



Engystol® Detail Aid Discussion Guide



-Heel

**FIGHT COLDS.
HELP YOUR
PATIENTS
ENJOY WINTER**

Give your patient's immune system a natural boost with

Engystol®

-Heel

Intended audience:

Professional: Pharmacists, primary care physicians, pediatricians and ENT specialists.

Tone and style:

This detail aid is designed to deliver the key points of the core Engystol® story in 2 minutes or less. There is also a tabbed section which allows discussion of additional aspects for those HCPs who are interested.

Front cover:

Key points:

- Winter brings a peak in patients suffering from colds, which can make it feel like a miserable season for many people.
- Engystol® is a natural way to boost your patient's immune system and fight off viruses to help your patients get back to enjoying their winter.

Probe:

- “Are you aware of Engystol® and its benefits?” – if yes, present the new pre-clinical data by Wronski et al. (p3 - and supplementary p9 if HCP is interested to know more) followed by a trial close:
- “So, would you prescribe/recommend Engystol® for the next few patients with colds that you see? I’ll come back in a few weeks and see how things have gone. When would suit you best?”



Taken early, **Engystol®** fights the common cold effectively and naturally.¹

Engystol® works naturally to stimulate your patient's immune system²⁻⁵ and to shorten the duration of symptoms,¹ helping them to enjoy an earlier recovery from colds this winter.⁶

Page two:

Key points:

- If your patients take Engystol® early, it can help them recover earlier from colds by stimulating their immune system.

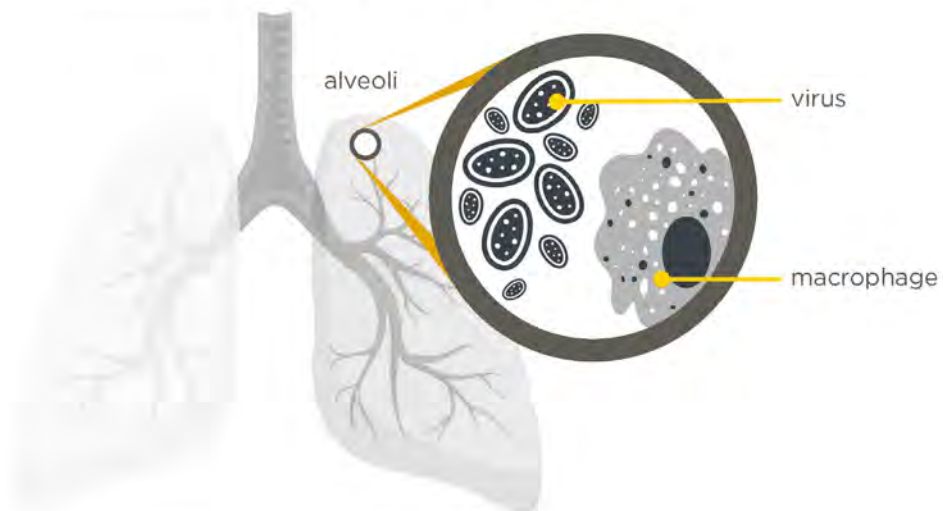
Discussion points:

This allows the opening of a discussion into the fact that Engystol®, a natural product, stimulates patients' immune systems to help them recover earlier from colds. This effect on the immune system underpins the beneficial effects seen on cold symptoms. It is expanded on, on the next page.

NEW
DATA!

Engystol® strengthens and supports the immune system during viral infection²⁻⁵

- Engystol® treatment markedly enhances the phagocytic capacity of alveolar macrophages following RSV* infection², thereby:
 - Significantly reducing early bronchoalveolar neutrophil and lymphocyte infiltration, and
 - Significantly reducing the release of inflammatory cytokines²
- **This points toward earlier resolution of the acute inflammatory response and associated symptoms²**



*RSV= Respiratory Syncytial Virus

Page three:

Key points:

- Engystol® strengthens and supports the immune system during viral infection. This points toward earlier resolution of the acute inflammatory response and associated symptoms, and thus toward earlier recovery.

Discussion points:

These are new data supporting the main claim for Engystol®, so for HCPs already familiar with Engystol®, this page should be presented first. The rest of the sales aid can be used as a reminder if needed.

