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(54) Title: PROCESS FOR THE PREPARATION OF FOSAPREPITANT, INTERMEDIATE AND PHARMACEUTICAL ACCEPTABLE SALT THEREOF

(57) Abstract: The present invention relates to an improved process for the manufacture of phosphorylated Aprepitant and intermediate thereof. The present invention further relates to an improved process for the manufacture of Fosaprepitant dimeglumine from the said intermediate.



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**PROCESS FOR THE PREPARATION OF FOSAPREPITANT, INTERMEDIATE
AND PHARMACEUTICAL ACCEPTABLE SALT THEREOF**

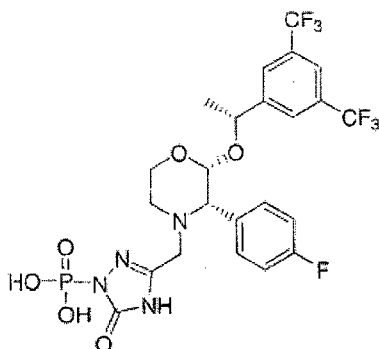
Field of the Invention

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The present invention relates to an improved process for the manufacture of phosphorylated Aprepitant and intermediate thereof. More particularly the present invention relates to an improved process for the manufacture of Fosaprepitant dimeglumine.

10 **Background of the Invention**

Phosphorylated aprepitant also commercially known as Fosaprepitant is an anti-emetic drug, administered intravenously. It is a prodrug of aprepitant. It has the structural formula



15 The compound (phosphorylated aprepitant) and related compounds are disclosed in EP0748320 which also discloses process for manufacturing this compound.

WO2006/060110 discloses a process for manufacturing of this compound and also describes the conversion of aprepitant to monobenzyl aprepitant and the subsequent conversion to fosaprepitant dimeglumine.

20

WO2010/018595 describes intermediates for preparing fosaprepitant dimeglumine, fosaprepitant in neutral form and amorphous dimeglumine and the process thereof.

Previously reported methods for making phosphorylated aprepitant involve use of hazardous, pyrophoric and expensive hindered bases like NaHMDS, n-butyl lithium, Lithium diisopropyl amide, tertiary butoxides, Sodamide etc. at low temperature in anhydrous solvent under inert atmosphere.

5

The present inventors have surprisingly developed a novel, convenient and efficient process which utilizes metal hydroxides like lithium hydroxide, monohydrate, sodium hydroxide, potassium hydroxide etc and sterically hindered amidine base like DBU (Diaza (1, 3) bicyclo [5.4.0]undecane), DBN (1,5-Diazabicyclo[4.3.0]non-5-ene) etc. in solvents like DMSO, DMF, NMP, Sulpholane etc. at ambient temperature to produce compound of formula (II) in a higher yield than the prior art synthesis and avoids a low temperature reaction. The present inventors have further surprisingly developed a novel process for preparation of fosaprepitant dimeglumine by using compound of formula (II).

10

15 The present inventors have developed a novel process which is not only energy efficient but it is also more productive allowing for a shorter time cycle and easily scalable.

The present invention has the following advantages namely improved reaction yield at ambient temperature, higher purity, shorter reaction time, avoids need of inert atmosphere and anhydrous solvents, Low cost bases no special safety requirement avoids the need for handling Hydrogen gas.

20

It is an object of the present invention to provide an improved process for the synthesis of phosphorylated aprepitant and its conversion to fosaprepitant dimeglumine with high purity and good yield.

25

It is another object of the present invention to provide an improved process for the synthesis of phosphorylated aprepitant and its conversion to fosaprepitant dimeglumine which does not employ any hazardous reagents.

It is a further object of the present invention to provide an improved process for the synthesis of phosphorylated aprepitant and its conversion to fosaprepitant dimeglumine which is energy efficient.

5 Summary of the Invention

According to an aspect of the present invention there is provided a process for the synthesis of phosphorylated aprepitant comprising the steps of:

- i. Charging Aprepitant to a mixture of a base in an organic solvent;
- 10 ii. Charging tetra benzyl pyrophosphate to the solution obtained in step i and stirring the reaction mixture at 25-35°C until completion of the reaction;
- iii. Isolating the title compound as yellow oil by solvent extraction.

