Tolerase® G

The only enzyme that effectively breaks down gluten

DSM
BRIGHT SCIENCE. BRIGHTER LIVING.

Tolerase® G, a *proline-specific endopeptidase* or *prolyl oligopeptidase*, is the only dietary enzyme scientifically proven to help break down gluten in the stomach.[1] It gives gluten sensitive consumers following a gluten-free diet more freedom, as they no longer need to worry about accidentally consuming the residual gluten 'hidden' in many foods.

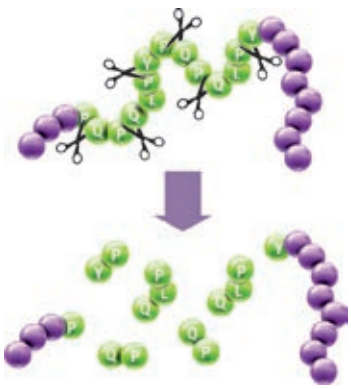
What is gluten?

Found in wheat, barley and rye, gluten is a protein complex that is rich in an amino acid called proline. The human body cannot break down proline-rich proteins efficiently and this may be why up to 13% of the world's population is sensitive to dietary gluten.[2]

Gluten is well-known for giving bread its shape, strength and texture. It is also in a surprisingly wide range of other foods, including confectionery products, processed meats and sauces.

'Hidden' gluten

While 1 in 4 global consumers try to avoid eating foods that contain gluten, this can be almost impossible when dining away from home.[3] Studies show that, even when adopting a gluten-free diet, unintentional gluten intake can range from 200 to 3,000 mg/day depending on how strictly the diet is followed.[4,5,6]



Tolerase® G cleaves peptides after a proline residue

Worry-free dining

Marketed at the growing number of gluten-sensitive individuals, Tolerase® G gives consumers the peace of mind to follow a gluten-free diet with more confidence:

- ✓ Scientifically proven to be more effective than any other commercially available supplement.
- ✓ Available in convenient on-the-go formats.

In short:

Backed by regulatory bodies in the United States, European Union (EU), Canada, Australia and New Zealand, Tolerase® G is an IP-protected and uniquely efficacious enzyme for gluten digestion in the stomach:

- ✓ Only enzyme that is scientifically proven to effectively digest proline-rich gluten epitope, in a gastrointestinal model and in humans.[8,9,10,11]
- ✓ Stable and active under acidic stomach conditions.
- ✓ Resistant to digestion by pepsin.
- ✓ Micro-granulated form with excellent flowability and compressibility for use in capsules and tablets.
- ✓ Manufactured in the EU.

Tolerase® G

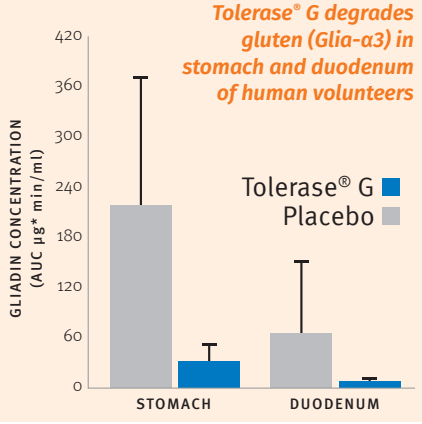
The only enzyme that effectively help break down residual gluten

Scientifically proven efficacy

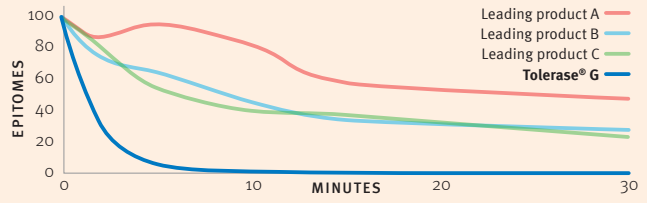
Tolerase® G is the only enzyme that is scientifically proven to effectively break down gluten:[8,9,10,11]

- Tolerase® G is stable and active under gastric conditions.
- Tolerase® G specifically degrades the immunogenic parts within gluten proteins. Other enzymes that are currently used in commercially available dietary supplements claiming to degrade gluten are much less effective.
- Gluten-sensitive T-cells still react to gluten degraded by current commercial gluten-digesting supplements, but not to gluten degraded with Tolerase® G.
- Tolerase® G degrades gluten in an *in vitro* system that mimics the human gastro-intestinal tract and in the human gastrointestinal tract.
- Tolerase® G digests gluten in the stomach of human volunteers before they enter the small intestine

Tolerase® G degrades gluten (Glia-α3) in stomach and duodenum of human volunteers



Currently available gluten-degrading enzyme supplements are not very effective[12]



Proven safety

Tolerase® G is safe for the general population, as tested in regulatory toxicity studies and shown in available clinical studies.[11]