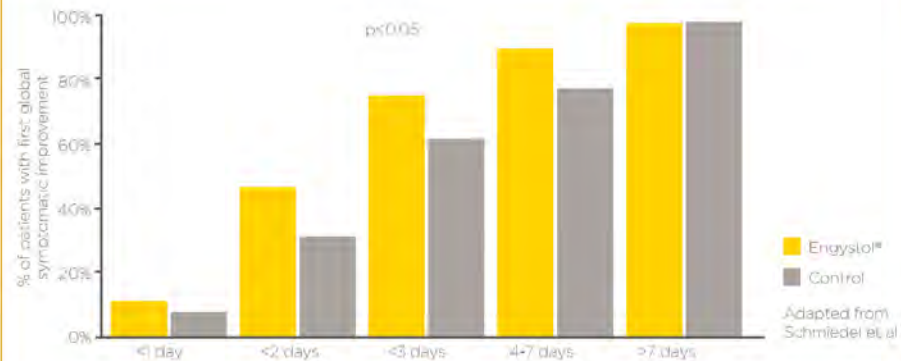
This page builds on the introduction of the immune system effects seen previously. It acts as a proof point for the following page, in which we look at earlier symptom improvement.

The specific cell activity can be explored further if the HCP is interested, but it is optional. Further information on this is available in the tabbed section toward the back of the sales aid.

Engystol[®] rapidly improves symptoms of the common cold¹

- >75% of patients reported significant relief of symptoms within 3 days¹
- Significantly more patients using Engystol[®] reported improvement within 3 days (77.1%) compared with the control group (61.7%)¹

Effect of treatment with Engystol[®] tablets on symptomatic improvement over time, compared with conventional OTC treatments (control)¹



Page four:

Key points:

- Over 75% of patients reported significant relief of symptoms within 3 days. That was significantly more than those on conventional OTC treatments.

Discussion points:

This is the pivotal page of the detail aid. It is the pay-off for the previous page, as it represents the practical benefit seen from the immune system effects.

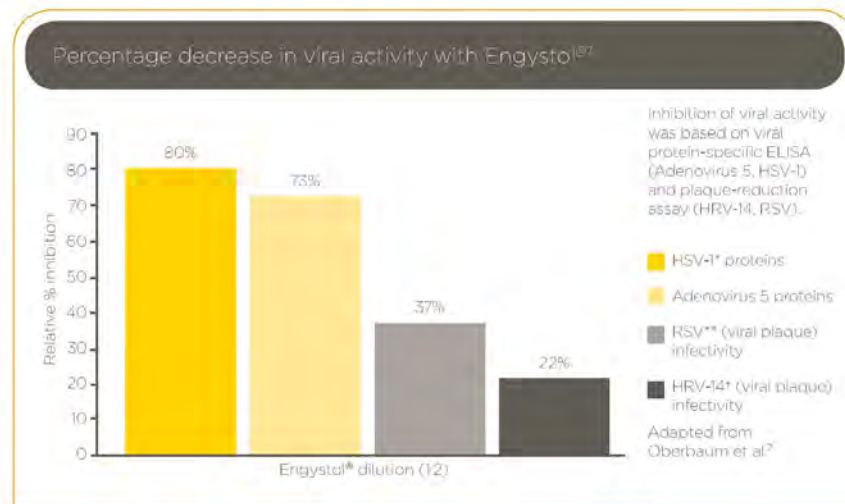
If the HCP strongly agrees at this point, then a trial close could again be appropriate:

Trial close

“So, would you prescribe/recommend Engystol[®] for the next few patients with colds that you see? I’ll come back in a few weeks and see how things have gone. When would suit you best?”

... and has demonstrated antiviral activity against several common viruses^{5,7}

- Engystol[®] demonstrates antiviral activity against HSV-1*, adenovirus 5, RSV** and HRV-14^{15,7}, possibly mediated via the interferon-based defense system (i.e. IFN- α , IFN- γ producing immune cells)^{4,5} or through a direct effect on viruses tested⁷



*HSV-1: Herpes Simplex Virus Type 1; **RSV: Respiratory Syncytial Virus; †HRV-14: Human Rhinovirus Type 14.

Page five:

Key points:

- In addition to the immune system effects and the improvement in symptoms, Engystol[®] has also demonstrated antiviral activity against several common viruses.

