MSN SCIENTIFIC SPARKLES

MSN
Research for Better Medicines

# MSN SPARSENTAN

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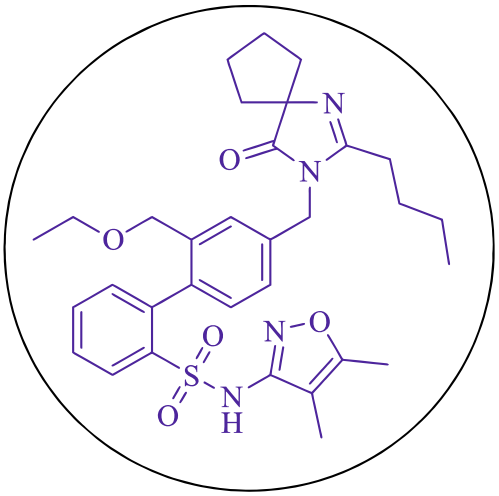
# MSN - HIGH PURE SPARSENTAN

## INTRODUCTION

Sparsentan was initially developed for the treatment of hypertension, however, it has shown to be efficient in the reduction of proteinuria in patients with IgAN and focal segmental glomerulosclerosis (FSGS). Compared to Irbesartan, Sparsentan reduces proteinuria to a greater extent. Furthermore, it is the first non-immunosuppressive therapy for the reduction of proteinuria in IgAN.

### SPARSENTAN STRUCTURE




## SYNTHESIS AND COMPLEXITY OF SPARSENTAN - OVERCOMING THE PURITY CHALLENGES

The active substance Sparsentan is synthesized with excellent optimized conditions to control impurities and produce good yields with consistent quality.

The complexity lies in the purification of intermediates and API, since all the intermediates are residues or oils as per the reported procedures in literature for Sparsentan and are purified by column chromatography which is not commercially viable.

MSN has developed a novel, robust and cost efficient purification process for Sparsentan and its intermediates by chemical and precipitation methods without the need of chromatographic purification.

The MSN - HIGH PURE SPARSENTAN is characterized by a simple and robust HPLC method.

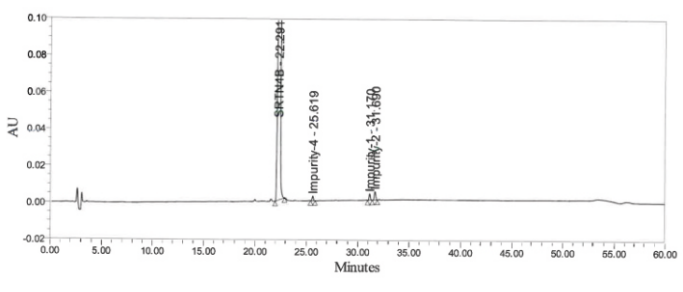
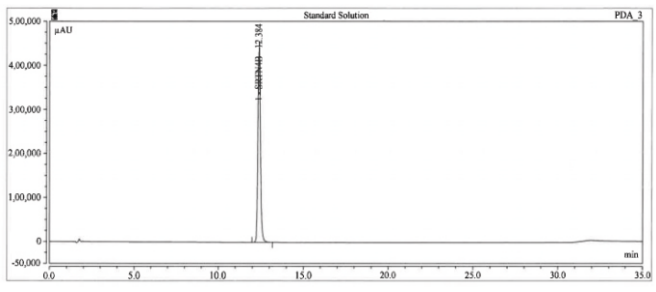
# STABILITY INDICATING REVERSE PHASE HIGH PERFORMANCE LIQUID CHROMATOGRAPHY METHODS FOR DETERMINATION OF ASSAY AND RELATED SUBSTANCES OF MSN - HIGH PURE SPARSENTAN

A sensitive, precise, specific Ion Pair Reverse Phase High Performance Liquid Chromatography (RP- HPLC) method for determination of related substances and assay of MSN - HIGH PURE SPARSENTAN.

In the development of said method, resolution of Impurity-1 and impurity-2 was critical. To resolve the issue, different stationary phase columns have been explored using gradient elution method. Out of the different columns we achieved better resolution using C18 column.

Study was carried out on different mobile phases using different buffers and better peak shapes were achieved when phosphate buffer was used along with acetonitrile in the mobile phase.

