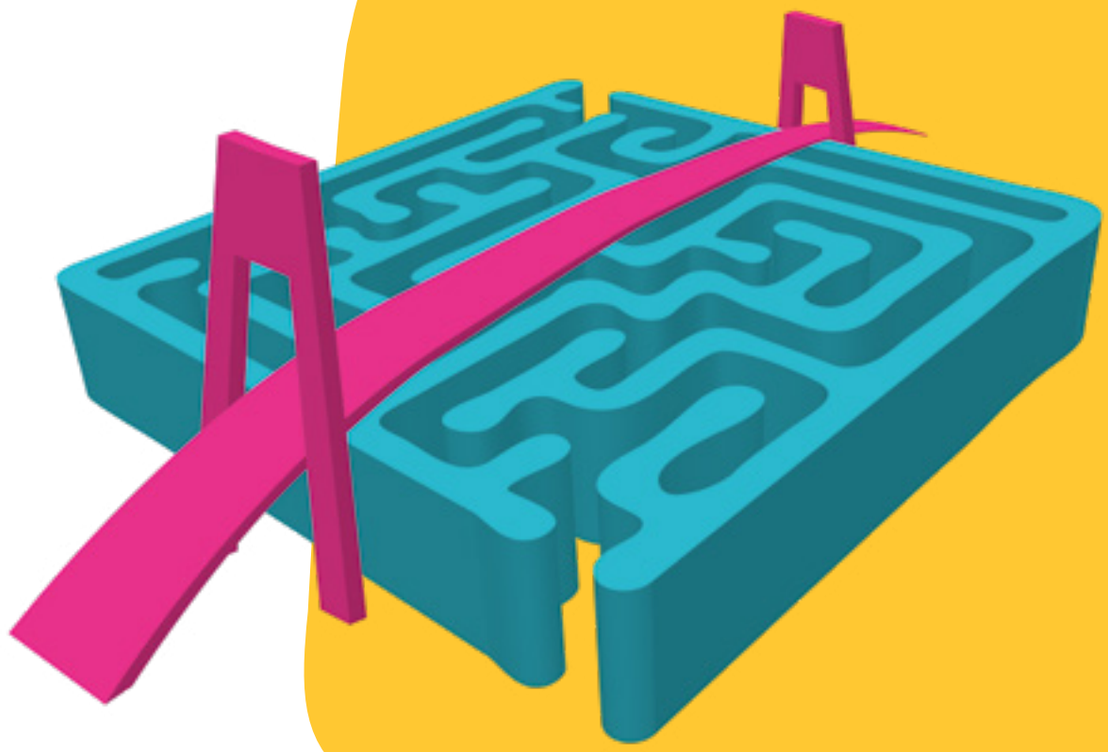
The Emprove® Program.



Ensuring the compliance of your pharmaceutical and biopharmaceutical products involves the compilation of a vast amount of data, which can be time- and resource-intensive. In order to facilitate and accelerate this process, we developed our **Emprove® Program**. It includes 400 pharma raw and starting materials and a selection of filtration and single-use products. Each product in the portfolio is complemented with three different types of dossiers supporting you throughout the different stages of your operations: qualification, risk assessment, and process optimization – all designed to help you speed your way through the regulatory maze.

Find out more: MerckMillipore.com/emprove

The Emprove® Suite provides 24/7 access to all Emprove® dossiers online. For more information on how to subscribe, visit: MerckMillipore.com/emprovesuite



PVA SAFETY

PVA has long been widely used in different applications in both food and pharma. As such, there is sound scientific evidence for its safety:

- A GRAS notice on the use of PVA in coatings (solid oral) has been filed.
- Statements on PVA toxicity, toxicity data, and guidelines on safe levels of intake have been published by the JECFA (Joint FAO/WHO Expert Committee on Food Additives), EFSA (European Food Safety Authority) and CIR (Cosmetic Ingredient Review).[1,2,3]
- Other publications on PVA toxicity are also available.[4,5,6]

We understand that the quality of a material is critical, especially in highly regulated application fields like ophthalmics. This is why we include additional specifications to support tolerability and patient safety:

- **Crotonaldehyde ≤ 10ppm**
  Crotonaldehyde is a known irritant to the skin and eye and also classified as a potential carcinogen.
- **Aerobic bacteria: ≤ 1·102 CFU/g**
  For formulations such as hydrogels that have a high water content, microbial contamination is a known critical risk to formulation stability and patient safety.