Discussion points:

This is additional support to the previous page. It strengthens the symptomatic messages by indicating that Engystol[®] may have a direct effect on the cause of the infection - viruses.

Further information is available in the tabbed section toward the back of the sales aid if the HCP is interested, but it is optional.

Engystol® has a good safety profile and is well tolerated¹ in a broad range of patient types⁸⁻¹⁰

- Pharmaceutical antiviral substances are associated with side effects¹¹⁻¹³
- Engystol® works naturally and is well tolerated¹
- Demonstrated safety and tolerability¹ in adults, infants and children⁸⁻¹⁰



Can be safely used alongside other medications^{9,14}

- Minimal adverse events observed
- No known interactions with other medications

Page six:

Key points:

- As a natural product, Engystol®'s safety and tolerability makes it suitable for a broad range of patient types: infants, children and adults, and elderly patients on polypharmacy.

Discussion points:

This really sets Engystol® apart from conventional antiviral drugs, most of which have side effects and restrictions on their use. This page is really reassurance that the benefits outlined previously come with minimal, if any, risk. The broad applicability message is conveyed further in the dose page that follows.

Dosing - Oral tablets

Unless otherwise prescribed:

Standard Dosage

Adults (and children 12 years and older):

1 tablet 3x daily

Pediatric:

6-11 years	1 tablet 2x daily
2-5 years	1 tablet 1-2x daily
Below 2 years	1 tablet 1x daily

Acute or Initial Dosage

Adults (and children 12 years and older):

1 tablet every $\frac{1}{2}$ to 1 hr, up to 12x daily, and then continue with standard dosage

Pediatric:

6-11 years	1 tablet every 1 to 2 hrs, up to 8x daily, and then continue with standard dosage
2-5 years	1 tablet every 1 to 2 hrs, up to 6x daily, and then continue with standard dosage
Below 2 years	1 tablet every 1 to 2 hrs, up to 4x daily, and then continue with standard dosage

Page seven:

Key points:

- Not only does Engystol®'s safety and tolerability make it suitable for a broad range of patients, but specific dosing is available for all age groups, including infants. This also includes an acute or initial dosage followed by a simple "1 tablet 1-3 times daily" regimen, depending on the age of the patient.

Discussion points:

From this page, in a normal call, the representative would skip to the rear cover, passing the tabbed section, unless there was a specific reason to show the HCP some of the tabbed information.

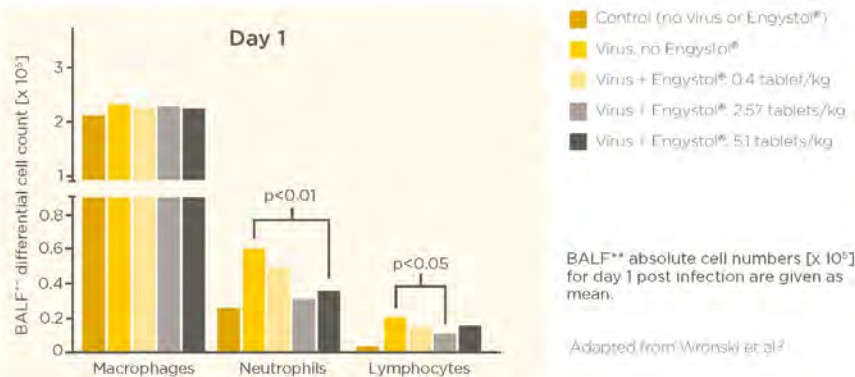
NEW
DATA!

Immune System Effects

Engystol® stimulates and supports the immune system in fighting colds²⁻⁵

- Helps fight early onset respiratory viral infection by modulating the immune response²
- In an *in vivo* study, Engystol® treatment markedly enhances the phagocytic capacity of alveolar macrophages following RSV* infection², thereby:
 - Significantly reducing early bronchoalveolar neutrophil and lymphocyte infiltration, and
 - Significantly reducing the release of inflammatory cytokines²

Inflammatory cell count in the lung following RSV* infection and Engystol® treatment²



*RSV: Respiratory Syncytial Virus; **BALF: Bronchoalveolar Lavage Fluid.

