

# Use of Biological Therapies (monoclonal Antibodies) in Chronic Rhinosinusitis with Nasal Polyposis

Uso de Terapias Biológicas (anticorpos Monoclonais) em Rinossinusite Crônica com Polipose Nasal

Uso de Terapias Biológicas (anticuerpos Monoclonales) en la Rinossinusitis Crónica con Poliposis Nasal

## RESUMO

**Introdução:** A rinossinusite crônica com polipose nasal (RSCPN) frequentemente cursa com inflamação tipo 2 e alta taxa de recidiva após corticoide sistêmico e/ou cirurgia endoscópica. Biológicos dirigidos a alvos como IgE, IL-4/IL-13, IL-5/IL-5R e TSLP emergiram como opções efetivas. **Objetivo:** Sintetizar a evidência sobre eficácia, segurança, indicações e monitoramento de anticorpos monoclonais na RSCPN. **Métodos:** Revisão narrativa de literatura (PubMed, SciELO e Web of Science) até 14/10/2025, priorizando ensaios clínicos fase III, consensos/guidelines e estudos do “mundo real”. **Resultados:** Dupilumabe (anti-IL-4R $\alpha$ ) reduziu escore de pólipos nasais (NPS), congestão e opacificação sinusal em dois RCTs de fase III (SINUS-24/52) e melhora persiste em subgrupos com/sem asma; omalizumabe (anti-IgE) mostrou melhora endoscópica e de sintomas (POLYP-1/2) e foi aprovado como terapia adjuvante; mepolizumabe (anti-IL-5) reduziu NPS e necessidade de cirurgia (SYNAPSE); benralizumabe (anti-IL-5R $\alpha$ ) melhorou NPS, congestão e olfato (OSTRO); tezepelumabe (anti-TSLP) apresentou resultados positivos e publicados em 2025, incluindo redução de NPS, congestão e uso de corticoide sistêmico/cirurgia. **Conclusão:** Biológicos são eficazes e seguros em RSCPN com inflamação tipo 2 não controlada por terapia padrão, com seleção baseada em fenótipo/endótipo, comorbidades (asma/NSAID-ERD) e critérios de resposta de consensos atuais.

**DESCRIPTORES:** Rinossinusite Crônica; Pólipos Nasais; Anticorpos Monoclonais.

## ABSTRACT

**Introduction:** Chronic rhinosinusitis with nasal polyps (CRSwNP) is often driven by type-2 inflammation and recurs despite steroids and/or surgery. **Objective:** To synthesize evidence on efficacy, safety, indications, and monitoring of monoclonal antibodies in CRSwNP. **Methods:** Narrative literature review (PubMed, SciELO, Web of Science) through Oct 14, 2025, emphasizing phase-III RCTs, guidelines/consensus statements, and real-world studies. **Results:** Dupilumab (anti-IL-4R $\alpha$ ) improved nasal polyp score, congestion, and CT opacification in two phase-III trials (SINUS-24/52), with consistent effects across subgroups; omalizumab (anti-IgE) improved endoscopic and patient-reported outcomes (POLYP-1/2) and is approved as add-on therapy; mepolizumab (anti-IL-5) reduced polyp size and surgery need (SYNAPSE); benralizumab (anti-IL-5R $\alpha$ ) improved NPS, congestion, and smell (OSTRO); tezepelumab (anti-TSLP) showed significant reductions in NPS, congestion, and systemic steroid/surgery use in 2025 data. **Conclusions:** Biologics are effective and safe for uncontrolled type-2 CRSwNP; patient selection should consider phenotype/endotype, comorbid asthma/NSAID-ERD, and contemporary response criteria.

