

# Novel process for preparation of Methotrexate disodium salt

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**Database number 682004**

**Published in the February 2021 paper journal**

**Published digitally 23 December 2020 13:24 UT**

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## Novel process for preparation of Methotrexate disodium salt

### Abstract:

A disclosure provides a novel process for preparation of methotrexate disodium salt.

### Introduction:

Methotrexate is one of the oldest chemotherapy drugs. It has been used in the treatment of various forms of cancer; Methotrexate is also used in non-cancerous conditions such as psoriasis and rheumatoid arthritis. A number of marketed products contain the sodium salt of methotrexate.

### Process for preparation of Methotrexate disodium salt.

The process comprising the step of 1) reacting 2, 4-diamino-6-hydroxymethylpteridine with thionyl chloride in presence of acetonitrile to obtain 2, 4-diamino-6-chloromethylpteridine hydrochloride, crystallized crude compound using mixture of acetic acid and formic acid to get 2, 4-diamino-6-chloro methylpteridine hydrochloride (acetic acid content ~ 10-35%); 2) condensation of obtained 2, 4-diamino-6-chloromethyl-pteridine hydrochloride with diethyl N (4-methyl aminobenzoyl) -L- glutamate in presence of KI and DMSO to obtain Methotrexate diethylester hydroiodide salt; 3) *in-situ* hydrolysis of ester salt using NaOH in presence of THF and water followed by addition of IPA; obtained solid filtered; washed with acetone; recrystallized with THF; washed with acetone to obtain crude methotrexate disodium salt; 4) purification of methotrexate disodium salt by dissolving in water and ethanol (1:2) at 65°C, followed by cooling to room temperature, filtered and dried under vacuum to obtain pure methotrexate disodium salt.

