

# Review of: "Severe Cutaneous Adverse Drugs Reactions: From Causes To Mechanisms"

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**Potential competing interests:** The author(s) declared that no potential competing interests exist.

The paper "Severe Cutaneous Adverse Drugs Reactions: from causes to mechanisms" focus an interesting topic and was a good effort to summarize some of the available literature. However, there are some aspects that should be revised:

- English should be revised throughout the manuscript. Additionally, some sentences are interrupted by a period that should not be there (e.g. first sentence of the "results and conclusions" in the abstract; sentence starting with "The task of pharmacovigilance is to provide..." in the introduction).
- Introduction: the first part of the background could be reduced. It is much more general than the major topic of the paper (severe cutaneous reactions to drugs) and seems to be too much explored while other relevant aspects are not included (such non-severe adverse drug reactions as opposed to severe or the relevance of cutaneous symptoms as a manifestation of ADR). Those aspects that support the relevance of your review, e.g. epidemiology, burden..., should be explored in the introduction, especially if not directly approached in the discussion.
- Introduction: the expression "Association to the exhibition for professional reasons" is not clear to me. It might be "exposure due to professional reasons" or "professional exposure"
- Methods: If you choose to present material and methods regarding your review (which I find important), consider providing additional data regarding (at least) the process used to select articles (e.g. inclusion / exclusion criteria) and extract data. In an author review there is no need to present a complete methodological description, but this additional information would strengthen the data you present.
- Results: a section with your results is missing. If you present "materials and methods" for your review, you should also include a results section to describe your findings (and not just a discussion).
- Discussion: the discussion should be improved and reorganized so that the message is better transmitted. Consider including subheadings to facilitate the reorganization. It is not clear which are severe cutaneous ADR or mild / moderate reactions (the authors go from urticaria and rashes (which are mostly non-severe) to TEN and DRESS (which are always severe) and then to contact dermatitis (also typically not included in severe cutaneous adverse reactions)). The characteristics of the reactions are not adequately presented, with the authors reporting that they appear after 15-20 days or within 24-48 hours without further explanation (namely on which types of reactions usually have one or another behaviour). They mix IgE-mediated urticarial eruptions, which, usually, are not considered severe cutaneous drug reactions, with Steven-Johnsons, TEN or DRESS which are typically severe. They should also distinguish allergic reactions from those with different mechanisms. Moreover, the inclusion of drug "rashes" as a clinical presentation of severe cutaneous drug ADR should be explained as most rashes are non-severe. A subheading concerning genetic susceptibility could be included. You should improve the inclusion of references to support your statements (e.g. there

is no reference to support the genetic susceptibility associated with reactions to carbamazepine or abacavir).

- Conclusion: it should be changed to focus on the most relevant aspects of the data you present and should not include new data (such as those concerning the reporting of ADR).