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Editorial

Highlights of the Spanish Asthma Guidelines (GEMA), Version 5.4

Aspectos destacados de la Guía Española para el Manejo del Asma (GEMA), versión 5.4

The Spanish Asthma Guidelines, commonly known as GEMA (Guía Española para el Manejo del Asma), is an evidence-based clinical practice guide for asthma management. Developed by a panel of experts representing 18 national and international scientific societies, GEMA is the primary Spanish-language reference for asthma globally. It exerts a significant influence on healthcare professionals in Spain, Portugal, and Latin American countries.

Rather than being an exhaustive collection of all scientific knowledge on the subject, it is a brief document containing essential information to assist healthcare professionals (specialized and non-specialized in asthma) in providing high-quality clinical care to their patients. As a result, it is a clear and concise guide, possessing crucial characteristics necessary for its successful application. Access to this resource is available for free download in various formats at www.gemasma.com. Particularly noteworthy is the existence of an artificial intelligence tool (iaGEMA) developed exclusively on these guidelines, which has shown exceptional responsiveness in assisting clinicians in making immediate decisions. While currently restricted to Spain, we expect it to become downloadable in other countries soon.

A prominent characteristic of GEMA is its yearly content revisions, meticulously conducted by members of the GEMA Executive Committee, with the support of the Pro-GEMA Commission (consisting of 4 external experts not affiliated with the GEMA Committee), who carefully choose asthma-related articles from indexed journals published in the previous year. These articles form the basis for the main modifications in the annual update of GEMA. The ongoing 5th phase of the guide in 2024 has advanced to update 5.4.[1]

While previous editions of GEMA updates introduced significant novel features, especially therapeutic ones, version 5.4 may not seem as remarkable at first glance. However, it remains equally relevant. The following text summarizes these changes.

In the epidemiological field, the inclusion of overweight or obese status during pregnancy as a novel risk factor for the development of asthma has been observed, owing to a study conducted in California involving 104,467 children, which revealed a slightly but significantly elevated prevalence of asthma.[2] Furthermore, extreme climate variations (hurricanes, tornadoes, thunderstorms, sandstorms, snowstorms, heat waves) have been identified as triggers for asthma crises or exacerbations, supported by a systematic literature review indicating elevated asthma morbidity and mortality risks in children and women.[3]

In the clinical setting, novel and robust evidence has emerged, highlighting the impact of recurrent exacerbations on asthma future risk. This results in an accelerated decline in pulmonary function and potentially diminished response to subsequent treatments.[4–6] Previous data on this topic were based on older studies with limited cohorts. However, recent studies strongly confirm these findings in significantly larger patient populations. For instance, Soremekun et al.[4] evaluated a dataset of 109,182 individuals, revealing that each additional exacerbation led to an estimated additional decrease of −1.34 L/min PEF per year (95% CI −1.23 to −1.50). Patients aged 18–24 years at baseline who experienced more than 2 asthma exacerbations per year suffered an additional −5.95 L/min PEF/year (95% CI −8.63 to −3.28) loss compared to those without exacerbations.

As a new concepts approach, this edition includes the most relevant conclusions of the recent REMAS (acronym from REMision in ASthma) consensus achieved by 120 experts coming from GEMA and SEPAR (Spanish Respiratory Society) Asthma Forum.[7] Among various innovations, it designates a three-year timeframe for ascertaining the potential achievement of complete remission or a proposal of a new subtype of complete remission, "remission in asthma and rhinosinusitis with nasal polyposis (RSC-PN)", when both conditions coexist in a patient. In the pediatric asthma field, the notions of "transition" and the "factors facilitating the transition" across different care levels, from pediatric to adult healthcare, during the shift from childhood to adulthood in asthmatic patients, are delineated. These concepts were produced by national[8] or international[9] working groups.

The section on Severe Asthma includes findings that validate the use of Dupilumab for individuals with elevated exhaled nitric oxide (FeNO > 25 ppb).[10] This applies regardless of eosinophil levels and other clinical attributes.

One of the most innovative and original contributions of GEMA 5.4 is the incorporation of combined treatment scenarios for patients with severe asthma (whether controlled or not, with or without monoclonal antibodies) and RSC-PN (whether previously surgically treated or not).[11] The rationale for this initiative arises from the observation that existing guidelines, such as GEMA and

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POLINA (Spanish acronym for "chronic rhinosinusitis and nasal polyposis consensus"), offered separate therapeutic approaches for each condition, overlooking the unique considerations that arise when both conditions manifest in a single patient. This combined scenario, on the other hand, is not uncommon in severe uncontrolled asthma (SUA). Consequently, a collaborative effort involving the authors of both guidelines was undertaken to identify eight potential clinical combinations and propose corresponding therapeutic strategies, acknowledging the limited evidence supporting some of these recommendations. Nevertheless, the authors believed that these recommendations could offer practical guidance to clinicians as further evidence is gathered.

