Management of Reported Side Effects of Patients Initiating Therapy on dimethyl fumarate

Jaspreet Abraham, RN, BSN, MSCS, Victoria Stokes, RN, BSN, Gina Remington, RN, BSN, MSCN, Diana Logan, RN, FNP-C, BC, MSCN, Teresa Frohman, MPAS, PA-C, Elliot Frohman, MD, PhD, FAAN

University of Texas Southwestern Medical Center at Dallas, Department of Neurology and Neurotherapeutics

**Objective**

To characterize patient-reported side effects in multiple sclerosis (MS), patients treated with dimethyl fumarate, and to ascertain whether pre-emptive symptom management strategies could impact upon these side effects and ultimately on treatment adherence.

**Background**

Dimethyl fumarate is an oral medication approved by the FDA in April 2013 for the treatment of relapsing-remitting Multiple Sclerosis (RRMS). Phase III pivotal clinical trials revealed common adverse events related to dimethyl fumarate (previously designated as BG-12), including flushing, diarrhea, nausea, abdominal pain, and itching. In an attempt to proactively manage these well-recognized, and not infrequently limiting side effects, providers recommended pre-treatment with a variety of medications including aspirin, anti-histamine agents, anti-cholinergic (e.g. glycopyrrolate) agents, and bismuth subsalicylate.

**Design/Methods**

In our large, academic, Clinical Center for MS at UT Southwestern Medical Center, 66 MS patients treated with dimethyl fumarate were systematically evaluated for treatment-associated symptoms, and their potential management. Patients were transitioned from various disease modifying therapies such as interferon beta-1a, interferon beta-1b, glatiramer acetate, azathioprine, fingolimod, natalizumab, or rituximab. Patients were followed via telephone and secure EMR messages. Additionally, data was collected at a clinical follow-up visit 3 months after initiating treatment with the new disease modifying therapy. Providers requested surveillance laboratory studies including complete baseline blood work (CBC and CMPL) as well as follow-up studies with CBC and CMPL repeated monthly for the first 3 months.

**Results**

Regardless of the symptom being reported, patients most commonly reported side effects as they titrated from the starting dose of 120 mg twice daily, to the maintenance dose of 240 mg twice daily. Similar to the Phase III clinical findings, patients most commonly reported flushing, abdominal pain, diarrhea, nausea, vomiting, and itching. Low dose aspirin (81mg BID) was recommended for flushing. Diphenhydramine or cetirizine was recommended for patients who experienced itching or rash. In some cases we prescribed bismuth subsalicylate or with prescription medicines montelukast and glycopyrrolate.

**Conclusions**

66 patients transitioned to dimethyl fumarate following final FDA approval and were monitored for reported adverse side effects. In a real-world environment, patients experienced symptoms including flushing, abdominal pain, diarrhea, and itching. These common side effects can be managed in the majority of patients if pre-treated with aspirin, diphenhydramine, cetirizine, loperamide or bismuth subsalicylate or with prescription medicines montelukast and glycopyrrolate.

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**References**

1. Jaspreet Abraham, RN, BSN, MSCS, Victoria Stokes, RN, BSN, Gina Remington, RN, BSN, MSCN, Diana Logan, RN, FNP-C, BC, MSCN, Teresa Frohman, MPAS, PA-C, Elliot Frohman, MD, PhD, FAAN. Management of Reported Side Effects of Patients Initiating Therapy on dimethyl fumarate. UT Southwestern Medical Center, Department of Neurology and Neurotherapeutics.

2. University of Texas Southwestern Medical Center at Dallas, Department of Neurology and Neurotherapeutics.

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