

## DYSAUTONOMIA INTERNATIONAL



AWARENESS



ADVOCACY



ADVANCEMENT

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Dear Preferred Shares Mylan Independent Board,

Dysautonomia International is a non-profit patient advocacy organization based in New York. We advocate for patients living with disorders of the autonomic nervous system in the US and abroad.

We would like to express our concern regarding the possible takeover of Mylan N.V. by Teva Pharmaceutical Industries Ltd. Our concern is that this organizational change may lead to shortages of midodrine, an essential drug for the patient population we serve. We are also concerned that this takeover will result in price increases, reduced competition and limited access to generic medications.

### **Background**

Mylan is one of the largest generic manufacturers in the world of midodrine hydrochloride (“midodrine”). Midodrine is an alpha-receptor agonist that results in constriction of the blood vessels, producing an increase in blood pressure. Midodrine is used to treat low blood pressure associated with numerous disorders of the autonomic nervous system, including neurogenic orthostatic hypotension, postural orthostatic tachycardia syndrome, orthostatic intolerance, multiple system atrophy and autonomic neuropathies. Most of these conditions are rare diseases, but collectively, they impact over 70 million people worldwide.

Due to a malfunction or loss of autonomic nerve fibers that control the blood vessels, these patients have blood pressure so low that they cannot stand up. Low blood pressure leads to frequent fainting, which can result in falls, injuries and even death. The functional disability seen in these patients is severe. Imagine being so lightheaded that you can't stand up without losing your vision, you can't think clearly because of limited blood flow to your brain, and you faint within 30 seconds of standing upright. Many patients who rely on midodrine would not be able to stand, walk, or even sit upright in a chair without this medication.

In the US, midodrine is one of only two drugs approved by the Food & Drug Administration to treat orthostatic hypotension, and it is lawfully prescribed by physicians to treat the other autonomic disorders listed above. Droxidopa, the other drug approved to treat orthostatic hypotension in the US, is not an exact replacement

for midodrine, as it works through a different physiological mechanism. Switching from midodrine to droxidopa is not an option for many patients with autonomic disorders as droxidopa increases blood pressure by increasing norepinephrine levels. Many patients already have excessive norepinephrine levels. Further increasing norepinephrine levels would worsen symptoms worse in these patients, thus it is important that midodrine remains available as an option for these patients.

Between April 2014 and April 2015, 928,833 prescriptions for midodrine were filled in the US. The demand for midodrine in the US is growing significantly, having almost doubled within the past five years. This is likely due to increased awareness of autonomic disorders, resulting in additional diagnoses, as well as the aging of the baby boomer generation. Some autonomic disorders that are treated with midodrine are more common in adults age 60 and over.

In the US, midodrine is manufactured by Mylan (55.8% of the market), Upsher-Smith (20.6%), Sandoz (12.6%) and Global (10.1%).

### **Stakeholder Concerns**

Compared to the other drugs within Mylan's portfolio, midodrine, as a rare disease drug, is not a big money maker. Since midodrine is not high on the list of Mylan's profit generating products, and since Teva has predicted \$2B in cost savings if it acquires Mylan, we are very concerned that Teva may choose to discontinue production of midodrine after acquiring Mylan. This would result in devastating consequences for our patient community.

**Drug Shortages** - With Mylan having 55.8% of the market, it would be difficult for other manufacturers to meet Mylan's production and distribution capabilities in a timely manner, if ever. Being that midodrine is not likely a money maker for the other generic companies either, it's possible that none of the other companies would seek to increase production or would have the capability of doing so. Even a temporary disruption in production can result in drug shortages that last months or years, as has been seen with other pharma products in the US in recent history (intravenous saline and generic hydroxychloroquine have both been in short supply for over a year and US regulators have done nothing to address this).

**Increased prices** - For a generic drug, midodrine is actually quite expensive in the US. Patients without insurance spend an average of \$500-\$1000 US per month to fill their midodrine prescriptions. Loss of competition and drug shortages will increase prices even further, resulting in harm to patients who are already financially disadvantaged, as many of them cannot work due to their health problems.

**Reduced Access To Care** - Both drug shortages and increased prices reduce overall access to the drug, presenting serious concerns for patients who have no other drug options, who literally can't stand up without taking midodrine several times per day.

**Increased Human Suffering and Death** - Patients with severe orthostatic hypotension who cannot access midodrine will become bedridden, unable to stand without fainting. Fainting results in falls that can cause broken bones, brain injuries and in some cases, death. Additionally, patients who cannot stand or walk due to untreated orthostatic hypotension become physically deconditioned quite rapidly, which leads to osteoporosis, loss of muscle mass, cardiac deconditioning, blood clots, depression and an overall increased risk of mortality.

**Increased Burden on Families** - Patients who cannot access midodrine will become even more functionally disabled than they currently are, which places increase economic and social strain on the families of these patients. Caregivers may have to stop working to care for bedridden patients full-time.

**Increased Burden on Society** - Loss of access to midodrine will result in increased hospitalizations and emergency room (A&E) visits for patients with autonomic disorders. This increases the strain on the overall healthcare system, as well as private and public health insurers. Patients who are no longer able to work due to the loss of midodrine are more likely to become dependent on the state.

**Loss of Overall Competition** - After a flurry of mergers and acquisitions over the past few years, there are only four large generic drug companies left: Teva, Mylan, Novartis (Sandoz) and Abbott. Combined, these companies control 43% of the marketplace. If Teva and Mylan merged, the combined company would control one-third of all prescriptions issued in the US and the next largest competitor would control only 10%. Less competition means higher drugs costs for consumers. Fewer large generic companies means fewer companies with the capability of addressing other drug shortages that may occur, and fewer pharmaceutical companies willing to take on high risk, low yield rare disease drugs.

## **Conclusion**

Given their focus on cost savings for shareholders, it seems unlikely that Teva will continue manufacturing midodrine. Mylan is a trusted source of this drug for our patient population around the world. In the event that the Teva/Mylan acquisition does proceed, we hope that measures will be put into place to ensure that Teva will be able to meet current and future global demand for midodrine and other rare disease drugs that Mylan currently manufactures.

We ask the Preferred Shares Mylan Independent Board to take our stakeholder concerns into consideration. There are serious real life consequences for millions of everyday people resulting from the decisions you will make. Please consider the impact these decisions will have on patients around the world.

Respectfully submitted,



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on behalf of the Board of Directors  
of Dysautonomia International

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