According to another aspect of the present invention there is provided a process for the preparation of fosaprepitant dimeglumine which comprises the steps of:

- i. Dissolving dibenzyl fosaprepitant (Compound of formula II) in methanol and adding ammonium formate and catalyst under stirring;
- ii. Filtering the catalyst and collecting the clear solution;
- iii. Stirring the clear solution of step ii at 25-30°C with N- methyl glucamine;
- 20 iv. Concentrating and isolating the title compound as an oily mass;
- v. Purifying the isolated compound of step iv to obtain pure fosaprepitant dimeglumine.

According to yet another aspect of the present invention there is provided a process for the preparation of fosaprepitant dimeglumine which comprises the steps of:

- i. Dissolving dibenzyl fosaprepitant (Compound of formula II) in suitable solvent;
- ii. Hydrogenating it in the presence of catalyst;

- iii. Filtering the reaction mixture of step (ii) to obtain a wet residue and adding methanol and N-methyl D- glucamine under stirring to get a clear solution;
- iv. Filtering the solution obtained in step (iii) and concentrating the filtrate;
- v. Dissolving the concentrate in methanol and adding it to isopropyl alcohol to get fosaprepitant dimeglumine.

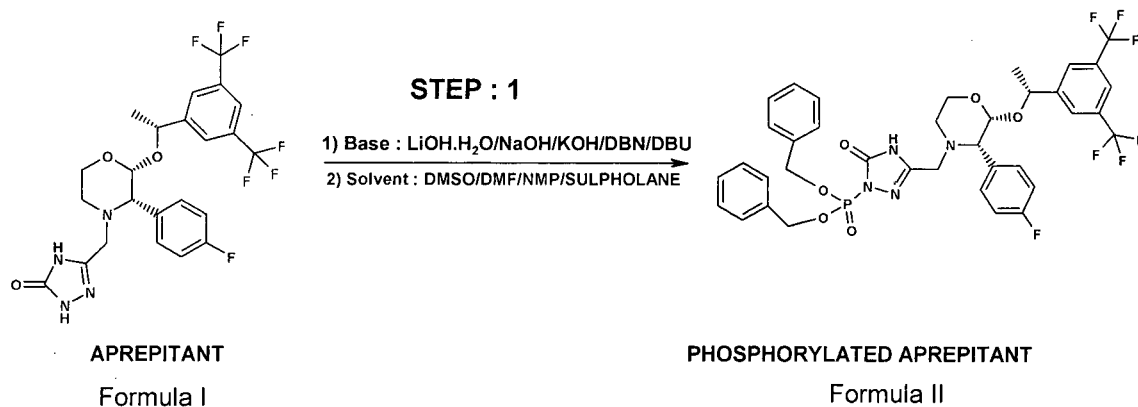
Detailed Description of the Invention

- 10 Phosphorylated aprepitant commercially known as Fosaprepitant is an anti-emetic drug, administered intravenously. It is a prodrug of aprepitant.

The present invention provides a robust, efficient and economical synthesis of phosphorylated aprepitant and its conversion to fosaprepitant dimeglumine in good yield.

15

The first embodiment of the present invention provides a process for the preparation of compound of Formula II from Aprepitant (Compound of formula 1). The reaction for synthesizing Phosphorylated aprepitant (fosaprepitant) can be represented in scheme I as follows:



20

Abbreviation

LiOH: Lithium hydroxide;

NaOH: Sodium hydroxide;

5 **KOH:** Potassium Hydroxide;

DMSO: Dimethyl Sulfoxide

DMF: Dimethylformamide

NMP: N-Methylpyrrolidone

DBU: Diaza (1, 3) bicyclo [5.4.0] undecane),

10 **DBN:** (1, 5-Diazabicyclo [4.3.0] non-5-ene).

