Drugs

Information for Healthcare Professionals: Reports of Altered Kidney Function in patients using Exenatide (Marketed as Byetta)

[11/02/2009] FDA has approved revisions to the drug label for Byetta (exenatide) to include information on post-marketing reports of altered kidney function, including acute renal failure and insufficiency.

Byetta, an incretin-mimetic, is approved as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

From April 2005 through October 2008, FDA received 78 cases of altered kidney function (62 cases of acute renal failure and 16 cases of renal insufficiency), in patients using Byetta. Some cases occurred in patients with pre-existing kidney disease or in patients with one or more risk factors for developing kidney problems. From April 2005 through September 2008, more than 6.6 million prescriptions[1] for Byetta were dispensed. Therefore, the 78 reported cases of altered renal function represent a small percentage of the total number of patients who have used the drug.

Some of the 78 patients reported nausea, vomiting, and diarrhea--the most common side effects associated with Byetta in clinical trials. These side effects may have contributed to the development of altered kidney function in the reported cases.

The revisions to the drug label allow healthcare professionals to better weigh the known benefits of Byetta with the potential risks that exist for certain patients. Changes include:

- **Information regarding post-market reports of acute renal failure and insufficiency, highlighting that Byetta should not be used in patients with severe renal impairment (creatinine clearance <30 ml/min) or end-stage renal disease.**
- **Recommendations to healthcare professionals that caution should be applied when initiating or increasing doses of Byetta from 5 mcg to 10 mcg in patients with moderate renal impairment (creatinine clearance 30 to 50 ml/min).**
- **Recommendations that healthcare professionals monitor patients carefully for the development of kidney dysfunction, and evaluate the continued need for Byetta if kidney dysfunction is suspected while using the product.**
- **Information about kidney dysfunction in the patient Medication Guide to help patients understand the benefits and potential risks associated with Byetta.**

This information reflects FDA's current analysis of data available to FDA concerning this drug. FDA intends to update this sheet when additional information or analyses become available.

To report any unexpected adverse or serious events associated with the use of this drug, please contact the FDA MedWatch program using the information at the bottom of the page.

Considerations for Healthcare Professionals:

- Discuss with patients the possibility of developing altered kidney function with Byetta, taking into account the clinical utility of Byetta, the risks/benefits of other antidiabetic therapies, and the risks associated with uncontrolled diabetes mellitus.
- Monitor for the emergence of signs and symptoms of altered kidney function, such as increased serum creatinine, changes in urination (color, frequency, amount), unexplained swelling in the extremities, increases in blood pressure, lethargy, changes in appetite or digestion, or dull ache in the mid to lower back.
- Consider discontinuation of Byetta if kidney dysfunction cannot be explained by other causes.
- Understand that altered kidney function can be a consequence of diabetes, independent of any risk associated with Byetta.
- Discuss with patients that chronic conditions such as hypertension and pancreatitis as well as medications, such as non-steroidal anti-inflammatory drugs (NSAIDs), diuretics, and antihypertensives, can increase the risk of developing altered renal function.
- Inform patients of the signs and symptoms of altered kidney function so they are aware of and able to notify their healthcare professional if they experience any unusual signs or symptoms.
- Tell patients to report nausea, vomiting, or dehydration, as these symptoms may contribute to altered kidney function.

Information for Patients:

- Altered kidney function, including acute kidney failure and renal insufficiency, has been reported in patients using Byetta. Some cases have been associated with dehydration from nausea, vomiting, and diarrhea, which are known side effects of Byetta.
- Reported cases of altered kidney function represent a very small percentage of the total number of patients who have used Byetta.
- Pay close attention for any signs or symptoms of altered kidney function, such as changes in urination (color, frequency, amount), unexplained swelling in the extremities, changes in blood pressure, lethargy, changes in appetite or digestion, or dull ache in mid to lower back.
- Contact your healthcare professional if you experience nausea, vomiting, diarrhea, or dehydration while using Byetta, as these symptoms may increase the likelihood of developing altered kidney function.

- Do not stop or change medicines that have been prescribed without first talking with your healthcare professional.
- Review the Medication Guide that accompanies each prescription of Byetta. It is provided to help patients understand the benefits and potential risks associated with Byetta.

Data Summary:
FDA has completed a review of 78 cases of altered kidney function reported in patients with diabetes using Byetta. The cases were reported to FDA's Adverse Event Reporting System (AERS) between April 28, 2005 and October 29, 2008. Sixty-two of the cases were classified as acute renal failure and 16 cases were classified as renal insufficiency. Cases of acute renal failure or insufficiency occurred as soon as 3 days and up to 2 years after initiation of Byetta. The patient ages ranged from 23 to 83 years, with an average age of 60 years.

The majority of patients, 74/78 (95%), had at least one contributory risk factor for altered kidney function, such as cardiac insufficiency, hypertension, pancreatitis, rhabdomyolysis, and urinary tract infection, as well as concomitant medications such as antiretrovirals, antihypertensives, diuretics, and non-steroidal anti-inflammatory drugs (NSAIDs). These factors could independently increase the risk for developing altered kidney function. Forty-two patients (54%) reported symptoms associated with volume depletion, such as diarrhea, and/or vomiting, which are also known risk factors for altered kidney function and are the most commonly reported adverse events associated with the use of Byetta.

Hospitalization was required in 71 of 78 (91%) patients and there were 4 deaths reported in the cases reviewed. Eighteen patients required dialysis and two patients required kidney transplantation after initiation of Byetta. Of those patients who required dialysis, six had no prior history of altered kidney function, two had a prior history of altered kidney function, and the remaining 10 patients reported no information regarding prior renal history.

Byetta was discontinued in 63 of 78 (80%) patients, with 39 (50%) patients reporting improved signs and symptoms after discontinuation of the drug. One patient experienced recurrent altered kidney function after re-initiation of Byetta.

Notably, 14 of the cases had past medical histories of chronic kidney disease, including four with chronic renal failure, despite recommendations against the use of Byetta in these patients in the current prescribing information.

Due to the serious potential consequences of altered kidney function and temporal relationship between the development of renal effects and initiation of Byetta, FDA has approved revisions to the drug label for Byetta to describe this risk.

References:
1. SDI Vector One®: National (VONA). clearance # C100003-2008-1392. received 10/15/2009.

Related Information

- Exenatide (marketed as Byetta) Information

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