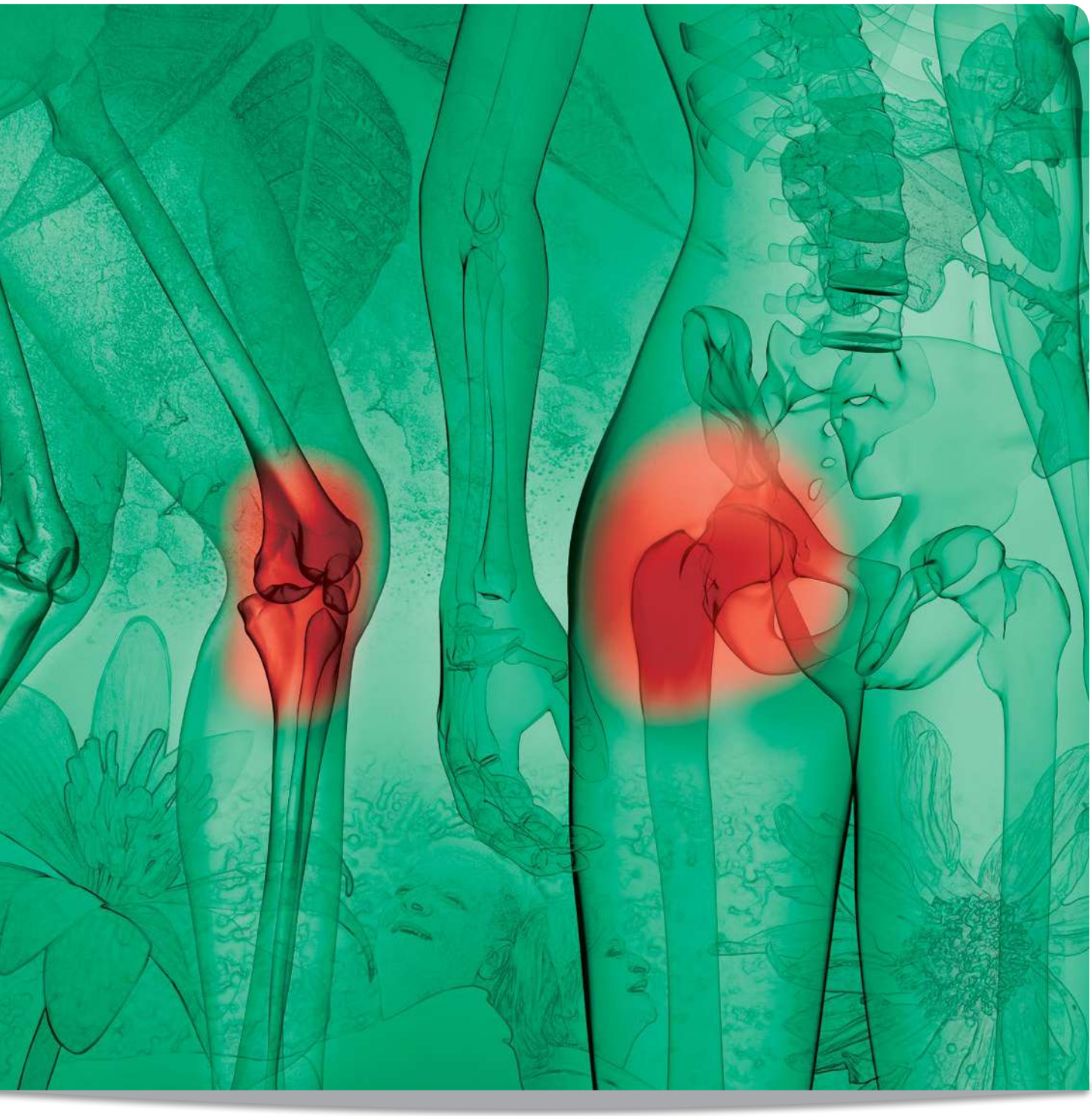
Naturally effective and safe therapy in osteoarthritis and rheumatic joint diseases

… As effective as common therapies but with a better safety and tolerability profile



