



MAYNE PHARMA RECEIVES FDA APPROVAL OF TOLSURA™ (SUBA®-ITRACONAZOLE CAPSULES) FOR THE TREATMENT OF CERTAIN FUNGAL INFECTIONS

12 December 2018, Adelaide Australia: Mayne Pharma Group Limited (ASX: MYX) is pleased to announce that the US Food and Drug Administration (FDA) has approved the New Drug Application (NDA) for Tolsura™ (SUBA®-itraconazole) 65mg capsules. Tolsura is a new formulation of itraconazole indicated for the treatment of certain systemic fungal infections in adult patients.

Tolsura is indicated for the treatment of blastomycosis (pulmonary and extrapulmonary), histoplasmosis (including chronic cavitory pulmonary disease and disseminated, non-meningeal histoplasmosis) and aspergillosis (pulmonary and extrapulmonary, in patients who are intolerant of or who are refractory to amphotericin B therapy). These serious infections most commonly occur in vulnerable or immunocompromised patients, for example, those with a history of cancer, transplants (solid organ or bone marrow), HIV/AIDS, or chronic rheumatic disorders, and are often associated with high mortality rates or long-term health issues.

Mayne Pharma's CEO, Mr Scott Richards said "We are very pleased to have received FDA approval of this patented formulation of itraconazole which incorporates Mayne Pharma's proprietary SUBA technology to improve the bioavailability of poorly soluble drugs. Reformulation of existing drugs plays an important role in improving patient compliance and clinical outcomes. We are proud to offer a new treatment option for patients with these life-threatening infections. We believe physicians will appreciate having access to Tolsura, which has been shown in clinical studies to have increased bioavailability and significantly reduced variability when compared to conventional oral itraconazole capsules."

"After many years of research and development and working closely with key global opinion leaders in infectious disease management, Tolsura represents a major milestone in the SUBA (SUper-BioAvailable) drug delivery platform at Mayne Pharma."

The Company will directly commercialise Tolsura and plans to launch in January 2019 with a new institutional sales team focused primarily on hospital-based infectious disease specialists. Tolsura has four granted patents from the United States Patent and Trademark Office with expiry dates ranging from 2023 to 2033.

The US anti-fungal triazole market has a current value of US\$600m according to IQVIA and based on the clear unmet clinical need in serious systemic infections, the addressable market is estimated at US\$200m¹.

Mayne Pharma directly markets more than 60 products in the US including three patent protected dermatology products Fabior® (tazarotene) foam, Sorilux® (calcipotriene) foam and Doryx® MPC (doxycycline) delayed-release tablets. The Company recently acquired Lexette® (halobetasol) foam used to treat plaque psoriasis which it expects to also launch in January 2019.

¹ Management estimate



ASX Announcement

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About Mayne Pharma

At Mayne Pharma we believe that everyone deserves medicines that are better, safe and more affordable. That's why our people are determined to create innovative products and services for our changing world.

Mayne Pharma is an ASX-listed specialty pharmaceutical company focused on applying its drug delivery expertise to commercialise branded and generic pharmaceuticals. Mayne Pharma also provides contract development and manufacturing services to more than 100 clients worldwide.

Mayne Pharma has a 30-year track record of innovation and success in developing new oral drug delivery systems and these technologies have been successfully commercialised in numerous products that have been marketed around the world.

Mayne Pharma has two product development and manufacturing facilities based in Salisbury, Australia and Greenville, USA with expertise in formulation of complex oral and topical dose forms including potent compounds, modified-release products and inherently unstable compounds.

About Tolsura (SUBA-itraconazole) capsules

Indications and Usage

TOLSURA is an azole antifungal indicated for the treatment of the following fungal infections in immunocompromised and non-immunocompromised adult patients:

- Blastomycosis, pulmonary and extrapulmonary
- Histoplasmosis, including chronic cavitary pulmonary disease and disseminated, non-meningeal histoplasmosis, and
- Aspergillosis, pulmonary and extrapulmonary, in patients who are intolerant of or who are refractory to amphotericin B therapy.

Limitations of Use:

TOLSURA is not indicated for the treatment of onychomycosis

TOLSURA is **NOT** interchangeable or substitutable with other itraconazole products

IMPORTANT SAFETY INFORMATION

WARNING: CONGESTIVE HEART FAILURE and DRUG INTERACTIONS

See full prescribing information for complete boxed warning.

- **Congestive Heart Failure**
TOLSURA can cause or exacerbate congestive heart failure (CHF). When itraconazole was administered intravenously to healthy human volunteers and dogs, negative inotropic effects were seen. If signs or symptoms of congestive heart failure occur or worsen during administration of TOLSURA, reassess the benefit-risk of continuing treatment.
- **Drug Interactions**
 - Co-administration of certain drugs that are metabolized by human CYP3A4 enzymes are contraindicated with TOLSURA because plasma concentrations of such drugs are increased.
 - Co-administration with colchicine, fesoterodine and solifenacin is contraindicated in subjects with varying degrees of renal or hepatic impairment.
 - Co-administration with eliglustat is contraindicated in poor or intermediate metabolizers of CYP2D6 and in subjects taking strong or moderate CYP2D6 inhibitors.
 - Increased plasma concentrations of some of these drugs can lead to QT prolongation and ventricular tachyarrhythmias including occurrences of torsades de pointes, a potentially fatal arrhythmia.

Contraindications

- Co-administration with certain drugs that either affect metabolism of itraconazole or whose metabolism is affected by itraconazole.
- Hypersensitivity to itraconazole

Warnings and Precautions

- **Hepatotoxicity**: Serious hepatotoxicity, including liver failure and death were reported with the use of itraconazole. Discontinue treatment if signs of liver dysfunction occur
- **Cardia Dysrhythmias**: Life-threatening cardiac dysrhythmias and/or sudden death have occurred in patients using certain drugs that are metabolized by human CYP450 enzymes concomitantly with oral itraconazole and/or other CYP3A4 inhibitors.
- **Peripheral Neuropathy**: This has been reported in patients on long-term therapy with itraconazole. Monitor and promptly evaluate neurologic symptoms.
- **Hearing loss**: Reversible or permanent has been reported in patients. Discontinue treatment if hearing loss occurs

Adverse Reactions

Most common adverse reactions (incidence $\geq 1\%$) are nausea, rash, vomiting, edema, headache, diarrhea, fatigue, fever, pruritus, hypertension, abnormal hepatic function, abdominal pain, dizziness, hypokalemia, anorexia, malaise, decreased libido, somnolence, albuminuria, impotence.

To report SUSPECTED ADVERSE REACTIONS, contact Mayne Pharma at 1-844-825-8500 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

For more information about Tolsura, please refer to the prescribing information available [here](#).