INVOKANA

LITIGATION UPDATE

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WHAT IS INVOKANA?

Invokana is a Type II diabetes medication that belongs to a class of drugs known as SGLT2 Inhibitors.

SGLT2 (sodium glucose co-transporter 2) is a protein that aids the body in its reabsorption of glucose (blood sugar) into the blood stream through the kidneys.

Invokana works by inhibiting SGLT2 and blocking the reabsorption of glucose in the kidneys. The excess glucose goes through the kidneys and is passed out through the urine, and blood glucose levels are lowered.

WHAT IS INVOKANA?

Approved as a Type II Diabetes Medication

Promoted Off-Label for Type I Diabetic Patients and for Weight Loss

Farxiga and Jardiance – Separate Litigations

WHO ARE DEFENDANTS?

Janssen Pharmaceuticals

Johnson & Johnson*

* Mitsubishi Tanabe Pharma Corporation was originally sued as a Defendant. In the MDL, this corporation is being dismissed without prejudice pursuant to the terms set forth in CMO 7.

INVOKANA INJURIES?

Diabetic Ketoacidosis

Kidney Injury

Amputations

Bone Fracture

Urinary Tract Infections

Cardiovascular/Stroke

DIABETIC KETOACIDOSIS

Serious complication of diabetes that occurs when there are high levels of blood acids called “ketones.” Ketones normally develop when the body is unable to produce enough insulin.

Insulin metabolizes glucose so the glucose can enter the cells as an energy source. When the body fails to produce enough insulin, glucose utilization is reduced and the body uses fat as an alternate fuel source. Ketones are produced as a byproduct of this process.

Typically DKA is seen in Type I diabetes patients and is diagnosed through tests that reveal: (1) elevated ketones in the the blood or urine; (2) elevated serum glucose; (3) ABG pH of < than 7.3; and/or (4) serum bicarbonate ≤ than 18 mEq per L.

However, Invokana-related DKA is being seen in Type II diabetes patients and the testing is revealing elevated ketones in the blood with normal or near-normal serum glucose counts. Further there is science specific to Invokana-related DKA that states not to use the urine ketone levels in making the diagnosis of DKA.

ACUTE KIDNEY INJURY

Health Canada performed safety review showing causal link announce in October 2015

Between March 2013 to October 2015, the FDA confirmed 73 adverse events of acute kidney injury associated with Invokana.

More than half the cases occurred within 1 month of Invokana being initiated.

Most cases required hospitalization with some resulting in death or permanent injuries

There may be kidney events associated with DKA.

STROKE/CARDIOVASCULAR INJURIES

FDA Advisory Committee

- At time of approval an FDA reviewer noted "an imbalance in early cardiovascular events" in the CANVAS trial, a 4,300-subject study assessing the cardiovascular effects of Invokana.
- In the first 30 days of use in the clinical trial, Invokana had a cardiovascular events "Hazard Ratio" of 6.9: i.e., that patients who were taking Invokana had a 690% higher likelihood of suffering a cardiovascular event than the patients who were taking placebo. (13 heart attacks/strokes in Invokana group vs. 1 in placebo group) In response to a question whether FDA Advisory Committee members had safety concerns about Invokana's cardiovascular risk, 8 voted "yes" and 7 voted "no"
- FDA approved Invokana but required completion of cardiovascular outcomes study (CANVAS) and 4 other post-marketing trials. Study completed in February 2017; Full CANVAS results not due until June 2017

Invokana has an acute diuretic effect. This could destabilize a patient with underlying coronary artery disease.

RAPIDLY CHANGING WARNINGS

- March 2013 – Invokana is Launched
- May 2015 – FDA issues Safety Announcement Regarding DKA
- September 2015 – FDA issues Safety Communication Regarding the Increased Risk of Bone Fractures
- October 2015 – Health Canada Announces Safety Review Had Revealed Evidence of Causal Link between Invokana and Acute Kidney Injury
- December 2015 – Warnings and Precaution Section Amended to Include DKA Warning and Severe Urinary Tract Infections

RAPIDLY CHANGING WARNINGS

- January 2016 – FDA Issues Safety Announcement Regarding Increased Risk of Bone Fracture
- May 2016 – FDA issues Safety Alert regarding Interim Safety Results that Revealed an Increase in Leg and Foot Amputations
- June 2016 – Warnings and Precaution Section Amended to Include Kidney Failure Warning
- August 2016 – Warnings and Precaution Section Amended to Include “Fatal” DKA Warning
- 2017 – CARDIOVASCULAR? June 2017

STATUS OF INVOKANA MDL

On December 7, 2016, MDL created by JPML and actions transferred to Judge Brian R. Martinotti of the District of New Jersey.

Prior to JPML transfer, Judge Martinotti had been transferred all DNJ Invokana actions.

- December 16, 2016 Protective Order
- December 26, 2016 ESI Protocol

STATUS OF INVOKANA MDL

295 Cases Filed as of April 21, 2017

Approx. 1.1 Million Documents Produced (Approx. 14 Million Pages)

Relevant Case Management Orders Entered:

- CMO 2 – Order Appointing Plaintiff Steering Committee
- CMO 4 – Direct Filing Order
- CMO 5 – Science Day – July 19, 2017
- CMO 6 – Common Benefit Order
- CMO 7 – Dismissal of Mitsubishi Tanabe Pharma Corporation
- Letter from Court - CM/ECF Registration is required

STATUS OF INVOKANA MDL

Case Management Orders to Look Out For:

- Service of Complaints and Defendants' Answer
- Plaintiff Fact Sheet/Defendant Fact Sheet
- "Unbundling" of Plaintiffs on Single Complaint
- Discovery Schedule/Selection of Bellwether Cases
- Privilege Log
- *Ex Parte* Contact with Healthcare Providers
- *Ex Parte* Contact with Current/Former Employees

STATE COURT LITIGATIONS

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