Regarding the management of severe asthma, the document addresses potential reasons for inadequate responses to biological treatments in SUA[12] and outlines a systematic approach involving five sequential steps before switching to a new biological treatment. These steps include assessing and addressing low treatment adherence, identifying and managing comorbidities, categorizing exacerbations as infectious or inflammatory, reassessing the inflammatory phenotype, and considering alternative biological agents or supplementary treatments such as azithromycin or thermoplasty if needed.[13]

Furthermore, this version introduces updated criteria for continuous oral glucocorticoid therapy (corticosteroid dependence) in asthma based on the recent Spanish consensus.[14]

The updated diagnostic and therapeutic criteria for eosinophilic granulomatosis with polyangiitis (EGPA) have been revised in alignment with international standards[15] and include the results of the MANDARA study comparing the efficacy between Benralizumab and Mepolizumab.[16]

However, one of the most significant innovations of this latest edition is the concurrent release of the updated version of GEMA Patients.[17] This document conveys the most pertinent information about GEMA in informal, lay language for individuals who are not healthcare professionals. The latest iteration of GEMA Patients is the third version, following the editions from 2005 to 2015. These editions were warmly welcomed by both healthcare practitioners and patients, with some facilities even using them as a supplementary resource for patients and caregivers as part of their Asthma Education Programs.

We believe that this new version, GEMA 5.4, will achieve at least the same level of recognition as its predecessors, along with extensive reach and influence among healthcare providers. This will enhance their education and, in turn, improve the standard of care they provide to their patients, which is the ultimate goal of these collective efforts.

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Authors' contributions

- VP: designed contents and wrote the manuscript draft.
- MB: revised, corrected and approved the final manuscript.
- JF: revised, corrected and approved the final manuscript.
- GG: revised, corrected and approved the final manuscript.
- AM: revised, corrected and approved the final manuscript.
- SQ: revised, corrected and approved the final manuscript.
- GSC: revised, corrected and approved the final manuscript.
- CA: revised, corrected and approved the final manuscript.

Conflicts of interest

- VP in the last three years received honoraria for speaking at sponsored meetings from Astrazeneca, Boehringer-Ingelheim, Chiesi, Gebro, GSK, Luminova-Medwell and Sanofi. Received help assistance to meeting travel from Astrazeneca and Chiesi. Act as a consultant for Astrazeneca, Chiesi, GSK and Menarini.
- MB in the last three years received honoraria for advisory and speaking at sponsored meetings from Astrazeneca, GSK, TEVA, SANOFI, Chiesi.
- JF in the last three years received honoraria for speaking at sponsored meetings from Astrazeneca, Bial, GSK, Sanofi, MSD, Tecnimed, Tecnifar, Medinfar and Inmunotek. Received help assistance to meeting travel from Astrazeneca, Bial, GSK, Sanofi, Tecnimed, Tecnifar, Medinfar and Inmunotek.
- GG in the last three years received honoraria for speaking at sponsored meetings from Chiesi, GSK, Novartis and Sanofi. Received help assistance to meeting travel from GSK and Sanofi. Act as a consultant for GSK and Sanofi and received honoraria for investigation clinical trials from GSK, Sanofi, Chiesi, WorldWide, PPD, Insmed, Fortrea, Areteia and AZ.
- AM in the last three years received honoraria for speaking at sponsored meetings from Astrazeneca, Bial, GSK, Leti, Medinfar, TEVA, Takeda and Viatris.
- SQ has been on advisory boards for and has received speaker's honoraria from Allergy Therapeutics, AstraZeneca, Chiesi, GlaxoSmithKline, Gebro, Novartis and Sanofi.
- GSC in the last three years received honoraria for speaking at sponsored meetings from Astrazeneca, Menarini, Aflorfam, Gebro, GSK and Sanofi. Received help assistance to meeting travel from Astrazeneca and Sanofi. Act as a consultant for Astrazeneca and Sanofi.
- CA in the last three years received honoraria for speaking at sponsored meetings from Astrazeneca, Boehringer-Ingelheim, Chiesi, Gebro, GSK, and Sanofi. Act as a consultant for Astrazeneca, Chiesi, GSK and Sanofi.

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