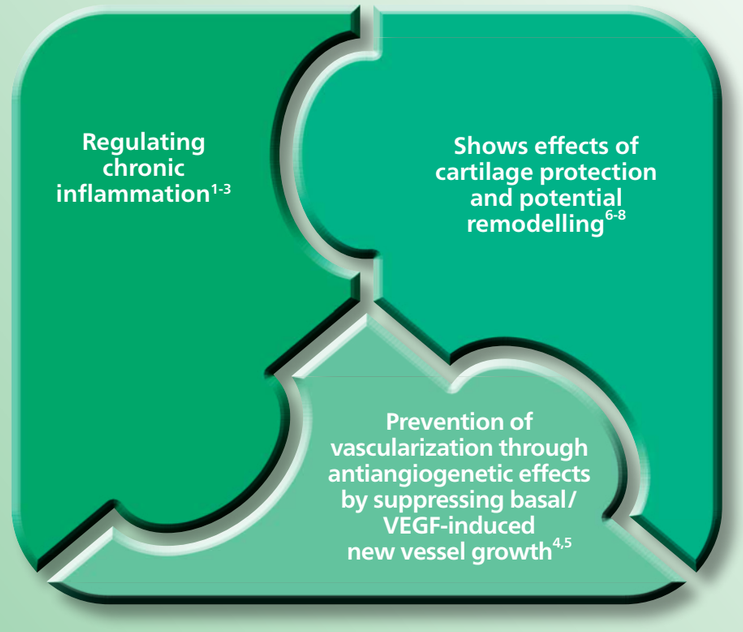
-Heel

Zeel® T

Zeel T is a **proven, natural, effective treatment** for osteoarthritis and rheumatic joint diseases

- Zeel T is effective in osteoarthritis and rheumatic joint diseases due to its multi-targeted mode of action that is mediated by its various natural ingredients:[1-8]

Multi-targeted mode of action of Zeel T



- Zeel T works by modulating both the 5-LOX and COX-1 and -2 inflammatory pathways[1-3]
- Zeel T inhibits the production of the leukotriene B4 (LTB4) which is elevated in chronic inflammatory joint diseases[1]

KEY FACT

The constituents of **Zeel T** act in a complementary manner to effectively relieve symptoms of osteoarthritis and rheumatic joint diseases and protect the cartilage.

Zeel T is **safe and easy to use** in a wide range of patients

NSAIDs/COX-2s/ glucocorticoids

Elderly and high-risk patients

NSAIDs/COX-2s have dose-dependent side effects which limit their use in elderly and high-risk patients; **glucocorticoids** are limited by their adverse effects and short-term use; the use of viscosupplements/hyaluronic acids are restricted by their questionable cost:benefit ratio, quality of evidence and lack of long-term data[9-17]

Patients with contra-indications

NSAIDs/COX-2s have known gastrointestinal, cardiovascular, renal and liver toxicities which limit their long-term use; glucocorticoids have long-term effects on bone and other systems, and many co-morbidities predispose patients to adverse events with **glucocorticoids**. These include diabetes, glucose intolerance, cardiovascular disease, peptic ulcer disease, recurrent infections, immunosuppression, and (risk factors of) glaucoma and osteoporosis[9-17]

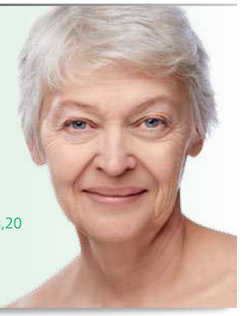
Patients using other medications

There are multiple drug interactions with **NSAIDs/COX-2s** that can restrict their use[9-17]

Zeel T

Zeel T is well tolerated[18,19]

Zeel T can be given long-term[18,20]



Side effects are very rarely reported with **Zeel T**[18,19]

Zeel T can be used safely in patients with cardiovascular disease, hypertension, gastrointestinal disturbance, renal disease and liver disease

Zeel T can be safely combined with natural or conventional medications or used as monotherapy[18,19]

Zeel T has no known drug interactions with other medications

- The side effect profile of common treatments make them less than ideal in the treatment of osteoarthritis and rheumatic joint diseases, which often require longer-term therapy and need to be used with other medications in patients with co-morbidities.

