MSN SCIENTIFIC SPARKLES

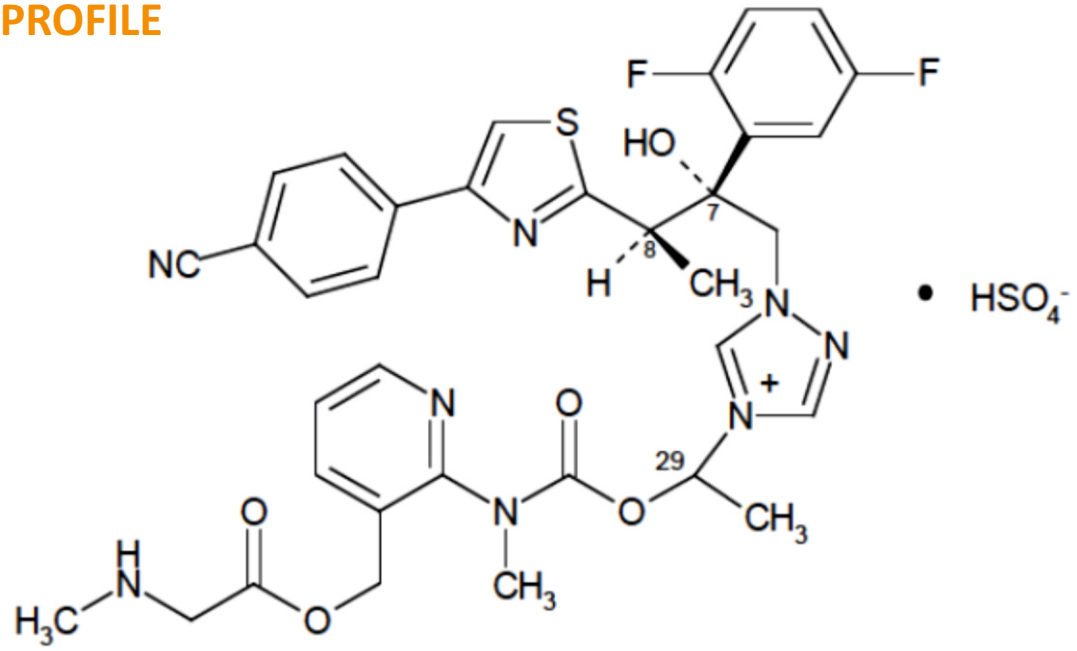
MSN
Research for Better Medicines

MSN ISAVUCONAZONIUM SULFATE

MSNSS No: 00006
Published on 19-JAN-2024

RELIABLE DELIVERY OF STABLE AND HIGHLY PURE ISAVUCONAZONIUM SULFATE

PRODUCT PROFILE



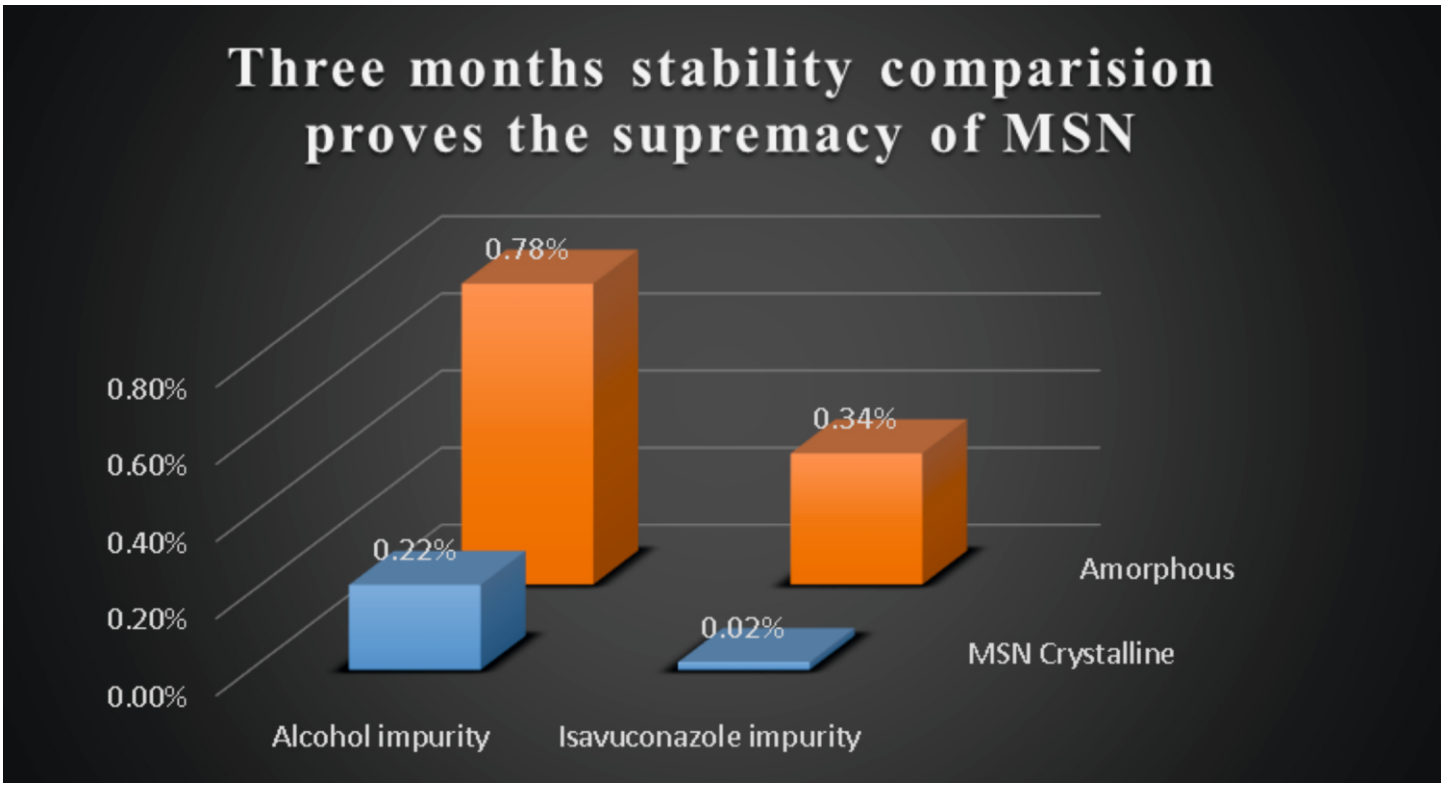
Isavuconazonium sulfate, a prodrug of isavuconazole is indicated for the treatment of invasive aspergillosis (IA) and invasive mucormycosis (IM). It is sold under the brand name of CRESEMBA by Astellas. It can be administered by oral or intravenous infusion. In December 2023, FDA also approved for the treatment of IA and IM in pediatric patients. Perhaps, it is the only azole antifungal drug approved for paediatric patients. The recent COVID-19 pandemic steered a surge in these serious and life-threatening fungal infections, presenting an even greater urgency to address this emerging unprecedented medical need. The reported literature processes beleaguered with stability and purity. To cater the global demand, MSN scientific team developed stable and highly pure Isavuconazonium sulfate and accomplished its process validation in multi-kilo level.

Novel crystalline polymorph of Isavuconazonium sulfate:

Currently Isavuconazonium sulfate is supplied as amorphous form in the market, which is undergoing degradation during the course of time. To circumvent the issue, MSN has developed novel and stable crystalline form of Isavuconazonium sulfate that is highly pure. MSN crystalline form has greatly remedied the drawbacks such as low stability and low quality associated with amorphous form. There are multiple impurities which could form in the preparation of the API and also there are few major degradation impurities formed even up on storage at low temperatures.

