cation stated on the summary of characteristics for use in patients with creatinine clearance rates <60ml/min, due to the risk of lactic acidosis. However, it can be used in patients with glomerular filtration rates (GFR) of as low as 30ml/min/1.73m^2 [sic].

Based on the recommendations provided by the NICE guidelines and studies such as Shaw et al. and Lipska et al., the authors later suggest a contraindication for metformin in patients with GFR<30ml/min/1.73m^2 and utilisation with precaution in patients with GFR<45ml/min/1.73 with risk factors for developing lactic acidosis, allowing for its use in patients with moderate chronic kidney disease (estimated GFR: 30-50ml/min/1.73m^2).[1]

We published an earlier article in the journal of *Nefrología* on this topic, in which we bring attention to the need for health care professionals that prescribe OAD, especially metformin (this being the OAD indicated in the initial treatment of patients with DM2 and the most heavily used), to be able to do so within the legal framework that regulates its use based solely on the drug summary of characteristics, not guidelines, consensus documents, or isolated studies.[2]

As such, and after reading the editorial in question, we continue with the same doubts that prompted our article. Is it illegal to administer metformin in patients with creatinine clearance rates <60ml/min, as described by the drug summary of characteristics and as recommended by the Spanish Society for Diabetes, which also contraindicates its use in patients with a GFR<60ml/min/1.73m^2?[3]

In addition, nephrologists treat a large number of diabetic patients with various levels of renal failure who are sent from other specialists and later transferred back to them. Should we prescribe medications outside of the guidelines established in their respective summary of characteristics to these patients, without generating potential legal conflicts in a medical society that is becoming more and more judicialised?

With this in mind, we would like to know the opinion of the authors of the aforementioned editorial, and would also like to highlight the need for Spanish research groups studying diabetes to contemplate these aspects when elaborating guidelines or research documents that serve as reference materials for proper medical practice.

Conflicts of interest

The authors declare that they have no conflicts of interest related to the contents of this article.

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Carlos del Pozo-Fernández[1], Carlos Pardo-Ruiz[2], Concepción Sánchez-Botella[3], Ramón López-Menchero[1]

[1] Sección de Nefrología. Hospital Virgen de los Lirios. Alcoy, Alicante. (Spain).

[2] Sección de Endocrinología. Hospital Virgen de los Lirios. Alcoy, Alicante. (Spain).

[3] Medicina de Familia y Comunitaria. Centro de Salud de San Vicente del Raspeig, Alicante. (Spain).

Correspondence: Carlos del Pozo Fernández
Sección de Nefrología, Hospital Virgen de los Lirios, Alcoy, Alicante. (Spain).
delpozo_car@gva.es

Authors reply:

Discrepancies between the summary of characteristics and the recommended use of metformin in the treatment of type 2 diabetes mellitus patients

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To the Editor:

We would like to thank Del Pozo et al.[1] for their interest in our review[2] and their thoughtful question. The use of metformin in patients with a glomerular filtration rate (GFR) <60ml/min/1.73m^2, that is to say, outside of the appropriate range established by the drug summary of characteristics, continues to be a source of substantial controversy, prompting discussion in several recent scientific conferences and consensus documents.[3-5]

The prescription of medications in conditions that fall outside of the recommendations established in summary of characteristics is a common practice in our profession, whenever approved and validated by the scientific community through a process of discussion of pros and cons or with the provision of informed consent. The summary of characteristics is a document that is not set in stone, must contain updated and current information regarding the medication, and tends to be modified whenever aspects of drug safety are updated or new indications come to light. However, this does not always occur, since the cost for modifying technical data sheets can be very high, and this can often produce a situation in which modifications are not cost-effective because the medication in question is quite inexpensive, such as in the case of metformin.