For more information on Tolerase® G,
visit **www.dsm.com/human-nutrition** or e-mail **info.dnp@dsm.com**

REFERENCES: 1 J. Konig at al, 'Aspergillus niger-derived enzyme AN-PEP efficiently degrades gluten in the stomach of gluten-sensitive subjects', Clinical Nutrition, 2016, vol 35 no 1, pS152. **2** Various sources, all available upon request. **3** Nielsen, 'What's in our food and on our minds: ingredient and dining out trends around the world', August 2016 [report]. **4** F. van Overbeek et al.. 'The daily gluten intake in relatives of patients with coeliac disease compared with that of the general Dutch population', Eur J Gastroenterol Hepatol, 1997, vol. 9, no. 11, p1097-9. **5** E. Hopman et al., 'Nutritional management of the gluten-free diet in young people with celiac disease in The Netherlands', J Pediatr Gastroenterol Nutr, 2006, vol. 43 no. 1, p102-8. **6** E. Hopman et al., 'Gluten tolerance in adult patients with celiac disease 20 years after diagnosis?', Eur J Gastroenterol Hepatol, 2008, vol 20 no 5, p423-9. **7** The University of Kentucky, 'The gluten-free choice: is it for me?' [report]. **8** D. Stepniak et al., Highly efficient gluten degradation with a newly identified prolyl endoprotease: implications for celiac disease', Am J Physiol Gastrointest Liver Physiol', 2006, vol 291 no 4:G621-9. **9** C. Mitea et al., 'Efficient degradation of gluten by a prolyl endoprotease in a gastrointestinal model: implications for coeliac disease', Gut, 2008, vol 57 no 1, p25-32. **10** G. Janssen, 'Ineffective degradation of immunogenic gluten epitopes by currently available digestive enzyme supplements', PLoS One, 2015, vol 10, no 6. **11** B. Salden et al., 'Randomised clinical study: Aspergillus niger-derived enzyme digests gluten in the stomach of healthy volunteers', Aliment Pharmacol Ther, 2015, vol 42 no 3, p273-85. König J, et al. Randomized clinical trial: Effective gluten degradation by Aspergillus niger-derived enzyme in a complex meal setting. Sci Rep. 2017 Oct 12;7(1):13100.

Claims and labelling

Tolerase® G is available as:

- FDA-notified New Dietary Ingredient in the US.
- Listed Natural Health Product Ingredient in Canada.
- Authorized Novel Food in the EU.
- Listed Complementary Medicine Ingredient in Australia.
- Listed permitted substance in New Zealand.

The list of available and approved claims varies between countries or regions. Please consult your local DSM team for the best possible positioning of your product.

Tolerase® G is not designed to replace a gluten-free diet. Therefore, consumer products made with Tolerase® G should not be presented as replacing a gluten-free diet and may need to carry the disclaimer:

"Tolerase® G is not suitable to replace a gluten-free diet. Tolerase® G is not suitable to treat or prevent celiac disease."

Tolerase® G is not intended for consumption by infants and young children (less than 36 months old). In the EU, the Novel Food authorization targets its use in food supplements for the general adult population.

Composition

Tolerase® G – or *Aspergillus niger*-prolyl endopetidase – is a prolyl endopeptidase from the food-grade fungus *Aspergillus niger*. In the EU, it is labelled as prolyl oligopetidase with a minimum activity of 580,000 PPI/g of product (PPI: Protease Picomol International).

Applications

- Tolerase® G is a micro-granulate with excellent flowability and compressibility for use in tablets and capsules.
- Tolerase® G has an off-white to orange-yellowish color, high solubility and a bland taste.
- Tolerase® G has a shelf life of 24 months at ≤ 15 °C.

Dosage

For best efficacy, gluten sensitive consumers who enjoy a gluten-free diet should take a product that contains Tolerase® G at the start of a meal. The dose rate is dependent on the sensitivity of gluten intolerance and the size of meal consumed. DSM experts remain at your disposal to advise on the most appropriate dose and the consumer intake.

Assuming an average accidental gluten exposure of about 0.5 g of gluten per day, about 80 000 PPI Tolerase® G per day spread over 3 meals would be required; i.e. 26 666 PPI with each meal, 3 times daily. This dose can be increased to 2 tablets per meal depending on the uncertainty of hidden gluten content in the meal.

Estimated gluten intake and Tolerase® G dosage/dosing:

80 000 PPI (26 666 PPI per meal) for 0.5 g hidden gluten per day

160 000 PPI (53 333 PPI per meal) for 1 g hidden gluten per day

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PRODUCTS CUSTOMIZED SOLUTIONS EXPERT SERVICES

DSM is more than an ingredients provider, we are a reliable, end-to-end, innovative, purpose-led partner powered by experts to deliver science-backed nutrition and health products and quality customized solutions.