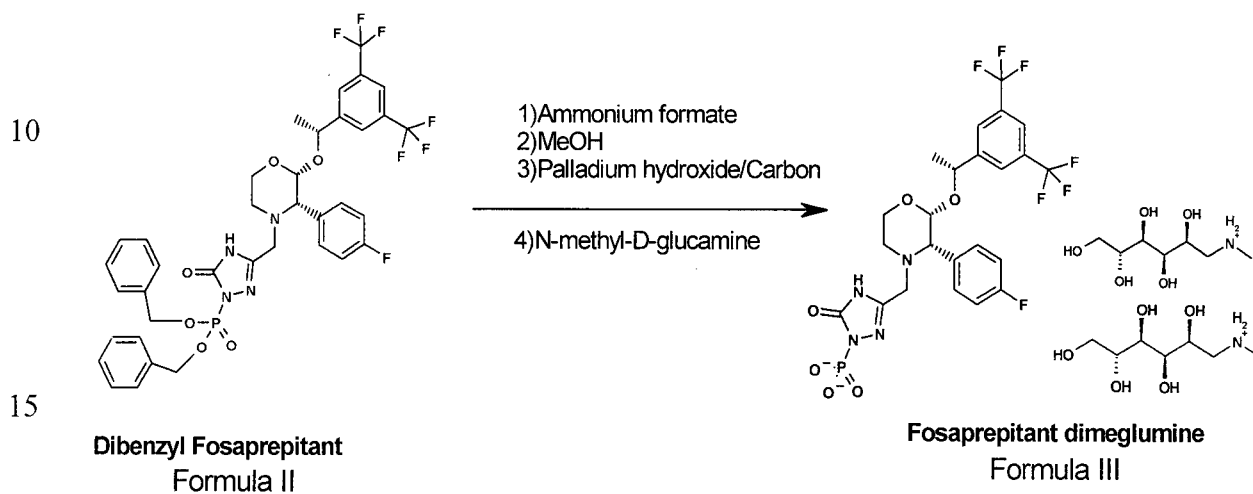
Preparation of phosphorylated aprepitant according to the process of the present invention is described in detail hereinafter.

15 The process for preparing phosphorylated aprepitant comprises introducing 0.4 gm (9.53 mmole) of lithium hydroxide monohydrate at ambient temperature in 10 ml of DMSO solution under stirring. Adding 1.0 gm (1.87 mmole) of aprepitant to the solution obtained and stirring the mixture for 30 mins to get clear solution. Adding 1.1 gm of (2.04 mmole) tetra benzyl pyrophosphate under stirring to the solution. Stir the clear solution for 30 mins at 25-
20 30°C Monitor reaction progress by HPLC. After completion of reaction (aprepitant < 0.5 %), Cool the reaction mass to 10-15 °C and Add 20 ml water slowly under stirring over 20-30 mins. Stir for 5 mins and add 10 ml of DCM solution under stirring. Stir the mixture for 30 mins and then separate the layers. Wash DCM layer with (2x 20 ml) water and (2x 20 ml) saturated sodium bi-carbonate solution. Dry the DCM layer over 1.0 gm anhydrous sodium
25 sulphate and concentrate under vacuum at ambient temperature to give yellow colored oil.

The present invention results in a product with overall yield 1.26 gm (85% theory) and an overall better process efficiency.

The compound of Formula II further finds application in the preparation of pharmaceutically acceptable formulation which is used to prevent nausea and vomiting caused by cancer treatment (chemotherapy).

- 5 The reaction for synthesizing fosaprepitant dimeglumine by transfer hydrogenation can be represented in scheme II as follows