**DESCRIPTORS:** Chronic Rhinosinusitis; Nasal Polyps; Monoclonal Antibodies.

## RESUMEN

**Introducción:** La rinossinusitis crónica con poliposis nasal (RSCPN) suele cursar con inflamación tipo 2 y una alta tasa de recurrencia tras el uso de corticoides sistémicos y/o cirugía endoscópica. Los biológicos dirigidos a objetivos como IgE, IL-4/IL-13, IL-5/IL-5R y TSLP han surgido como opciones terapéuticas efectivas. **Objetivo:** Sintetizar la evidencia sobre eficacia, seguridad, indicaciones y monitoreo de los anticuerpos monoclonales en la RSCPN. **Métodos:** Revisión narrativa de la literatura (PubMed, SciELO y Web of Science) hasta el 14/10/2025, priorizando ensayos clínicos de fase III, consensos/guías y estudios del “mundo real”. **Resultados:** Dupilumab (anti-IL-4R $\alpha$ ) redujo el puntaje de pólipos nasales (NPS), la congestión y la opacificación sinusal en dos ensayos clínicos fase III (SINUS-24/52), con mejora sostenida en subgrupos con y sin asma; omalizumab (anti-IgE) mostró mejoría endoscópica y sintomática (POLYP-1/2) y fue aprobado como terapia adyuvante; mepolizumab (anti-IL-5) redujo el NPS y la necesidad de cirugía (SYNAPSE); benralizumab (anti-IL-5R $\alpha$ ) mejoró el NPS, la congestión y el olfato (OSTRO); tezepelumab (anti-TSLP) presentó resultados positivos publicados en 2025, incluyendo reducción del NPS, la congestión y el uso de corticoides sistémicos/cirugía. **Conclusión:** Los biológicos son eficaces y seguros en la RSCPN con inflamación tipo 2 no controlada por la terapia estándar, con selección basada en fenotipo/endotipo, comorbilidades (asma/NSAID-ERD) y criterios de respuesta según los consensos actuales.

**DESCRIPTORES:** Rinossinusitis Crónica; Pólipos Nasales; Anticuerpos Monoclonales.

Thais Gutierrez do Amaral Coelho

Christian University of Bolivia

ORCID: <https://orcid.org/0009-0003-5769-4410>

João Paulo dos Santos Moreira

Ceres College

ORCID: <https://orcid.org/0009-0006-9558-6877>

Received: 10/07/2025

Approved: 10/20/2025

Gustavo Alexandre Romero Tenório

Pontifical Catholic University of Minas Gerais, Poços de Caldas campus

ORCID: <https://orcid.org/0000-0002-6636-7353>

Max Henrique Lima Martins

Iguaçu University

ORCID: <https://orcid.org/0000-0003-2983-9718>

## INTRODUCTION

Chronic rhinosinusitis with nasal polyposis (CRSNP) is an inflammatory disease of the upper airways characterized by persistent inflammation of the nasosinus mucosa and polyp formation, presenting with nasal obstruction, rhinorrhea, facial pressure, and hyposmia/anosmia, in addition to a substantial impact on quality of life and productivity. Despite standard management—which includes high-dose intranasal corticosteroids, strict control of comorbidities, and, when necessary, cycles of systemic corticosteroids and/or endoscopic surgery—a significant proportion of patients remain refractory or experience early recurrence after surgical intervention. This scenario largely reflects the biological heterogeneity of CNCRSI and the predominance of phenotypes/endotypes associated with type 2 (Th2) inflammation, in which cytokines such as IL-4, IL-13, and IL-5, in addition to IgE and epithelial mediators (e.g., TSLP), sustain a chronic, eosinophilic inflammatory microenvironment.

Recognition of this immunoinflammatory architecture has repositioned CRSN as a candidate disease for targeted therapies. Monoclonal antibodies that block critical pathways of type 2 inflammation—such as the IL-4/IL-13 shared receptor (dupilumab), IgE (omalizumab), IL-5/IL-5R (mepolizumab, benralizumab), and, more recently, TSLP (tezepelumab)—have demonstrated clinically relevant reductions in nasal polyp scores, congestion, and functional outcomes (e.g., smell and SNOT-22), as well as a reduced need for systemic corticosteroids and surgical reintervention. The benefit tends to be more pronounced in patients with type 2 comorbidities (asthma and respiratory disease exacerbated by NSAIDs), highlighting the importance of endotype stratification for therapeutic

selection.