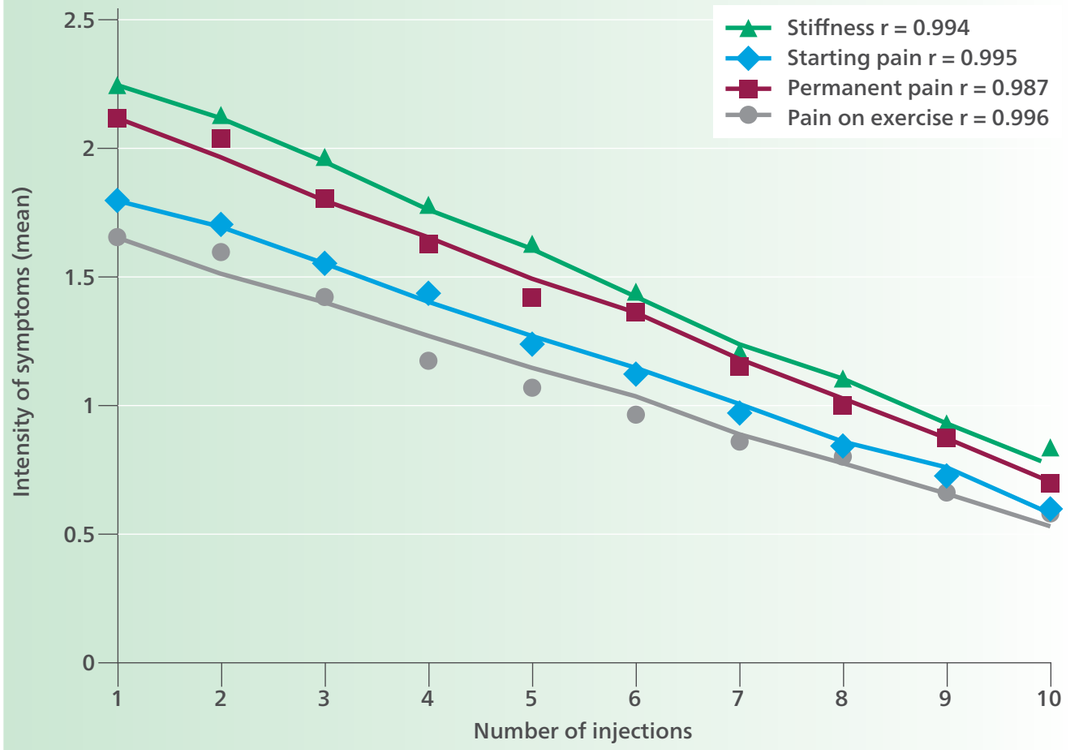
"Use oral NSAIDs/COX-2 inhibitors at the lowest effective dose for the shortest possible period of time."[10]

KEY FACT

In contrast to NSAIDs/COX-2s, **Zeel T** can be used in all patients without concerns about safety or drug interactions.

Zeel T – periarticular injections have **demonstrated effective** symptom relief in knee osteoarthritis

Change in the intensity of symptoms during 10 injections of Zeel T solution for injection, with correlation coefficients for change in symptoms and the number of injections[18]



An observational cohort study in which 100 patients with osteoarthritis of the knee received peri-articular injection of Zeel T solution for injection for 4-6 weeks.[18]