Page nine:

Key points:

- In this new *in vivo* study, Engystol® treatment markedly enhanced the phagocytic capacity of alveolar macrophages and significantly reduced early neutrophil and lymphocyte infiltration as well as the release of inflammatory cytokines following RSV infection.
- This study strongly supports the claim of “Engystol® boosting the immune system” in viral infections.

Discussion points:

This is an optional page for HCPs interested in the immune system effects of Engystol® and builds on the information given on page 3.

As mentioned in the discussion points for page 3, for HCPs already familiar with Engystol®, page 3 should be presented first, and then this page, if the HCP wishes to know more about the new data. The rest of the sales aid can be used as a reminder if needed.

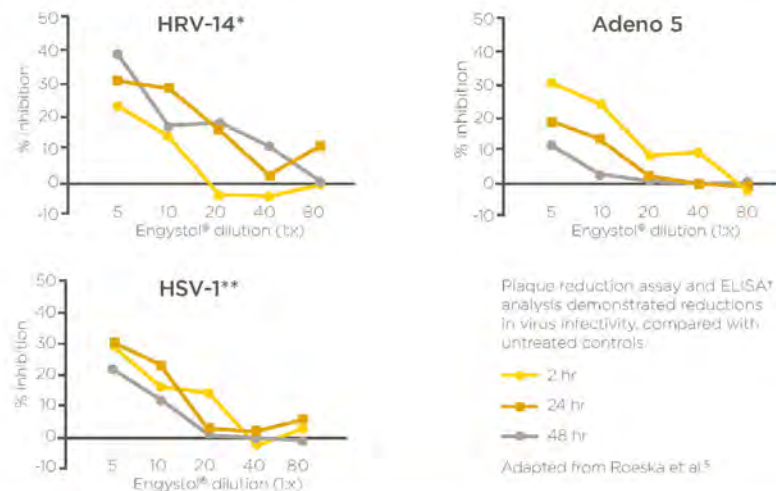
The findings of this study could explain Engystol®’s effects on earlier symptom relief and recovery, given that many symptoms are due to the immune response to viral infection.

Use of this page requires familiarity with the Wronski et al. publication.

Engystol® is effective in treating viral infections of the upper respiratory tract^{1,14}

- Demonstrates antiviral activity against HRV-14*, adenovirus 5, HSV-1** and RSV†^{5,7}, possibly mediated via the interferon-based defense system (i.e. IFN-α, IFN-γ producing immune cells)^{4,5} or through a direct effect on viruses tested⁷

Antiviral effect of Engystol® against HRV-14*, adenovirus 5 and HSV-1**⁵



*HRV-14: Human Rhinovirus Type 14; **HSV-1: Herpes Simplex Virus Type 1; †ELISA: Enzyme Linked Immunosorbent Assay; RSV: Respiratory Syncytial Virus.

Antiviral Effect

Page eleven:

Key points:

- Engystol® demonstrated antiviral activity against several common viruses that can cause infections of the upper respiratory tract.
- This was measured using ELISA and plaque reduction assays to demonstrate reductions in virus infectivity compared with untreated controls.

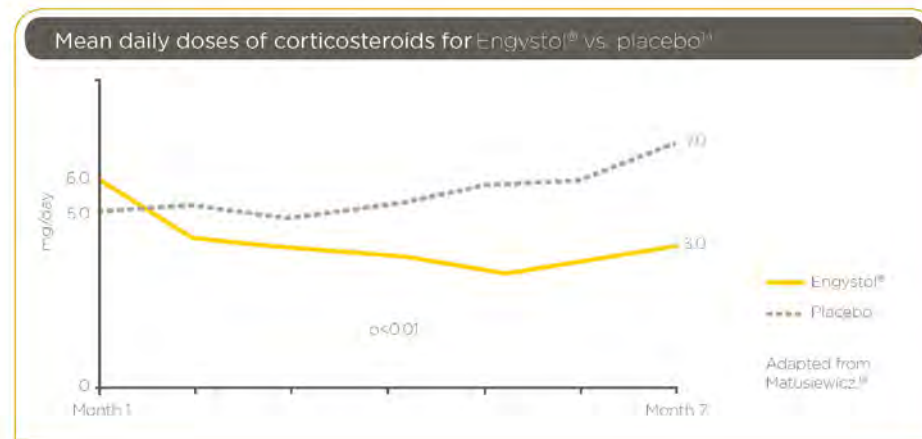
Discussion points:

This is an optional page for those doctors expressing an interest in the antiviral effects introduced on page 5.