Emprove® Program **Packaging & Ordering**

[1] Sixty-first meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA), Polyvinyl alcohol, in Safety evaluation of certain food additives and contaminants, World Health Organization, Editor. 2004: Geneva. p. 137-153.

[2] European Food Safety Authority, Opinion of the Scientific Panel on Food Additives, Flavourings, Processing Aids and Materials in Contact with Food on a request from the Commission related to the use of polyvinyl alcohol as a coating agent for food supplements; Question number EFSA-Q-2005-017. The EFSA Journal, 2005. 294: p. 1-15.

[3] Nair, B. and Cosmetic Ingredient Review Expert Panel, Final Report On the Safety Assessment of Polyvinyl Alcohol. International Journal of Toxicology, 1998. 17(5 suppl): p. 67-92.

[4] DeMerlis, C.C. and D.R. Schoneker, Review of the oral toxicity of polyvinyl alcohol (PVA). Food and Chemical Toxicology, 2003. 41(3): p. 319-326.

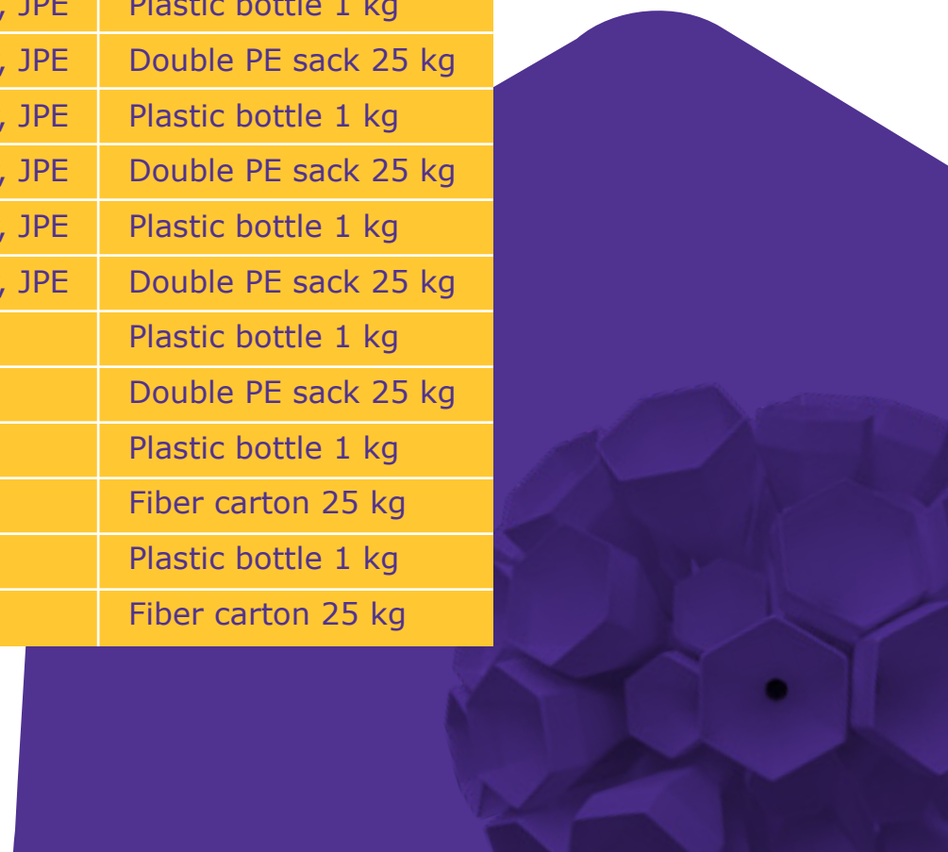
[5] Kelly, C.M., et al., Subchronic toxicity study in rats and genotoxicity tests with polyvinyl alcohol. Food and Chemical Toxicology, 2003. 41(5): p. 719-727.