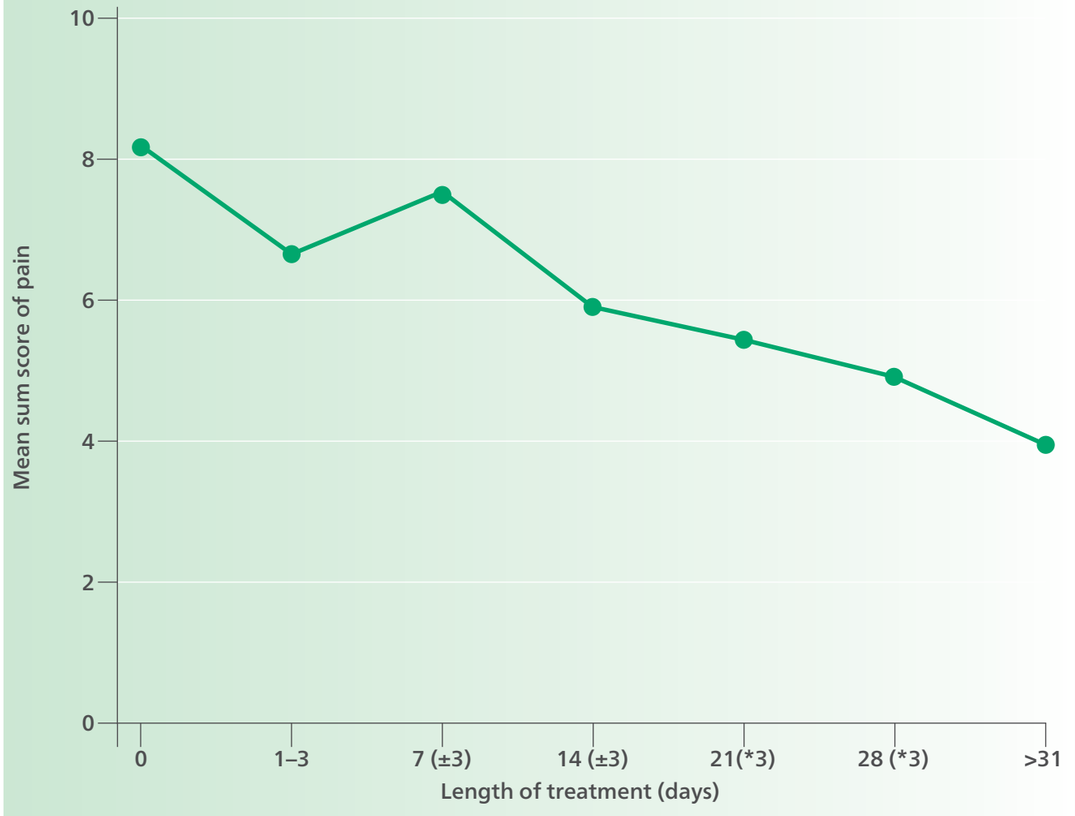
Zeel® T

KEY FACT

Zeel T effectively **relieves** symptoms in osteoarthritis of the knee.

Zeel T – ointment proven effective in reducing pain in degenerative articular disorders

Mean sum score of pain (night pain + starting pain + movement pain) for all patients (n=498)[20]*



A prospective, multi-centre cohort study in 498 patients with degenerative articular disorders; all patients received Zeel T ointment.[20]
* In 24% of the patients this was a combination therapy.

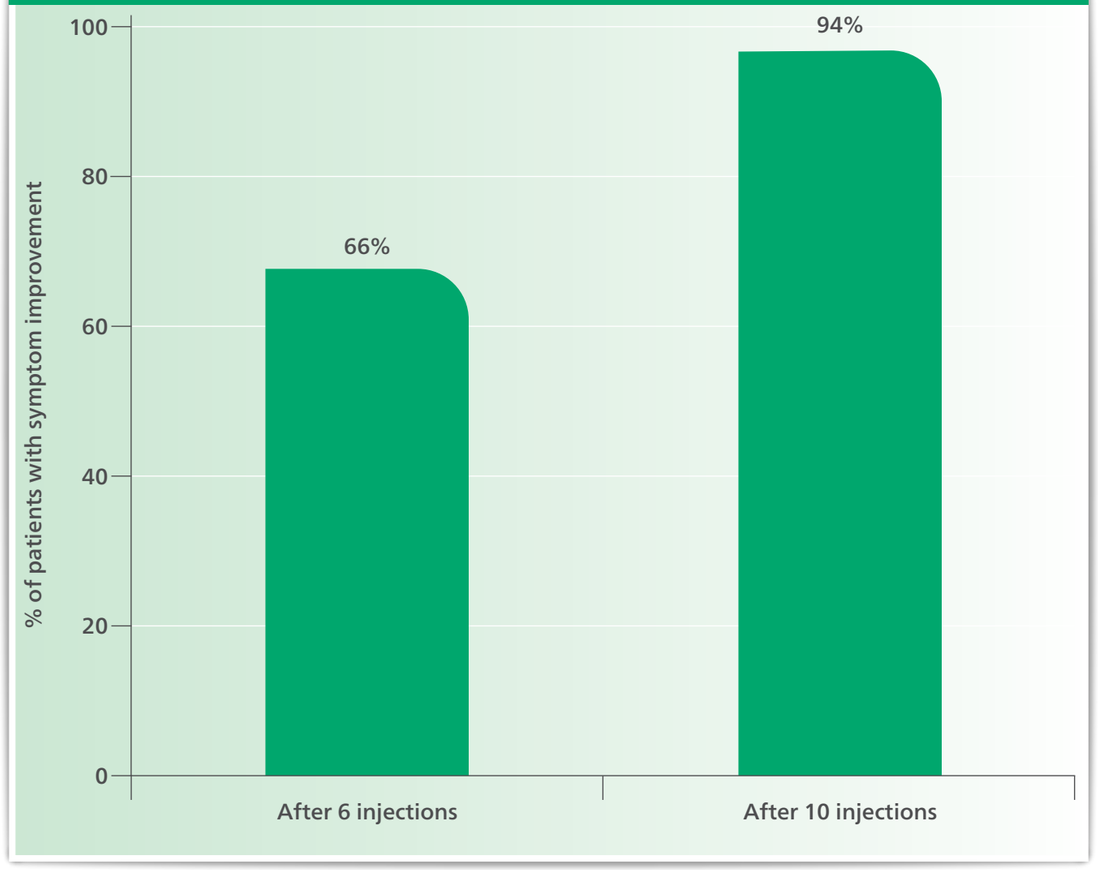
KEY FACT

Zeel T – effectively **reduces** pain in degenerative articular disorders.