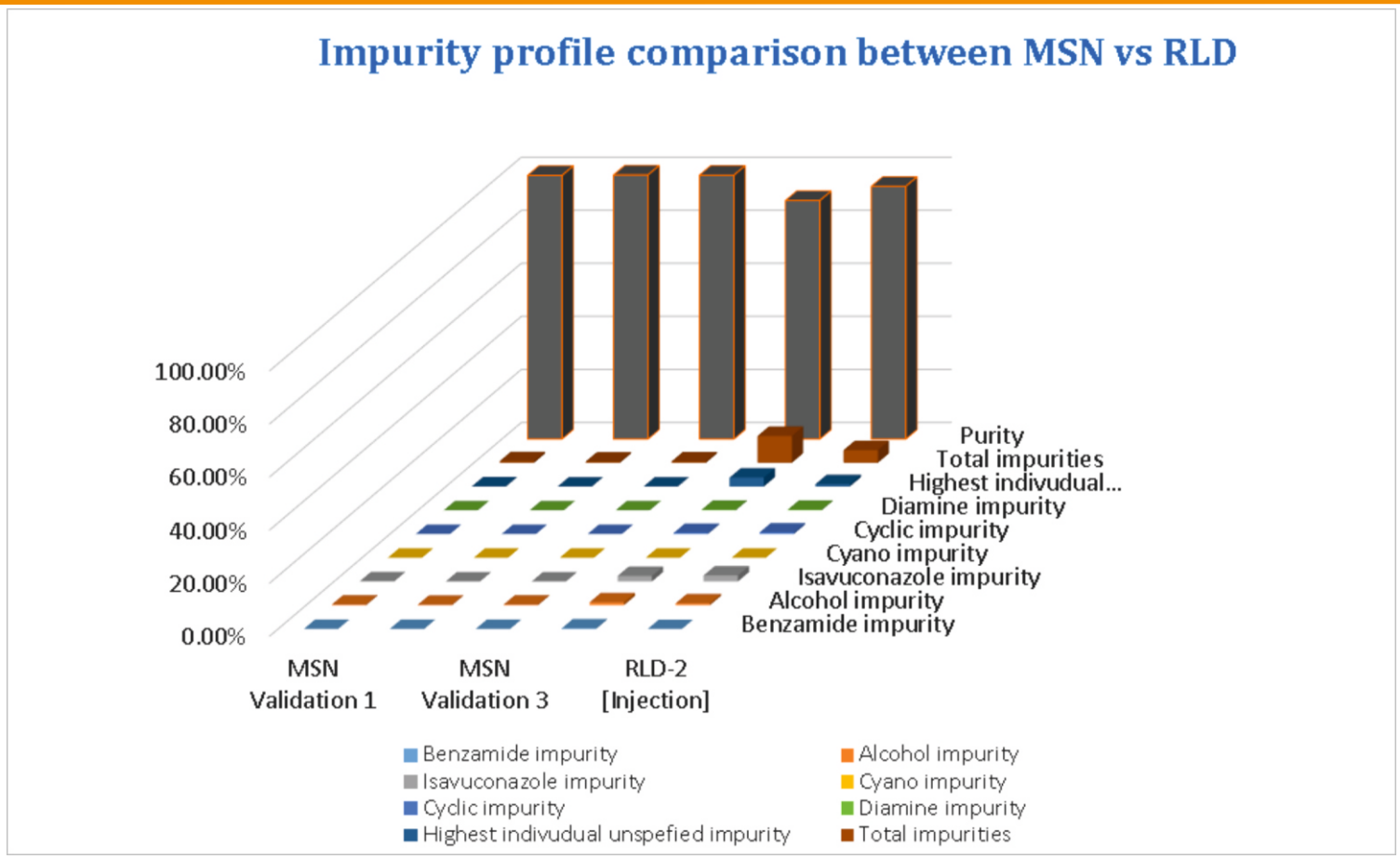
Stability of MSN Isavuconazonium sulfate:

The crystalline form of Isavuconazonium sulfate manufactured by MSN has superior quality when compared to amorphous polymorph. Amorphous polymorph is vulnerable in stability with a gradual reduction in purity and increment in degradation impurities such as alcohol impurity and Isavuconazole impurity. On the other hand, MSN crystalline form is highly pure and is not undergoing any degradation when stored at established in-house storage condition and hence is highly stable.