Use of this page requires familiarity with both the Roeska et al. and Oberbaum et al. publications.

Engystol[®] reduces respiratory infections and corticosteroid use in chronic asthma patients¹⁴

- In a randomized, double-blind, placebo controlled study involving 40 corticosteroid-dependent asthma patients, aged 24-28 years, corticosteroid usage was halved when patients were treated with Engystol[®]¹⁴
- Engystol[®] treatment resulted in a significant reduction of recurrence of upper respiratory infections from 5-6 per year to 1-2 per year¹⁴



Patients with complications

Page thirteen:

Key points:

- In this interesting study, adult asthma patients experienced fewer recurrent upper respiratory infections and reduced their steroid requirement over the observation period.
- Whilst it shows the benefits of Engystol[®] use in this patient group, it is important to note that the study does not support proactive reduction in steroid dose.

Discussion points:

This is an optional page for those doctors involved in the treatment of adult patients with asthma.

The study shows the beneficial effects of Engystol[®] when used in adult patients with asthma – their steroid use over time reduced as their symptoms improved, probably as a result of the reduction in the number of upper respiratory infections.

It can NOT be used to recommend the reduction of steroid use in asthma patients treated with Engystol[®] as this could be dangerous and potentially life-threatening in this patient group.

Use of this page requires familiarity with the Matusiewicz publication.

Engystol®: Trusted the World Over



- Used for over **70 years**
- Available in over **40 countries**
- More than **1,500,000 packs** sold globally every year
- Multiple studies support the effectiveness and tolerability of Engystol®^{9,14}

Page fifteen:

Key points:



- Engystol® is a widely used product globally, with a well-studied effectiveness and tolerability profile.

Discussion points:

This is an optional page for use with doctors who are unaware of Engystol® and may be concerned about how well established it is.

Active ingredients

- Engystol® contains 2 main active ingredients to stimulate the body's own defences²⁻⁵ and influence inflammatory aspects of the immune response²

Active and inactive ingredients	Active ingredient proposed actions ¹⁶	Oral tablets (per one of 301.5 mg)	Injectable solution (ampoule of 1.1 ml)
<i>Vincetoxicum hirsutum</i> (swallowwort) 	Stimulation of the body's own defenses with vascular and sympathetic action, e.g. in feverish viral diseases, such as influenza, mumps, etc.	<i>Vincetoxicum hirsutum</i> D6, 75.0 mg <i>Vincetoxicum hirsutum</i> D10, 75.0 mg <i>Vincetoxicum hirsutum</i> D30, 75 mg	<i>Vincetoxicum hirsutum</i> D6, 6.6 mg <i>Vincetoxicum hirsutum</i> D10, 6.6 mg <i>Vincetoxicum hirsutum</i> D30, 6.6 mg
Sulfur (sulphur) 	Reactant in all chronic diseases, e.g. acute and chronic inflammation of the respiratory organs, catarrh of the upper respiratory tract, dyspnea, bronchial asthma, throbbing headache	Sulfur D4, 37.5 mg Sulfur D10, 37.5 mg	Sulfur D4, 3.3 mg Sulfur D10, 3.3 mg
Lactose	-	300 mg	-
Magnesium stearate	-	1.5 mg	-
Sodium chloride	-	-	8.78 mg
Water for injections	-	-	1.073, 60 mg

Engystol® ingredients

Page seventeen:

Key points:

- Engystol® contains 2 main active ingredients, swallowwort and sulfur, to stimulate the body's own defences and influence inflammatory aspects of the immune response.

Discussion points:

This is an optional page to be used with HCPs enquiring about the ingredients and the rationale for their use.