Zeel® T

Zeel T – injections offer **rapid** symptom relief in various forms of arthritis

Percentage of patients with symptom improvement over time[19]

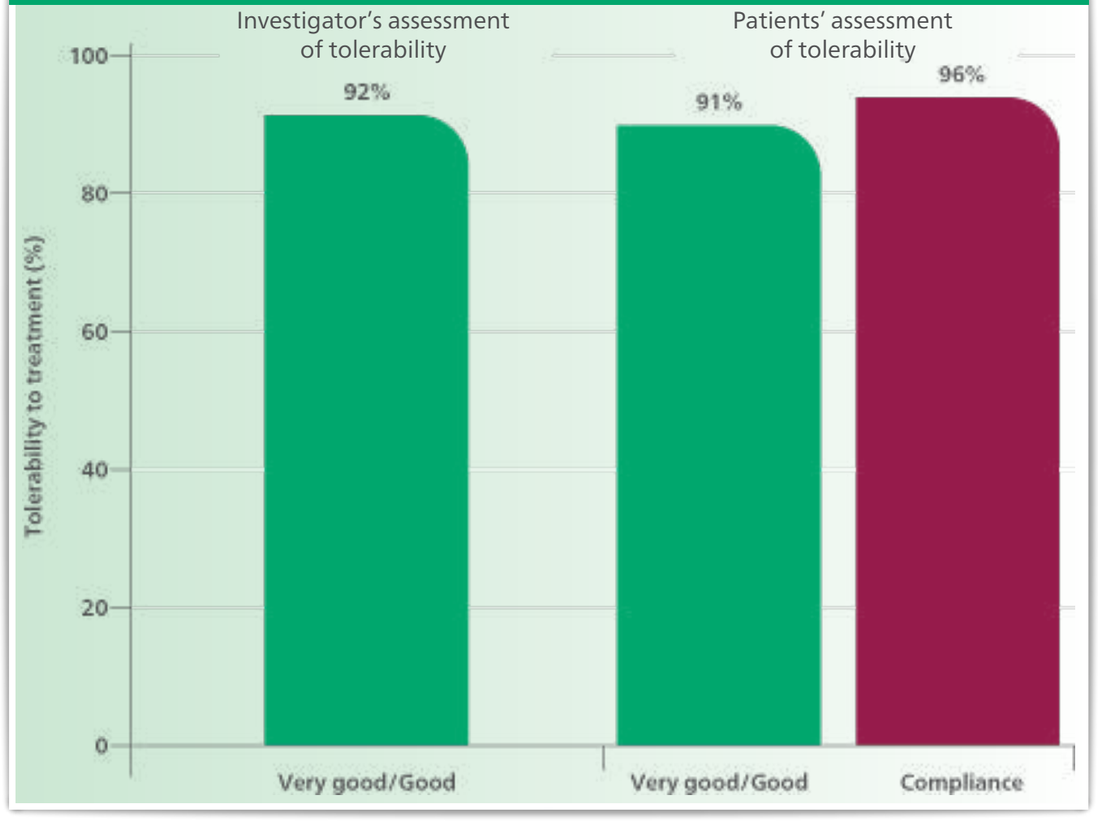


An open study in 523 patients with various types of arthritis in which all patients received Zeel T solution for injection (intra-articular, peri-articular or intramuscular).[19]

Zeel T injections - tolerability is **rated highly** by patients and physicians

- 92% of investigators and 91% of patients rate treatment with Zeel T as 'very good' or 'good'[18]
- Compliance with Zeel T is 96[18]

Zeel T is rated highly by investigators and patients[18]



An observational cohort study in which 100 patients with osteoarthritis of the knee received peri-articular injection of Zeel T solution for injection for 4-6 weeks. Efficacy assessments; by patients and investigators according to a 5-point rating scale: very good (no more complaints), good (significant improvement), moderate (slight improvement), without success (no change) or deterioration.[18]

Zeel® T

KEY FACT

Zeel T injections - an effective alternative to long-term NSAIDs or COX-2 inhibitors in various forms of arthritis.