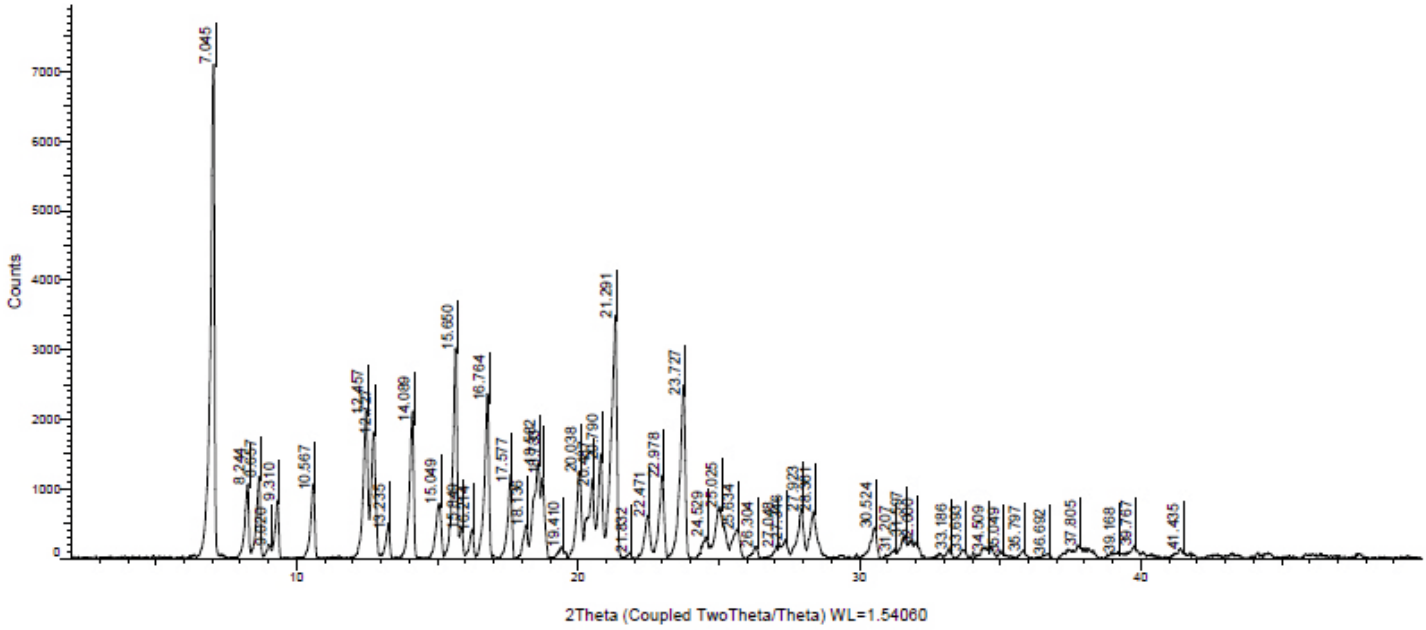
The statistical validation parameters such as linearity, accuracy, precision, inter-day and intra-day variation were checked. Limit of detection (LOD) and limit of quantitation (LOQ) of Sparsentan were found to be 0.01% and 0.03% respectively. Recovery and assay studies of Sparsentan were within 99 to 102% indicating that the proposed method can be adopted for routine quality control analysis of Sparsentan.

| TYPICAL CHROMATOGRAM OF SPARSENTAN RELATED SUBSTANCES BY HPLC | TYPICAL HPLC CHROMATOGRAM OF ASSAY BY HPLC |
|---|---|
|  |  |

## Powder X-Ray Diffraction Pattern of the crystalline Sparsentan API manufactured by MSN:

Powder X-Ray diffraction pattern of the Sparsentan API manufactured by MSN was measured with Bruker D8, Advance Davinci X-ray powder diffractometer, equipped with Cu irradiation source =1.54184 A, Lynxeye XE detector.

## PXRD pattern of the Sparsentan API




## MANUFACTURE AND SUPPLY ASSURANCE

Sparsentan is first in its class and orally active and was discovered by merging the structural elements of Irbesartan, an AT1R antagonist and Biphenyl Sulfonamide, an ETAR antagonist.

We manufacture Sparsentan API at our cGMP API manufacturing facilities, which were inspected by international regulatory authorities and approved.

Our manufacturing process involves complex chemical transformation across multiple synthetic steps, completely backward integrated to the basic starting materials.

With a dedicated manufacturing facility in place, all the synthetic steps to manufacture raw materials and final drug substance are developed and manufactured by MSN.

*We are amongst the earlier generic API manufacturers and formulators. In addition, we can provide country-specific regulatory filings in various countries to support global market expansion.*

## SUPPLY CHAIN MANAGEMENT AND MANUFACTURING:

- State of the art manufacturing facility to manufacture Sparsentan is the capability of MSN.
- Raw materials are procured from reliable GMP compliant sources and also from In-house manufacturing facilities.
- Multi kilogram level production capacity is available.
- MSN QC/QA department is capable to test and release all CQAs.