Summary of Product Characteristics

Engystol® Tablets and injection solution

Compositions: **Tablets:** 1 tabl. contains: Active ingredients: Sulfur D4 37.5 mg, Sulfur D10 37.5 mg, Vincetoxicum hirundinaria D6 75.0 mg, Vincetoxicum hirundinaria D30 75.0 mg, Vincetoxicum hirundinaria D10 6.60 mg, Vincetoxicum hirundinaria D30 6.60 mg. Excipients: Magnesium stearate 1.5 mg, contains lactose. **Injection solution:** 1 ampoule of 11 ml (=11 g) contains: Active ingredients: Sulfur D4 3.30 mg, Sulfur D10 3.30 mg, Vincetoxicum hirundinaria D6 6.60 mg, Vincetoxicum hirundinaria D10 6.60 mg, Vincetoxicum hirundinaria D30 6.60 mg. Excipients: Sodium chloride 8.78 mg, Water for injections 1.073, 60 mg. **Indications:** **Tablets, injection solution:** To reduce severity and duration of symptoms in viral infections, particularly in colds and influenza-like illnesses by supporting the immune system during or in upcoming flu season. **Contraindications:** **Tablets, injection solution:** Known allergy (hypersensitivity) to one or more of the ingredients. **Special warnings and special precautions for use:** **Tablets:** Patients with rare hereditary problems of galactose intolerance, Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicinal product. **Injection solution:** None. **Side effects:** **Tablets:** Like all medicinal products, this homeopathic medicinal product can cause side effects, although not everybody gets them. In isolated cases transient

skin reactions (e.g. rash, pruritus or erythema) and gastrointestinal complaints (e.g. abdominal pain or discomfort) have been reported. **Injection solution:** Like all medicinal products, this homeopathic medicinal product can cause side effects, although not everybody gets them. In isolated cases transient reactions (e.g. skin allergies, redness/swelling at the injection site) have been reported. **Interaction with other medicaments:** **Tablets, injection solution:** No interactions have been reported, and none are expected due to the homeopathic dilutions. **Pregnancy and lactation:** **Tablets, injection solution:** For this product no clinical data on pregnancy and lactation are available. Homeopathic dilutions of the substances present in this medicament are not known to be toxic during pregnancy and lactation. No adverse effects have so far been reported. **Effects on ability to drive and use machines:** **Tablets, injection solution:** No effects on the ability to drive and use machines have been reported, and none are expected due to the homeopathic dilutions. **Dosage:** **Tablets:** Standard dosage: Adults (and children 12 yrs. and older): 1 tablet 3x daily. Below 2 yrs.: 1 tablet 1x daily, 2-5 yrs.: 1 tablet 1-2x daily. 6-11 yrs.: 1 tablet 2x daily. **Acute or initial dosage:** Adults (and children 12 yrs. and older): 1 tablet every ½ to 1 hr, up to 12x daily,

and then continue with standard dosage. Below 2 yrs.: 1 tablet every 1 to 2 hrs., up to 4x daily, and then continue with standard dosage. 2-5 yrs.: 1 tablet every 1 to 2 hrs., up to 6x daily, and then continue with standard dosage. 6-11 yrs.: 1 tablet every 1 to 2 hrs., up to 8x daily, and then continue with standard dosage. **Method of administration:** Preferably allow the tablet to dissolve in the mouth, and then swallow. For children it is possible to crush the tablet and add to a small amount of water. This medicine should be taken away from meals. **Injection solution:** Standard dosage: Adults (and children 12 yrs. and older): 1 ampoule 1 to 3x weekly. 2-5 yrs.: ½ ampoule 1 to 3x weekly. 6-11 yrs.: ¼ of an ampoule 1 to 3x weekly. **Acute or initial dosage:** Adults (and children 12 yrs. and older): 1 ampoule daily, and then continue with standard dosage. 2-5 yrs.: ½ ampoule daily, and then continue with standard dosage. 6-11 yrs.: ¼ of an ampoule daily, and then continue with standard dosage. **Method of administration:** Injection solution may be administered by the s.c., i.d., i.m. or i.v. route. **Overdose:** **Tablets, injection solution:** No cases of overdose have been reported, and none are expected due to the homeopathic dilutions. **Package sizes:** **Tablets (9830):** Packs containing 50 and 250 tablets. **Injection solution (8546):** Packs containing 5, 10, 50 and 100 ampoules of 11 ml.