Quality of MSN Isavuconazonium sulfate:

The validated manufacturing process of Isavuconazonium sulfate has been the result of insightful investigations and innovations with cutting edge technologies. API produced with validated process demonstrated superior quality. The quality comparison between the validation batches of MSN and RLD samples is given below.

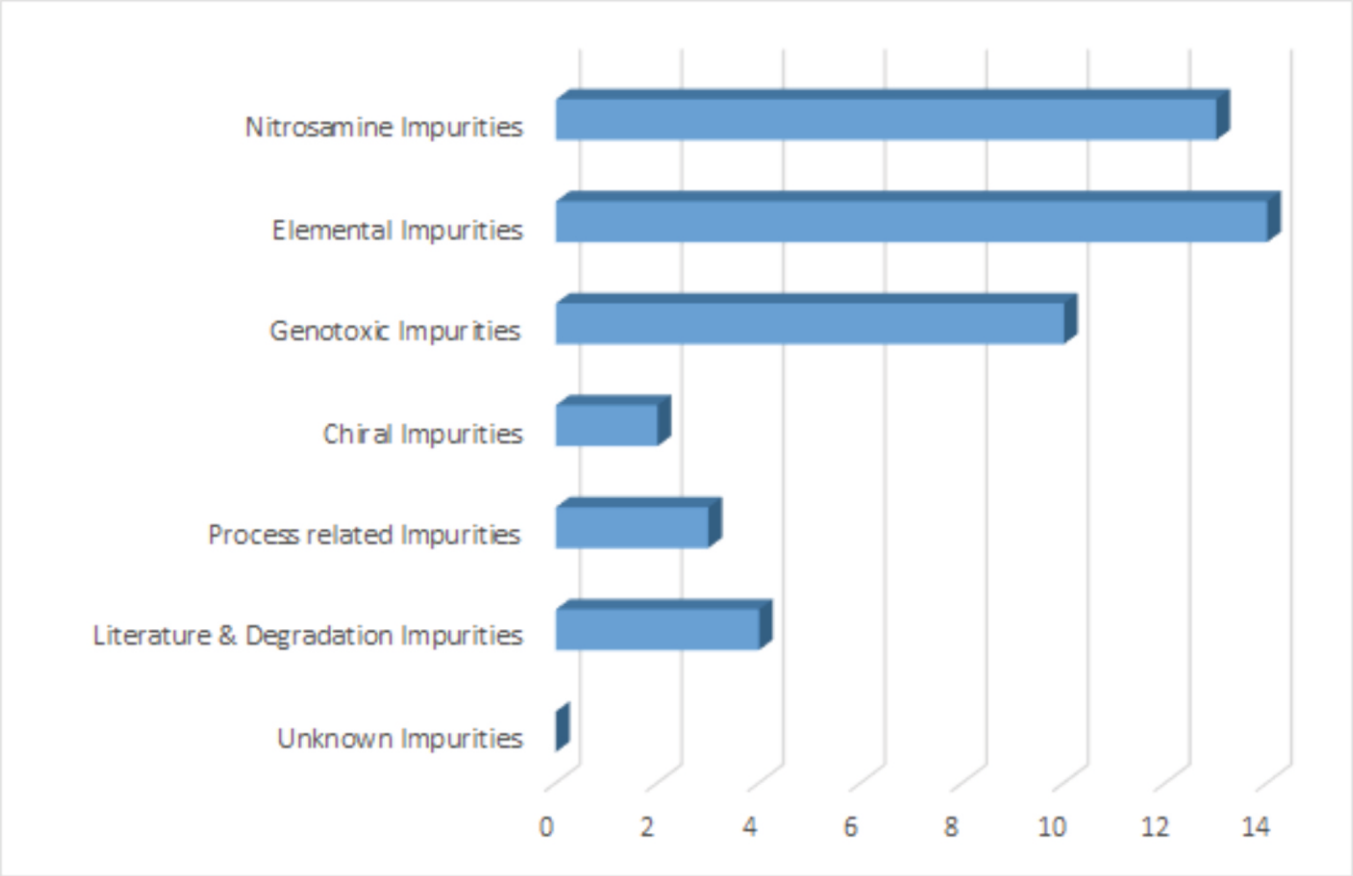


Isavuconazonium sulfate produced by MSN is having purity of >99.0% with the control of majority of the impurities below 0.09%.