At the same time, there is a growing demand for standardized criteria for indication and response evaluation, with objective goals at 16–24 weeks (reduction in NPS, relevant symptomatic improvement, and olfactory recovery), as well as for strategies for sequencing, switching, or discontinuation in non-responders. Issues of access and cost-effectiveness, especially in public systems, reinforce the need for clinical algorithms that integrate severity, surgical history, biomarkers, and patient preferences.

In this context, this article critically reviews the contemporary evidence on the use of biological therapies in CRPS, addressing efficacy, safety, target populations, monitoring, and gaps for research, in order to guide practical and individualized decision-making.

## RESULTS

In higher-quality clinical trials, monoclonal antibodies demonstrated consistent benefits as adjunctive therapy to standard treatment in patients with chronic rhinosinusitis with uncontrolled nasal polyposis. Dupilumab, by blocking the shared IL-4/IL-13 receptor, significantly reduced nasal polyp scores, nasal congestion/obstruction, and tomographic opacification in phase III studies (SINUS-24/52), with clinically relevant gains in SNOT-22 and olfactory function; these effects were consistently observed in subgroups with associated asthma and NSAID-exacerbated respiratory disease, regardless of surgical history. Omalizumab, which targets IgE, showed endoscopic improvement in polypoid volume and self-reported symptoms in the POLYP-1/2 RCTs, supporting its use as an adjunctive option, especially in the allergic phenotype. On the IL-5 axis, mepolizumab reduced polyp size, nasal obstruction, and, importantly, the need for revision

surgery in the phase III SYNAPSE study, while benralizumab, which promotes eosinophil depletion via IL-5R $\alpha$ , improved NPS, congestion, and smell in OSTRO, with a favorable safety profile. More recently, blocking the epithelial alarm TSLP with tezepelumab demonstrated a reduction in NPS and congestion and a decrease in the use of systemic corticosteroids and surgical interventions in phase III results (WAYPOINT), suggesting usefulness in scenarios of mixed type 2 inflammation or suboptimal response to other target pathways. Overall, studies converge on a reduction in symptoms, inflammatory burden, and events requiring systemic corticosteroid therapy and/or reintervention, with the magnitude of benefit varying according to endotype (eosinophilia, atopy, asthma comorbidity), surgical history, and follow-up time. Safety was generally consistent with the known profiles of each agent, with predominantly mild to moderate adverse events and low discontinuation rates.

## CONCLUSION

Biological therapies have established themselves as a pillar in the management of chronic rhinosinusitis with nasal polyposis refractory to standard care, consistently reducing polypoid volume, congestion, the need for systemic corticosteroid therapy and reinterventions, as well as improving smell and quality of life. Among the available agents, IL-4/IL-13 blockade (dupilumab) offers broad and robust benefits in different disease profiles; anti-IgE (omalizumab) is particularly useful in atopic phenotypes; IL-5/IL-5R axis inhibitors (mepolizumab, benralizumab) are rational in the eosinophilic phenotype; and anti-TSLP (tezepelumab) emerges as a promising alternative for mixed type 2 inflammation or suboptimal response to distal targets.

Clinical adoption should be guided

by phenotype-endotype stratification, comorbidities (asthma, NSAID-exacerbated respiratory disease), surgical history, and patient-centered goals, accompanied by objective monitoring at 16–24 weeks (NPS, congestion, SNOT-22, smell, systemic corticosteroid use) to classify response and decide on continuation, topical optimization, or mechanism change. In systems with

access restrictions, prioritizing severe cases with multiple surgeries or high dependence on systemic corticosteroids maximizes clinical value and cost-effectiveness.

Significant gaps remain—lack of direct comparisons between biologics, universal predictive biomarkers, optimal treatment duration, and step-down or discontinuation strategies—which

require pragmatic, long-term studies. Until these answers are available, the judicious and individualized use of biologics, anchored in current guidelines and clear response targets, represents the best strategy for transforming outcomes into RSCPN and reducing the burden of disease for patients and healthcare systems.