Zeel® T

Zeel T is available in a **range of formulations** for flexible dosing in adults and children

		Zeel T ampoules for injection	Zeel T ointment	Zeel T tablets
				
Standard dosage: *Unless otherwise prescribed*	Adults & children >12yrs 	**1 ampoule** 1 to 3 x weekly	**Apply** 2 to 4 x daily	**1 tablet** 3 x daily
	6–11yrs 	**⅔ of an ampoule** 1 to 3x weekly	**Apply** 2 to 4x daily	**1 tablet** 2x daily
Acute or initial dosage	Adults & children >12yrs 	**1 ampoule** daily, and then continue with standard dosage		**1 tablet** every ½ to 1 hr., up to 12 x daily, and then continue with standard dosage
	6–11yrs 	**⅔ of an ampoule** daily, and then continue with standard dosage		**1 tablet** every 1 to 2 hrs., up to 8x daily, and then continue with standard dosage

Zeel® T

Prescribing information

Zeel® T: Tablets • Injection solution • Ointment

Compositions: ***Tablets:*** 1 tablet = 301.5 mg containing: Active ingredients: Acidum DL-alpha liponicum D6 0.03 mg, Acidum silicicum D6 3.00 mg, Arnica montana D1 0.60 mg, Cartilago suis D4 0.30 mg, Coenzym A D6 0.03 mg, Embryo totalis suis D4 0.30 mg, Funiculus umbilicalis suis D4 0.30 mg, Nadidum D6 0.03 mg, Natrium diethyloxalaceticum D6 0.03 mg, Placenta totalis suis D4 0.30 mg, Rhus toxicodendron D2 0.54 mg, Sanguinaria canadensis D3 0.45 mg, Solanum dulcamara D2 0.15 mg, Sulfur D6 0.54 mg, Symphytum officinale D8 0.15 mg. Excipients: Lactose monohydrate 296.94 mg, magnesium stearate 1.50 mg. ***Injection solution:*** 2.0 g containing: Active ingredients: Acidum DL-alpha liponicum D8 2.0 mg, Arnica montana D4 200.0 mg, Cartilago suis D6 2.0 mg, Coenzym A D8 2.0 mg, Embryo totalis suis D6 2.0 mg, Funiculus umbilicalis suis D6 2.0 mg, Nadidum D8 2.0 mg, Natrium diethyloxalaceticum D8 2.0 mg, Placenta totalis suis D6 2.0 mg, Rhus toxicodendron D2 10.0 mg, Sanguinaria canadensis D4 3.0 mg, Solanum dulcamara D3 10.0 mg, Sulfur D6 3.6 mg, Symphytum officinale D6 10.0 mg. Excipients: Sodium chloride 17.6 mg, water for injections 1747.4 mg. ***Ointment:*** 100 g containing: Active ingredients: Arnica montana D3 1.500 g; Calendula officinalis Ø, Hamamelis virginiana Ø, 0.450 g each; Chamomilla recutita Ø, Acidum DL-alpha liponicum D6 0.010 g, Acidum silicicum D6 1.000 g, Arnica montana D2 0.300 g, Cartilago suis D2 0.001 g, Coenzym A D6 0.010 g, Embryo totalis suis D2 0.001 g, Funiculus umbilicalis suis D2 0.001 g, Nadidum D6 0.010 g, Natrium diethyloxalaceticum D6 0.010 g, Placenta totalis suis D2 0.001 g, Rhus toxicodendron D2 0.270 g, Sanguinaria canadensis D2 0.225 g, Solanum dulcamara D2 0.075 g, Sulfur D6 0.270 g, Symphytum officinale D8 0.750 g. Excipients: Cetostearyl alcohol (type A), emulsifying 8.007 g; ethanol 96% (V/V) 9.565 g; paraffin, liquid 9.342 g; white soft paraffin 9.342 g; water, purified 60.810 g.

Indications: ***Tablets, injection solution, ointment:*** Arthrosis/osteoarthritis, and/or rheumatic joint diseases.

Contraindications: ***Tablets, injection solution, ointment:*** 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. ***Ointment:*** Cetylstearyl alcohol may cause local skin reactions (e.g. contact dermatitis). Avoid contact with eyes, mucosae, open wounds or broken skin.

