MEDWATCH The FDA Safety Information and Adverse Event Reporting Program

Metformin-containing Drugs: Drug Safety Communication - Revised Warnings for Certain Patients With Reduced Kidney Function

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FDA 檢視醫學研究文獻，重新評估 Metformin 使用於輕度至中度腎功能不佳患者的安全性，結論為 Metformin 可安全的使用於輕度腎功能損傷的患者，和部分中度腎功能損傷的患者，因此 FDA 要求含 Metformin 成分的降血糖藥品將使用於腎功能不全患者的具體建議更新至仿單。

病患是否適合接受 Metformin 治療需考量腎功能損傷的程度，FDA 同時也要求廠商於仿單上修改評估腎功能損傷的檢驗項目，建議以腎小球過濾率(glomerular filtration rate estimating equation (eGFR))取代血清肌酸酐濃度 (blood creatinine concentration)，這是因為除了血清肌酸酐濃度，腎小球濾過率考慮到其他重要的參數，如患者的年齡，性別，種族和/或體重。

建議：

醫療人員開立含 Metformin 成分的降血糖藥物於腎損傷患者時，應遵循最新的仿單建議：

- 開立 Metformin 前，先取得病患腎功能 eGFR 的檢驗數值
- eGFR<30 mL/minute/1.73 m^2 是使用 Metformin 的禁忌
- eGFR 介於 30-40 mL/minute/1.73 m^2 不建議初次使用 Metformin
- 使用 Metformin 治療的患者，每年至少追蹤一次腎功能 eGFR，有增加腎功能損傷風險的人，如年長者，其腎臟功能的監測應該更頻繁
- 使用 Metformin 治療期間，如果 eGFR 低於 45 mL/minute/1.73 m^2 時，需評估繼續使用 Metformin 治療的利弊，一旦 eGFR<30 mL/minute/1.73 m^2 就必須停用 Metformin
- 接受含碘顯影劑造影檢查前，如果病患 eGFR 介於 30-60 mL/minute/1.73 m^2，或是有肝臟、酗酒、心衰竭病史，或是將接受血管攝影的患者，應該暫停使用 Metformin，直到檢查完 48 小時後，評估腎臟功能沒有惡化才能繼續使用 Metformin

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AUDIENCE: Pharmacy, Nephrology, Internal Medicine, Patient

ISSUE: FDA is requiring labeling changes regarding the recommendations for metformin-containing medicines for diabetes to expand metformin's use in certain patients with reduced kidney function. The current labeling strongly recommends against use of metformin in some patients whose kidneys do not work normally. FDA was asked to review numerous medical studies regarding the safety of metformin use in patients with mild to moderate impairment in kidney function, and to change the measure of kidney function in the metformin drug labeling that is used to determine whether a patient can receive metformin.

FDA concluded, from the review of studies published in the medical literature, that metformin can be used safely in patients with mild impairment in kidney function and in some patients with moderate impairment in kidney function. FDA is requiring changes to the metformin labeling to reflect this new information and provide specific recommendations on the drug's use in patients with mild to moderate kidney impairment.

FDA is also requiring manufacturers to revise the labeling to recommend that the measure of kidney function used to determine whether a patient can receive metformin be changed from one based on a single laboratory parameter (blood creatinine concentration) to one that provides a better estimate of renal function (i.e., glomerular filtration rate estimating equation (eGFR)). This is because in addition to blood creatinine concentration, the glomerular filtration rate takes into account additional parameters that are important, such as the patient's age, gender, race and/or weight. See the FDA Drug Safety Communication for additional information, including a data summary and a list of metformin-containing drugs.

BACKGROUND: Metformin-containing medicines are available by prescription only and are used along with diet and exercise to lower blood sugar levels in patients with type 2 diabetes. When untreated, type 2 diabetes can lead to serious problems, including blindness, nerve and kidney damage, and heart disease. Metformin-containing medicines are available as single-ingredient products and also in combination with other drugs used to treat diabetes. The current drug labeling strongly recommends against metformin use in some patients whose kidneys do not work normally because use of metformin in these patients can increase the risk of developing a serious and potentially deadly condition called lactic acidosis, in which too much lactic acid builds up in the blood.

RECOMMENDATION: Healthcare professionals should follow the latest recommendations when prescribing metformin-containing medicines to patients with impaired kidney function. Patients should talk to their health care professionals if they have any questions or concerns about taking metformin.

The labeling recommendations on how and when kidney function is measured in patients receiving metformin will include the following information:

- Before starting metformin, obtain the patient's eGFR.
- Metformin is contraindicated in patients with an eGFR below 30 mL/minute/1.73 m^2.
- Starting metformin in patients with an eGFR between 30-45 mL/minute/1.73 m^2 is not recommended.
- Obtain an eGFR at least annually in all patients taking metformin. In patients at increased risk for the development of renal impairment such as the elderly, renal function should be assessed more frequently.
- In patients taking metformin whose eGFR later falls below 45 mL/minute/1.73 m^2, assess the benefits and risks of continuing treatment. Discontinue metformin if the patient's eGFR later falls below 30 mL/minute/1.73 m^2.
- Discontinue metformin at the time of or before an iodinated contrast imaging procedure in patients with an eGFR between 30 and 60 mL/minute/1.73 m^2; in patients with a history of liver disease, alcoholism, or heart failure; or in patients who will be administered intra-arterial iodinated contrast. Re-evaluate eGFR 48 hours after the imaging procedure; restart metformin if renal function is stable.