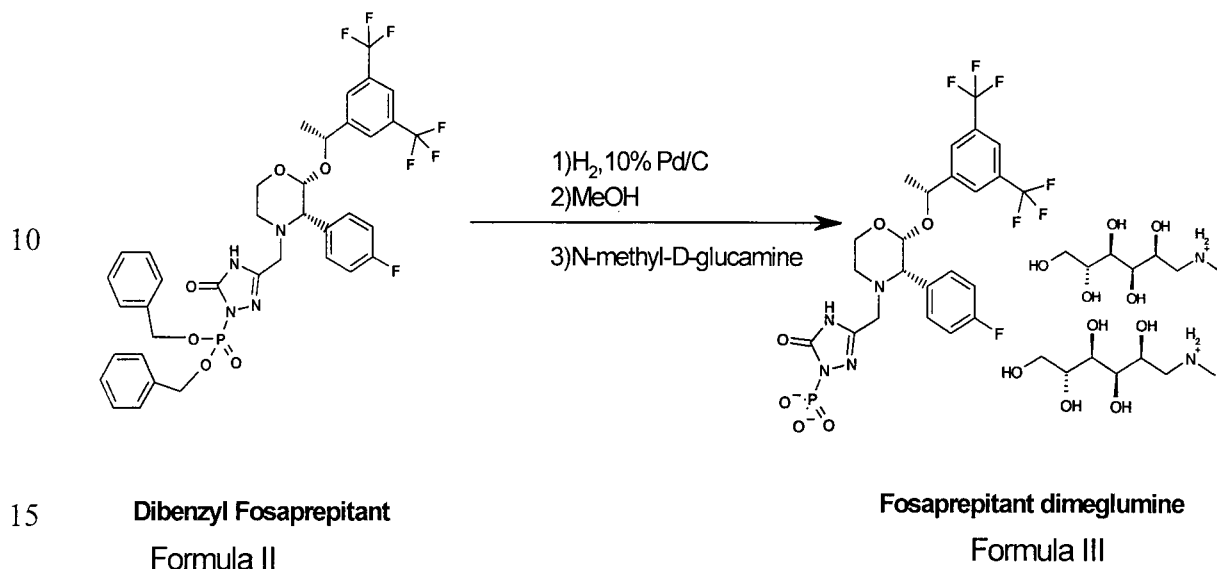


In an embodiment of the present invention provides a process for the synthesis of fosaprepitant dimeglumine (Compound of Formula III) comprising the steps of:

- i. Dissolving dibenzyl fosaprepitant in methanol and adding ammonium formate and catalyst under stirring;
- ii. Filtering the catalyst and collecting the clear solution;
- iii. Stirring the clear solution of step ii at 25-30°C with N- methyl glucamine;
- iv. Concentrating and isolating the title compound as an oily mass;
- v. Purifying the isolated compound of step iv to obtained pure fosaprepitant dimeglumine.

The catalyst of step (i) includes, but is not limited to, Palladium hydroxide, Palladium over carbon.

The reaction for synthesizing fosaprepitant dimeglumine (Compound of Formula III) using catalyst and hydrogen gas and can be represented in scheme III as follows



In an embodiment of the present invention there is provided a process for the synthesis of fosaprepitant dimeglumine (Compound of Formula III) comprising the steps of:

- 20
- i. Dissolving dibenzy fosaprepitant in suitable solvent;
 - ii. Hydrogenating it in the presence of catalyst;
 - iii. Filtering the reaction mixture of step (ii) to obtain a wet residue and adding methanol and N-methyl D- glucamine under stirring to get a clear solution;
- 25
- iv. Filtering the solution obtained in step (iii) and concentrating the filtrate;
 - v. Dissolving the concentrate in methanol and adding it to isopropyl alcohol to get fosaprepitant dimeglumine.

The solvent of step (i) includes, but is not limited to, ethanol, methanol, isopropanol, THF, MTBE.

The catalyst of step (ii) includes, but is not limited to Palladium hydroxide, Palladium over carbon, Raney nickel, Pearlman's catalyst

The present invention is illustrated by way of the following non-limiting examples.

EXAMPLES

10

Example-1: Process for the Preparation of phosphorylated aprepitant using DMSO and Lithium hydroxide monohydrate.

15 Taken 10 ml of DMSO under stirring and added 0.4 gm (9.53 mmole) lithium hydroxide monohydrate at ambient temperature. Added 1.0 gm (1.87 mmole) of aprepitant and stirred for 30 mins to get clear solution. Added 1.1 gm of (2.04 mmole) tetra benzyl pyrophosphate under stirring. Stirred the clear solution for 30 mins at 25-30°C. Monitored reaction progress by HPLC. After completion of reaction (aprepitant < 0.5 %), cooled the reaction mass to 10-15 °C. Added 20 ml water slowly under stirring over 20-30 mins. Stirred for 5 mins and
20 added 10 ml DCM under stirring and stirred for 30 mins. Separated the layers. Washed DCM layer with (2x 20 ml) water and (2x 20 ml) saturated sodium bi-carbonate solution. Dried DCM layer over 1.0 gm anhydrous sodium sulphate and concentrated under vacuum at ambient temperature to give yellow coloured oil. Yield-1.26 gm (85% theory).