Defining quality of Isavuconazonium sulfate by controlling the Impurities

Nearly 50 impurities were identified, synthesised, characterized and confirmed its control or absence at different steps of Isavuconazonium sulfate manufacturing process. The impurities belong to different classes such as process related, degradation, nitrosamine, genotoxic.

Genotoxic and nitrosamine impurities are having better control than RLD.

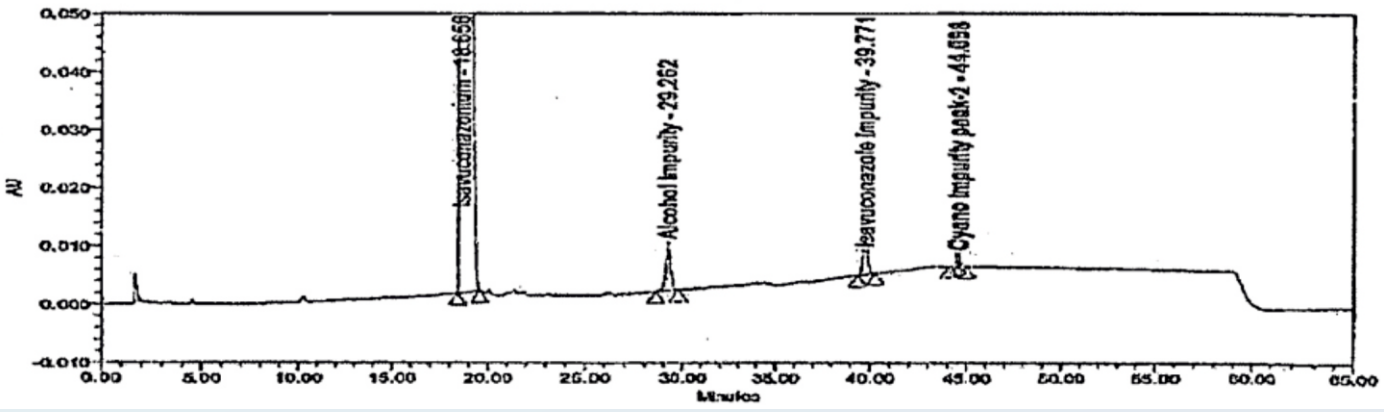


MSN scientists have overcome the challenges during scale-up of the technology by a tailor made equipment mapping.

Analysis of MSN Isavuconazonium sulfate

A precise HPLC method was developed and validated to quantify diastereomers, process related impurities and degradation impurities of Isavuconazonium sulfate. The following HPLC SST chromatograms demonstrate the method capability for identification of all isomeric, degradation and process related impurities.

TYPICAL CHROMATOGRAM OF SYSTEM SUITABILITY (SST) SOLUTION



The API is characterized using orthogonal analytical techniques such as physico-chemical properties by intact mass, 1D and 2D NMR, IR, UV, PXRD, DSC, TGA, SOR, IC etc.

Merits of MSN Isavuconazonium sulfate:

- Novel crystalline form of Isavuconazonium sulfate is the uniqueness of MSN.
- High quality Isavuconazonium sulfate (Purity >99.0 %) by controlling majority of the impurities below 0.09%.
- Identified, synthesised and characterised nearly 50 impurities of different classes to ensure their control/absence and delivery of highly pure Isavuconazonium sulfate.
- Nitrosamine impurities are well controlled in API.
- Elemental impurities are in compliance with ICH Q3D.
- Precise and validated HPLC methods are in hand to ensure high quality Isavuconazonium sulfate.
- State of the art manufacturing facility designed to manufacture Isavuconazonium sulfate at multi kilo level to cater the global demand.
- Material manufactured at FDA approved site.
- MSN has pool of scientists with an expertise in process development, scale up and analytical capability with integrated understanding of IP, Regulatory affairs of different regions.
- Polymorph stress study data is available.
- Stability study data is available.