Side effects: ***Tablets, injection solution:*** Like all medicinal products, homeopathic medicines may cause side effects. In isolated cases transient skin allergies have been reported. The frequency of these effects is not known. ***Ointment:*** Like all medicinal products, homeopathic medicines can cause side effects in isolated cases, such as transient allergic reactions. The frequency of these effects is not known.

Interactions with other medication: ***Tablets, injection solution, ointment:*** No interactions have been reported, and none are expected due to the homeopathic dilutions.

Pregnancy and lactation: ***Tablets, injection solution, ointment:*** 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. ***Ointment:*** Not applicable.

Dosage: ***Tablets:*** Standard dosage: Adults (and children 12 yrs. and older): 1 tablet 3× daily; 6–11 yrs. 1 tablet 2× daily; Acute or initial dosage: Adults (and children 12 yrs. and older): 1 tablet every ½ to 1 hr., up to 12× daily, and then continue with standard dosage; 6–11 yrs.: 1 tablet every 1 to 2 hrs., up to 8× 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 3× weekly. 6–11 yrs.: ⅔ of an ampoule 1 to 3× weekly. Acute or initial dosage: Adults (and children 12 yrs. and older): 1 ampoule daily, and then continue with standard dosage; 6–11 yrs.: ⅔ of an ampoule daily, and then continue with standard dosage. Method of administration: Solution for injection may be administered by the s.c., i.d., i.m., i.a. or i.v. route. ***Ointment:*** Standard dosage: Adults (and children 12 yrs. and older): Apply 2 to 4× daily, 6–11 yrs.: Apply 2 to 4× daily. Method of administration: For external use only. Apply a thin layer over the affected area.

Overdose: ***Tablets, injection solution:*** No cases of overdose have been reported, and none are expected due to the homeopathic dilutions. ***Ointment:*** No cases of overdose have been reported, and none are expected due to the homeopathic dilutions and external use.

Package sizes: ***Tablets:*** Packs containing 50, 100 and 250 tablets. ***Injection solution:*** Packs containing 10, 50 and 100 ampoules of 2.0 ml each. ***Ointment:*** Tubes containing 50 and 100 g.