In patients with moderate chronic kidney disease (CKD), the lack of therapeutic alternatives following the interruption of metformin may require the use of much more costly medications (such as dipeptidyl peptidase-4 inhibitors) or insulin treatment, which prompts some reluctance

in the affected patients. In addition, the exclusion of patients with CKD from the majority of clinical trials severely limits the breadth of the therapeutic arsenal available to these individuals, as can be seen in paediatric patients as well. In both situations (children and patients with CKD), it is a lack of conclusive study results, not issues with toxicity or efficacy, that limit the indications described on the drug technical data sheet in many cases. In two publications concerning paediatric patients (both in primary care and the hospital setting)[6-7] that compiled the available data from 11 studies, between 36% and 100% of patients were prescribed medications under conditions that fell outside of the recommended situations described in the drug summary of characteristics.

With this in mind, to address the question posed by Del Pozo et al[1] regarding whether one can say if it is illegal to employ metformin in patients with an estimated GFR<60ml/min/1.73m^2, we can state that the use of metformin in patients with an estimated GFR of 30-60ml/min/1.73m^2 does not fall within the legal regulations governing its use.

As such, and given the important benefits and low costs associated with this drug, we believe that the implicated scientific societies, health authorities, and pharmaceutical companies should place emphatic priority on the process of reviewing the technical data sheet for metformin in the interest of revising it. This modification should establish the indications for administering metformin in patients based on estimated GFR (ml/min/1.73m^2), which is the format recommended by current guidelines and consensus documents,[8] instead of using creatinine clearance values as recommended by the current drug technical data sheet. Secondly, the estimated range of GFR within which metformin can be used should be expanded. This modification, which has already been supported by expert consensus opinion, retrospective and observational studies, and meta-analyses,[3-5] should express the reasonable use of metformin, with precautionary measures taken and reduced doses, in patients with a GFR of 30-60ml/min/1.73m,[2] with interruprion of treatment with metformin in patients with a GFR<45ml/min/1.73m^2 and risk factors for developing lactic acidosis (peripheral hypoperfusion, diabetic foot, heart failure, advanced liver disease, or a history of previous episodes of lactic acidosis or metabolic acidosis).

It is only a matter of time, but the wait until evidence is provided and clinical trials have been completed could involve years of delay in optimising the treatment of hyperglycaemia in patients with CKD among the millions of people afflicted with diabetes mellitus all over the globe.

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José L. Górriz[1], Alberto Martínez-Castelao[2], Eva Sola[3], Carlos Morillas[3], Ana Jover[3], Francisco Coronel[4], Juan F. Navarro-González[5], Fernando de Álvaro[6]

[1] Servicio de Nefrología. Hospital Universitario Dr. Peset. GEENDIAB. REDINREN. S.E.N. Valencia.
[2] Servicio de Nefrología. Hospital Universitario de Bellvitge. IDIBELL. GEENDIAB. REDINREN. S.E.N. Hospitalet de Llobregat, Barcelona. (Spain).
[3] Servicio de Endocrinología. Hospital Universitario Dr. Peset. Valencia. (Spain).
[4] Servicio de Nefrología. Hospital Clínico de San Carlos. Madrid. (Spain).
[5] Servicio de Nefrología. Hospital Universitario Nuestra Señora de Candelaria. GEENDIAB. REDINREN. S.E.N. Santa Cruz de Tenerife. (Spain).
[6] Servicio de Nefrología. Hospital Universitario Infanta Sofía. GEENDIAB. REDINREN. S.E.N. Madrid. (Spain).

Correspondence: José L. Górriz
Servicio de Nefrología.
Hospital Universitario Dr. Peset. Valencia.
jlgorriz@senefro.org

B) BRIEF PAPERS ON RESEARCH AND CLINICAL EXPERIMENTS

Autosomal dominant polycystic kidney disease with contralateral renal agenesis

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To the Editor:

Autosomal dominant polycystic kidney disease (ADPKD) is the most common hereditary cause of terminal chronic renal failure (CRF), with an incidence of 1 in 500-1000. This disease is produced by mutations to the genes *PKD1* (16p13.3, 85%) or *PKD2* (4q22.1, 15%). In ADPKD, the growth of renal cysts produces a progressive increase in renal volume and destruction of the parenchyma, leading to terminal CRF at approximately 50-60 years of age (in PKD1 mutations). Although ADPKD is bilateral, renal involvement may be asynchronous and asymmetrical,[2] and in PKD2 mutations, terminal CRF may