25 **Example-2: Process for the Preparation of phosphorylated aprepitant using DMSO and Sodium hydroxide.**

Taken 10 ml of DMSO under stirring and added 0.19 gm (4.75 mmole) sodium hydroxide at ambient temperature. Added 0.5 gm (0.93 mmole) of aprepitant and stirred for 30 mins to get

clear solution. Added 0.5 gm of (0.93 mmole) tetra benzyl pyrophosphate under stirring. Stirred the clear solution for 30 mins at 25-30°C. Monitored reaction progress by HPLC. After completion of reaction (aprepitant < 20 %), cooled the reaction mass to 10-15 °C. Added 20 ml water slowly under stirring over 20-30 mins. Stirred for 5 mins and added 10 ml toluene under stirring and stirred for 30 mins. Separated the layers. Washed toluene layer with (2x 20 ml) water and (2x 20 ml) saturated sodium bi-carbonate solution. Dried toluene layer over 1.0 gm anhydrous sodium sulphate and concentrated under vacuum at ambient temperature to give yellow colored oil. Yield-0.62 gm (83.5% theory).

10 **Example-3: Process for the Preparation of phosphorylated aprepitant using DMSO and Potassium hydroxide.**

Taken 10 ml of DMSO under stirring and added 0.26 gm (4.64 mmole) potassium hydroxide at ambient temperature. Added 0.5 gm (0.93 mmole) of aprepitant and stirred for 30 mins to get clear solution. Added 0.5 gm of (0.93 mmole) tetra benzyl pyrophosphate under stirring. Stirred the clear solution for 30 mins at 25-30°C. Monitored reaction progress by HPLC. After completion of reaction (aprepitant < 20 %), cooled the reaction mass to 10-15 °C. Added 20 ml water slowly under stirring over 20-30 mins. Stirred for 5 mins and add 10 ml toluene under stirring and stir for 30 mins. Separated the layers. Washed toluene layer with (2x 20 ml) water and (2x 20 ml) saturated sodium bi-carbonate solution. Dried toluene layer over 1.0 gm anhydrous sodium sulphate and concentrated under vacuum at ambient temperature to give yellow colored oil. Yield-0.61 gm (82% theory).

25 **Example-4: Process for the Preparation of phosphorylated aprepitant using NMP and Lithium hydroxide monohydrate.**

Taken 10 ml of NMP under stirring and added 0.23 gm (5.47 mmole) lithium hydroxide monohydrate at ambient temperature. Added 0.5 gm (0.93 mmole) of aprepitant and stirred for 30 mins to get clear solution. Added 0.56 gm of (1.04 mmole) tetra benzyl pyrophosphate

under stirring. Stirred the clear solution for 30 mins at 25-30°C. Monitored reaction progress by HPLC. After completion of reaction (aprepitant < 0.5 %), cooled the reaction mass to 10-15 °C. Added 20 ml DCM under stirring. Separated the layers. Washed organic layer with (4x 25 ml) water and (2x 10 ml) saturated sodium bi-carbonate solution. Dried DCM layer over 1.0 gm anhydrous sodium sulphate and concentrated under vacuum at ambient temperature to give yellow colored oil. Yield-0.65gm (87.4% theory).

Example-5: Process for the Preparation of phosphorylated aprepitant using Sulpholane and Lithium hydroxide monohydrate.

Taken 20 ml of Sulpholane under stirring and added 0.20 gm (4.76 mmole) lithium hydroxide monohydrate at ambient temperature. Added 0.5 gm (0.93 mmole) of aprepitant and stirred for 30 mins to get clear solution. Added 0.55 gm of (1.02 mmole) tetra benzyl pyrophosphate under stirring. Stirred the clear solution for 30 mins at 25-30°C. Monitored reaction progress by HPLC. After completion of reaction (aprepitant < 1.0 %), cooled the reaction mass to 10-15 °C. Added 40 ml water slowly under stirring over 15 mins. Extracted with (2x20 ml) DCM under stirring and stir for 30 mins. Separated the layers. Washed DCM layer with (2x 20 ml) water and (2x 20 ml) saturated sodium bi-carbonate solution. Dried DCM layer over 1.0 gm anhydrous sodium sulphate and concentrated under vacuum at ambient temperature to give yellow colored oil. Yield-0.63 gm (85% theory).