Zeel® T

References

1. Jäggi R, Würgler U, Grandjean F, Weiser M. Dual inhibition of 5-lipoxygenase/cyclooxygenase by a reconstituted homeopathic remedy; possible explanation for clinical efficacy and favourable gastrointestinal tolerability. *Inflamm* Res. 2004 Apr;53(4):150-7.
2. Birnesser H. Stolt P, The homeopathic preparation Zeel comp. N: A review of the molecular and clinical data. *Explore* (NY) 2007;3(1):16-22.
3. Tunon H, Olavsdotter C, Bohlin L. Evaluation of anti-inflammatory activity of some Swedish medicinal plants. Inhibition of prostaglandin biosynthesis and PAF induced exocytosis. *J Ethnopharmacol*. 1995;48:61-76.
4. Basini G, Santini SE, Bussolati S, Grasselli F. Sanguinarine inhibits VEGF-induced Akt phosphorylation. *Ann N Y Acad Sci*. 2007 Jan;1095:371-6.
5. Basini G, Bussolati S, Santini SE, Grasselli F. Sanguinarine inhibits VEGF-induced angiogenesis in a fibrin gel matrix. *Biofactors*. 2007;29(1):11-8.
6. Schmolz M. Transforming Growth Factor beta (TGF-ß): eine neue Regelstrecke für antiphlogistische Therapien? *Biol Med*. 2000;29(1):31-34.
7. Schmolz M, Heine H. Homöopathische Substanzen aus der antihomotoxischen Medizin modulieren die Synthese von TGF-ß1 in menschlichen Vollblutkulturen. *Biol Med*. 2001;30(2):61-65.
8. Stančíková M, Bély M, Švík K, Metelmann HW, Schmolz MW, Ištok R, Fano R. Effects of Zeel comp. on experimental osteoarthritis in rabbit knee. *Rheumatologia* 1999;13(3): 101-108.
9. Hochberg MC, Altman RD, April CT, Benkhalti M, Guyatt G, McGowan J, Towheed T, Welch V, Wells G, and Tugwell P. American College of Rheumatology (ACR). Recommendations for the Use of Nonpharmacologic and Pharmacologic Therapies in Osteoarthritis of the Hand, Hip, and Knee. *Arthritis Care & Research*. 2012;64(4):465 -474.
10. NICE guideline. CG177 Osteoarthritis; Care and management in adults, February 2014, at: http://guidance.nice.org.uk/CG177. Accessed November 2015.
11. Brown GA. American Academy of Orthopaedic Surgeons (AAOS) clinical practice guideline: treatment of osteoarthritis of the knee: evidence-based guideline, 2nd edition. *J Am Acad Orthop Surg*. 2013 Sep;21(9):577-9.
12. Zhang W, Nuki G, Moskowitz RW, Abramson S, Altman RD, Arden NK, Bierma-Zeinstra S, Brandt KD, Croft P, Doherty M, Dougados M, Hochberg M, Hunter DJ, Kwoh K, Lohmander LS, Tugwell P. Osteoarthritis Research Society International (OARSI) recommendations for the management of hip and knee osteoarthritis. Part III: changes in evidence following systematic cumulative update of research published through January 2009. *Osteoarthritis and Cartilage* 2010;18:476-499.
13. Duru N, van der Goes MC, Jacobs JW, Andrews T, Boers M, Buttgereit F, Caeyers N, Cutolo M, Halliday S, Da Silva JA, Kirwan JR, Ray D, Rovensky J, Severijns G, Westhovens R, Bijlsma JW. The European League Against Rheumatism (EULAR) evidence-based and consensus based recommendations on the management of medium to high-dose glucocorticoid therapy in rheumatic diseases. *Ann Rheum Dis.* 2013 Dec;72(12):1905-13.
14. Rheumatoid arthritis: The management of rheumatoid arthritis in adults. National Institute for Health and Care Excellence (NICE) clinical guideline 79. 2009, last modified 2013, at: www.guidance.nice.org.uk/cg79. Accessed November 2015.
15. British National Formulary (BNF), at www.bnf.org. Accessed November 2015.
16. Management of early rheumatoid arthritis - A national clinical guideline. Scottish Intercollegiate Guidelines Network (SIGN), Guideline 123. 2011, at: http://www.sign.ac.uk. Accessed November 2015.
17. Safety Concerns Associated with Over-the-Counter Drug Products Containing Analgesic/ Antipyretic Active Ingredients for Internal Use. 2004. Food and Drug Administration (FDA).
18. Gottwald R, Weiser M. Treatment of osteoarthritis of the knee with Zeel T. *Medicina Biológica* 2000;13(4):109-113.
19. Lesiak A, Gottwald R, Weiser M. Skutecznosc kuracji preparatem Zeel T w iniekcjach dostawowych okolostawowych I domiesniowych w chorobie zwyrodnieniowej stawow. *Medycyna Biologiczna* 2001; kwiecień czerwiec zeszyt 2:30-36.
20. Wodick RE. Steininger K, Zenner S. The biological treatment of articular affections - results of a study conducted with 498 patients. *Biologische Medizin.* 1993;3:127-135.

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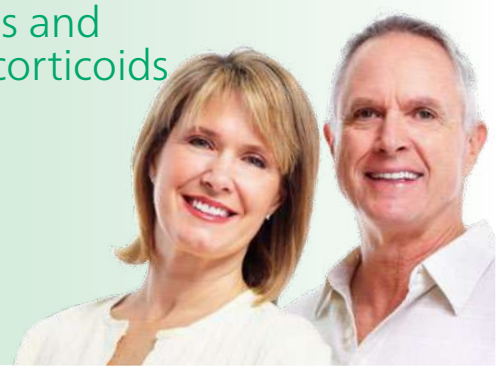
Effective, **safe** and **natural therapy** for osteoarthritis and rheumatic joint diseases

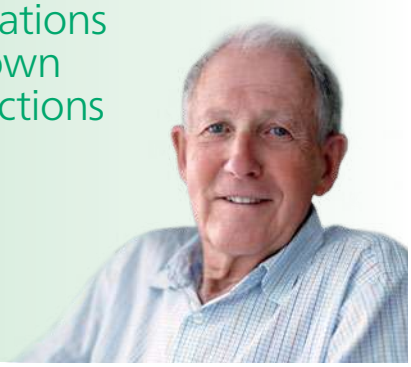
Zeel T is an effective long-term treatment

- Reduces symptoms[18-20]
- Reduces pain[18-20]
- Works reliably[18-20]

Favourable safety profile compared to NSAIDs, COX-2s and glucocorticoids



Very rarely reported adverse effects, few contraindications and no known drug interactions



Flexible range of formulations for patient convenience

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