References

- Schmiedel V, Klein P. A complex homeopathic preparation for the symptomatic treatment of upper respiratory infections associated with the common cold: An observational study. *Explore*. 2006;2(2):109-114. doi:10.1016/j.explore.2005.12.008
- Wronski S, Dannenmaier J, Schild S, et al. Engystol reduces onset of experimental respiratory syncytial virus-induced respiratory inflammation in mice by modulating macrophage phagocytic capacity. *PLoS One* 2018;13(4): e0195822. doi:10.1371/journal.pone.0195822
- Wagner H, Jurcic K, Doenicke A, Behrens N. Influence of Homeopathic Drug Preparations on the Phagocytosis Capability of Granulocytes: In-vitro tests and controlled single-blind studies. *Biol Ther*. 1993;11(1):43-49.
- Enberg H. Effects of the homeopathic preparation Engystol on interferon-gamma production by human T-lymphocytes. *Immunol Invest*. 2006;35(1):19-27. doi:10.1080/08820130500496753
- Roaska K, Selheimer B. Antiviral activity of Engystol(R) and Gripp-Heel(R): an in-vitro assessment. *J Immune Based Ther Vaccines*. 2010;8(1):6. doi:10.1186/1476-8518-8-6
- Hallmann A. A combination injection preparation as a prophylactic for flu and common colds. *Biol Ther*. 1994;12(4):249-253.
- Oberbaum M, Glatthaar-Saalmüller B, Stolt P, Weiser M. Antiviral activity of Engystol: an in vitro analysis. *J Altern Complement Med*. 2005;11(5):855-862. doi:10.1089/acm.2005.11.855
- Torbicka E, Brzozowska-Binda A, Wilczynski J, Uzarowicz A. RSV infections in infants: therapy with a homeopathic preparation. *Biomed Ther*. 1998;16(4):256-260.
- Herzberger G, Weiser M. Homeopathic treatment of infections of various origins: a prospective study. *Biomed Ther*. 1997;15(4):123-127.
- Tiraspolski I, V. Kuzmin VN, Kashirina TN, Busorgina O V. Antihomotoxische Therapie primärer Zytomegalie-Virusinfektionen bei Schwangeren. *Biol Medizin*. 1998;27(5):206-211.
- Nguyen H. Influenza Treatment & Management. Medscape website. <https://medscape.com/article/219557-treatment#d9>. Published 2018. Accessed August 16, 2018.
- Gompf S. Adenovirus. Medscape website. <https://medscape.com/article/211738-overview#showall>. Published 2016. Accessed August 20, 2018.
- Krilov L. Respiratory Syncytial Virus Infection. Medscape Reference website. <https://medscape.com/article/97148-overview>. Published 2017. Accessed August 21, 2018.
- Matusiewicz R. The effect of a homeopathic preparation on the clinical condition of patients with corticosteroid-dependent bronchial asthma. *Biomed Ther*. 1997;15(5):70-74.
- Biotherapeutic Index: A Medical Compendium for Health Care Professionals*. 8th rev ed. Queenswood, Pretoria, South Africa: Briza Publications; 2012.

Fight colds. Help your patients enjoy winter

Recommend taking **Engystol®** early to:

- Stimulate and support the immune system in fighting colds²⁻⁵
- Rapidly – within 3 days – improve symptoms of the common cold¹
- Effectively treat viral infections of the upper respiratory tract^{1,14}

Engystol® is:

- Well tolerated¹ in a broad range of patient types⁸⁻¹⁰
- Suitable for use alongside other medications with no known interactions^{9,14}
- Convenient to take – sublingual, oral dosing

Give their immune system a natural boost²⁻⁵ with



-Heel

Biologische Heilmittel Heel GmbH
Dr.-Reckeweg-Straße 2-4
76532 Baden-Baden, Germany
Phone +49 7221 501-00
www.heel.com

© 07/2019 by Biologische Heilmittel Heel GmbH,
Baden-Baden, Germany

Back cover:

Key points:

- Engystol®, when taken early, provides rapid symptom improvement of the common cold by naturally stimulating and supporting the immune system. It has a favorable safety profile and is well tolerated and is available as an oral formulation that suits all patients.

Close:

“So, I hope I have convinced you of the benefits and effectiveness of Engystol® and I will leave you some samples so that you can prescribe/recommend Engystol® for the next few patients with colds that you see. I’ll come back in a few weeks and see how things have gone. When would suit you best?”

© 07/2019 by Biologische Heilmittel Heel GmbH, Baden-Baden, Germany

FOR INTERNAL USE ONLY