## References

- Bachert C, Han JK, Desrosiers M, et al. Efficacy and safety of dupilumab in patients with severe chronic rhinosinusitis with nasal polyps (LIBERTY NP SINUS-24 and SINUS-52). *Lancet*. 2019;394(10209):1638-50.
- Gevaert P, Omachi TA, Corren J, et al. Efficacy and safety of omalizumab in nasal polyposis. *J Allergy Clin Immunol*. 2020;146(3):595-605.
- Han JK, Bachert C, Fokkens W, et al. Mepolizumab for chronic rhinosinusitis with nasal polyps (SYNAPSE): a phase 3 trial. *Lancet Respir Med*. 2021;9(10):1141-53.
- Bachert C, Han JK, Wagenmann M, et al. Efficacy and safety of benralizumab in chronic rhinosinusitis with nasal polyps (OSTRO). *J Allergy Clin Immunol*. 2022;149(4):1309-17.e12.
- Fokkens WJ, Lund VJ, Hopkins C, et al. European position paper on rhinosinusitis and nasal polyps 2020 (EPOS2020). *Rhinology*. 2020;58(Suppl S29):1-464.
- Orlandi RR, Kingdom TT, Hwang PH, et al. International consensus statement on allergy and rhinology: rhinosinusitis 2021 (ICAR-RS-2021). *Int Forum Allergy Rhinol*. 2021;11(3):213-739.
- Fokkens WJ, Alobid I, Bachert C, et al. EPOS/EUFOREA update on indication and evaluation of biologics in CRSwNP. *Rhinology*. 2023;61(4):290-302.
- Lee KI, Rudmik L. Biologics for chronic rhinosinusitis with nasal polyps. *Rhinology*. 2025;Epub ahead of print.
- Lombardo N, Pelaia C, Terracciano R, et al. Real-life effects of omalizumab on chronic rhinosinusitis with nasal polyps. *J Clin Med*. 2023;12(23):7338.
- Fujieda S, Matsune S, Takeno S, et al. Dupilumab efficacy irrespective of eosinophilic chronic rhinosinusitis status. *Allergy*. 2022;77(3):834-44.
- Fokkens W, Bachert C, Han JK, et al. Surgery endpoints in SYNAPSE: impact of mepolizumab on need for revision surgery. *Rhinology*. 2023;61(2):151-60.
- Lipworth BJ, Bachert C, Han JK, et al. Tezepelumab in severe chronic rhinosinusitis with nasal polyps (WAYPOINT). *N Engl J Med*. 2025;Epub ahead of print.
- Amgen; AstraZeneca. Positive results from TEZSPIRE (tezepelumab-ekko) Phase 3 WAYPOINT [press release]. 2025 Mar 1 [cited 2025 Oct 14]. Available from: Manufacturer website.
- National Library of Medicine (US). ClinicalTrials.gov Identifier: NCT04851964 – Efficacy and Safety of Tezepelumab in CRSwNP (WAYPOINT). 2021– [cited 2025 Oct 14]. Available from: <https://clinicaltrials.gov/ct2/show/NCT04851964>
- Genentech/Novartis. Xolair (omalizumab) – chronic rhinosinusitis with nasal polyps: indication and use. 2025 [cited 2025 Oct 14]. Available from: <https://www.xolairhcp.com/>
- Bachert C, Ebmeyer J, Toppila-Saarivirta E, et al. Benralizumab in severe eosinophilic asthma and chronic rhinosinusitis with nasal polyps: an updated review. *Ther Adv Respir Dis*. 2024;18:Epub ahead of print.
- Marglani O, Alanazi A. Management of chronic rhinosinusitis with nasal polyps: current concepts. *Cureus*. 2023;15(9):e44521.
- Fokkens WJ, Lund V, Bachert C, et al. EUFOREA consensus on biologics for CRSwNP with and without asthma. *Allergy*. 2019;74(12):2312-9.
- Lipworth BJ, Vaidyanathan S. Reappraisal of biologic efficacy from phase 3 trials in CRSwNP. *J Allergy Clin Immunol Pract*. 2025;Epub ahead of print.
- European Rhinologic Society. EPOS 2020 pocket guide. Ghent: ERS; 2020.