Example-6: Process for the Preparation of phosphorylated aprepitant using DMF and Lithium hydroxide monohydrate.

Taken 10 ml of DMF under stirring and added 0.45 gm (10.7 mmole) lithium hydroxide monohydrate at ambient temperature. Added 1.0 gm (1.87 mmole) of aprepitant and stirred for 30 mins to get clear solution. Added 1.1 gm of (2.04 mmole) tetra benzyl pyrophosphate under stirring. Stirred the clear solution for 30 mins at 25-30°C. Monitored reaction progress by HPLC. After completion of reaction (aprepitant < 1.0 %), added the reaction mass slowly

to a precooled (0-5°C) mixture of 20 ml water under stirring over a period of 15 mins. Separated the layers. Aqueous layer extracted with (20 ml) MTBE. Combined organic layer washed with (20 ml) water. Dried organic layer over 1.0 gm anhydrous sodium sulphate and concentrated under vacuum at ambient temperature to give yellow colored oil. Yield-1.3 gm (87.4 % theory).

Example 7: Process for the Preparation of phosphorylated aprepitant using DMF and DBU.

Taken mixture of 10 ml of DMF and added 0.9 gm (5.92 mmole) Diaza (1, 3) bicyclo [5.4.0] undecane, (DBU) at ambient temperature, add 1.0 gm (1.87 mmole) of aprepitant and stirred for 30 mins to get clear solution. Added 1.1 gm of (2.04 mmole) tetra benzyl pyrophosphate under stirring. Stirred the clear solution for 30 mins at 25-30°C. Monitored reaction progress by HPLC. After completion of reaction (aprepitant < 1.0 %), added the reaction mass slowly to a pre-cooled (0-5°C) mixture of 20 ml water under stirring over a period of 15 mins. Separated the layers. Aqueous layer extracted with (20 ml) MTBE. Combined organic layer washed with (20 ml) water. Dried organic layer over 1.0 gm anhydrous sodium sulphate and concentrated under vacuum at ambient temperature to give yellow colored oil. Yield-1.26 gm (85 % theory).

Example 8: Process for the Preparation of phosphorylated aprepitant using DMF and DBN.

Taken mixture of 10 ml of DMF and added 1.0 gm (8.05 mmole) 1,5-Diazabicyclo[4.3.0]non-5-ene (DBN) at ambient temperature, added 1.0 gm (1.87 mmole) of aprepitant and stirred for 30 mins to get clear solution. Added 1.1 gm of (2.04 mmole) tetra benzyl pyrophosphate under stirring. Stirred the clear solution for 30 mins at 25-30°C. Monitored reaction progress by HPLC. After completion of reaction (aprepitant < 1.0 %), added the reaction mass slowly to a pre-cooled (0-5°C) mixture of 20 ml water under stirring over a period of 15 mins. Separated the layers. Aqueous layer extracted with (20 ml) MTBE.

Combined organic layer washed with (20 ml) water. Dried organic layer over 1.0 gm anhydrous sodium sulphate and concentrated under vacuum at ambient temperature to give yellow colored oil. Yield-1.27 gm (85.4 % theory).

5 **Example 9: Process for the preparation of Fosaprepitant dimeglumine using transfer hydrogenation technique:**

2.0 gm (2.51 mmole) of phosphorylated aprepitant was dissolved in methanol at 25 °C. 0.79 gm of ammonium formate (1.25 m mole) and 0.4 gm of palladium hydroxide/C was added
10 under stirring. Reaction mass was heated to 40 ° C and stirred for 1 hr at this temperature. Monitor the progress of the reaction till starting material is less than 0.5 %. The catalyst was filtered through celite bed and washed the bed with methanol. Filtrate was stirred with N-methyl-D-Glucamine for 30 mins at 25°C to make salt. The clear solution was concentrated in vacuum till no solvent distill out to get oily mass. The oil was dissolved in methanol and
15 added slowly to isopropanol over a period of 30 mins. The precipitated compound was filtered under nitrogen and washed with 10 ml of IPA. Wet cake was dried under vacuum to get crude Fosaprepitant dimeglumine.
Yield- 1.8 gm (72 % theory).