[6] Rodwell, D.E., et al., Effects of polyvinyl alcohol administered in the diet to rats on fertility, early embryonic development, growth and development. Food and Chemical Toxicology, 2003. 41(5): p. 729-737.

PACKAGING AND ORDERING INFORMATION

Our PVA is available in grades 4-88, 5-88, 8-88, 18-88, 26-88, 40-88 and 28-99 as granules (with the first digit characterizing the average viscosity in mPa·s and the second digit characterizing the average hydrolysis grade in %). We also offer PVA-based Parteck® MXP excipient and Parteck® SRP 80 excipient for specific applications.

CAT. NO.	PRODUCT	PACK SIZE
1.41350.1000	Polyvinyl alcohol 4–88 suitable for use as excipient EMPROVE® exp Ph Eur, USP, JPE	Plastic bottle 1 kg
1.41350.9029	Polyvinyl alcohol 4–88 suitable for use as excipient EMPROVE® exp Ph Eur, USP, JPE	Double PE sack 25 kg
1.41354.1000	Polyvinyl alcohol 5–88 suitable for use as excipient EMPROVE® exp Ph Eur, USP, JPE	Plastic bottle 1 kg
1.41354.9029	Polyvinyl alcohol 5–88 suitable for use as excipient EMPROVE® exp Ph Eur, USP, JPE	Double PE sack 25 kg
1.41351.1000	Polyvinyl alcohol 8–88 suitable for use as excipient EMPROVE® exp Ph Eur, USP, JPE	Plastic bottle 1 kg
1.41351.9029	Polyvinyl alcohol 8–88 suitable for use as excipient EMPROVE® exp Ph Eur, USP, JPE	Double PE sack 25 kg
1.41355.1000	Polyvinyl alcohol 18–88 suitable for use as excipient EMPROVE® exp Ph Eur, USP, JPE	Plastic bottle 1 kg
1.41355.9029	Polyvinyl alcohol 18–88 suitable for use as excipient EMPROVE® exp Ph Eur, USP, JPE	Double PE sack 25 kg
1.41352.1000	Polyvinyl alcohol 26–88 suitable for use as excipient EMPROVE® exp Ph Eur, USP, JPE	Plastic bottle 1 kg
1.41352.9029	Polyvinyl alcohol 26–88 suitable for use as excipient EMPROVE® exp Ph Eur, USP, JPE	Double PE sack 25 kg
1.41353.1000	Polyvinyl alcohol 40–88 suitable for use as excipient EMPROVE® exp Ph Eur, USP, JPE	Plastic bottle 1 kg
1.41353.9029	Polyvinyl alcohol 40–88 suitable for use as excipient EMPROVE® exp Ph Eur, USP, JPE	Double PE sack 25 kg
1.41356.1000	Polyvinyl alcohol 28–99 suitable for use as excipient EMPROVE® exp Ph Eur, JPE	Plastic bottle 1 kg
1.41356.9029	Polyvinyl alcohol 28–99 suitable for use as excipient EMPROVE® exp Ph Eur, JPE	Double PE sack 25 kg
1.41464.1000	Parteck® MXP (Polyvinyl alcohol) EMPROVE® ESSENTIAL Ph Eur, JPE, USP	Plastic bottle 1 kg
1.41464.9025	Parteck® MXP (Polyvinyl alcohol) EMPROVE® ESSENTIAL Ph Eur, JPE, USP	Fiber carton 25 kg
1.41439.1000	Parteck® SRP 80 (Polyvinyl alcohol) EMPROVE® ESSENTIAL Ph Eur, USP, JPE	Plastic bottle 1 kg
1.41439.9025	Parteck® SRP 80 (Polyvinyl alcohol) EMPROVE® ESSENTIAL Ph Eur, USP, JPE	Fiber carton 25 kg



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