20 **Example 10: Process for the preparation of Fosaprepitant dimeglumine using transfer hydrogenation technique.**

2.0 gm (2.51 mmole) of phosphorylated aprepitant obtained as above was dissolved in methanol at 25 °C. 0.79 gm of ammonium formate (1.25 m mole) and 0.4 gm of Pd/C
25 catalyst was added under stirring. Reaction mass was heated to 40 ° C and stirred for 1 hr at this temperature. Monitor the progress of the reaction till starting material is less than 0.5 %. The catalyst was filtered through celite bed and washed the bed with methanol. Filtrate was stirred with N-methyl-D-Glucamine for 30 mins at 25°C to make salt. The clear solution was concentrated in vacuum till no solvent distill out to get oily mass. The oil was dissolved in

methanol and added slowly to isopropanol over a period of 30 mins. The precipitated compound was filtered under nitrogen and washed with 10 ml of IPA. Wet cake was dried under vacuum to get crude Fosaprepitant dimeglumine. Yield- 1.7 gm (68 % theory).

5 **Example 11: Process for the Preparation of Fosaprepitant Dimeglumine.**

50 gm of Dibenzyl Fosaprepitant was dissolved in about 1.0 litre of methanol. The reaction mixture is subjected to the hydrogenation using Pd/C catalyst and monitored the reaction by HPLC till its completion. The reaction mixture is filtered and residue washed with methanol
10 containing N-methyl-D-glucamine. The clear filtrate of methanol is added slowly to Isopropyl alcohol, filtered the precipitated slurry and dried under vacuum to get pure fosaprepitant dimeglumine salt with any individual impurities less than 0.05%.
Yield – 47 (75%), HPLC Purity 99.7%.

15 **Example 12: Process for the Preparation of Fosaprepitant Dimeglumine.**

1 gm of Dibenzyl Fosaprepitant was dissolved in about 20 ml of ethanol. The reaction mixture is subjected to the hydrogenation using Pd/C catalyst and monitored the reaction by HPLC till its completion. The reaction mixture is filtered and residue washed with methanol
20 containing N-methyl-D-glucamine. The clear filtrate of methanol is added slowly to Isopropyl alcohol, filtered the precipitated slurry and dried under vacuum to get pure fosaprepitant dimeglumine salt with any individual impurities less than 0.05%.
Yield – 0.93 gm (74%).

25 **Example 13: Process for the Preparation of Fosaprepitant Dimeglumine.**

1 gm of Dibenzyl Fosaprepitant was dissolved in about 30 ml of Isopropanol. The reaction mixture is subjected to the hydrogenation using Pd/C catalyst and monitored the reaction by HPLC till its completion. The reaction mixture is filtered and residue washed with methanol

containing N-methyl-D-glucamine. The clear filtrate of methanol is added slowly to Isopropyl alcohol, filtered the precipitated slurry and dried under vacuum to get pure fosaprepitant dimeglumine salt with any individual impurities less than 0.05%.

Yield – 0.92 gm (73%),

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Example 14: Process for the Preparation of Fosaprepitant Dimeglumine.

1 gm of Dibenzyl Fosaprepitant was dissolved in about 30 ml of MTBE. The reaction mixture is subjected to the hydrogenation using Pd/C catalyst and monitored the reaction by HPLC till its completion. The reaction mixture is filtered and residue washed with methanol containing N-methyl-D-glucamine. The clear filtrate of methanol is added slowly to Isopropyl alcohol, filtered the precipitated slurry and dried under vacuum to get pure fosaprepitant glucamine salt with any individual impurities less than 0.05%.

Yield – 0.93 gm (74%),

15

Example 15: Process for the Preparation of Fosaprepitant Dimeglumine.

1 gm of Dibenzyl Fosaprepitant was dissolved in about 30 ml of THF. The reaction mixture is subjected to the hydrogenation using Pd/C catalyst and monitored the reaction by HPLC till its completion. The reaction mixture is filtered and residue washed with methanol containing N-methyl-D-glucamine. The clear filtrate of methanol is added slowly to Isopropyl alcohol, filtered the precipitated slurry and dried under vacuum to get pure fosaprepitant dimeglumine salt with any individual impurities less than 0.05%.

Yield – 0.95 gm (75%),

25

Example 16: Process for the Preparation of Fosaprepitant Dimeglumine.

1 gm of Dibenzyl Fosaprepitant was dissolved in about 20 ml of methanol. The reaction mixture is subjected to the hydrogenation using Raney Ni catalyst and monitored the reaction

by HPLC till its completion. The reaction mixture is filtered and residue washed with methanol containing N-methyl-D-glucamine. The clear filtrate of methanol is added slowly to Isopropyl alcohol, filtered the precipitated slurry and dried under vacuum to get pure fosaprepitant dimeglumine salt with any individual impurities less than 0.05%.

5 Yield – 0.93 gm (74%),

Example 17: Process for the Preparation of Fosaprepitant Dimeglumine.

1 gm of Dibenzyl Fosaprepitant was dissolved in about 20 ml of methanol. The reaction
10 mixture is subjected to the hydrogenation using Pearlman's catalyst and monitored the reaction by HPLC till its completion. The reaction mixture is filtered and residue washed with methanol containing N-methyl-D-glucamine. The clear filtrate of methanol is added slowly to Isopropyl alcohol, filtered the precipitated slurry and dried under vacuum to get pure fosaprepitant dimeglumine salt with any individual impurities less than 0.05%.

15 Yield – 0.92 gm (73%),

CLAIMS

1. A process for the synthesis of phosphorylated aprepitant (Compound of formula II) comprising the steps of:
 - 5 i. Charging Aprepitant to a mixture of a base in an organic solvent;
 - ii. Charging tetra benzyl pyrophosphate to the solution obtained in step i and stirring the reaction mixture at 25-35°C until completion of the reaction;
 - iii. Isolating the title compound as yellow oil by solvent extraction.
- 10 2. The process according to claim 1 wherein the base in step (i) is selected from Lithium hydroxide (LiOH), Sodium hydroxide (NaOH) or Potassium hydroxide (KOH), Diaza (1, 3) bicyclo [5.4.0]undecane) and (1,5-Diazabicyclo[4.3.0]non-5-ene.
- 15 3. The process according to claim 1 wherein the organic solvent in step (i) is selected from Dimethyl Sulfoxide (DMSO); Dimethylformamide (DMF) N-Methylpyrrolidone (NMP) or Sulpholane.
- 20 4. A process for the preparation of fosaprepitant dimeglumine which comprises the steps of:
 - i. Dissolving dibenzyl fosaprepitant (Compound of formula II) as obtained in claim 1 in methanol and adding ammonium formate and catalyst under stirring;
 - ii. Filtering the catalyst and collecting the clear solution;
 - iii. Stirring the clear solution of step ii at 25-30°C with N- methyl glucamine;
 - 25 iv. Concentrating and isolating the title compound as an oily mass;
 - v. Purifying the isolated compound of step iv to obtain pure fosaprepitant dimeglumine.

5. The process according to claim 4 wherein the catalyst of step (i) is selected from Palladium hydroxide, Palladium over carbon.
6. A process for the preparation of fosaprepitant dimeglumine which comprises the steps of:
- i. Dissolving dibenzyl fosaprepitant (Compound of formula II) as obtained in claim 1 in suitable solvent;
 - ii. Hydrogenating it in the presence of catalyst;
 - iii. Filtering the reaction mixture of step (ii) to obtain a wet residue and adding methanol and N-methyl D- glucamine under stirring to get a clear solution;
 - iv. Filtering the solution obtained in step (iii) and concentrating the filtrate;
 - v. Dissolving the concentrate in methanol and adding it to isopropyl alcohol to get fosaprepitant dimeglumine.
7. The process according to claim 6 wherein the solvent of step (i) is selected from ethanol, methanol, isopropanol, THF, MTBE.
8. The process according to claim 6 wherein the catalyst of step (ii) is selected from Palladium hydroxide/C, Palladium over carbon, Raney nickel.