|  |  |
| --- | --- |
| **Composition** | Each uncoated tablet contains Ursodeoxycholic Acid:- 150 mg |
| **Description** | A White Circular flat bevelled edged tablet with bisecting mark on one side. |
| **Mfg. License No.** | DL-513 M |
| **Effective Batch No.** | 12233 |
| **Manufacturing Site** | Tablet Department |
| **Storage Condition** | Store protected from light & moisture at a temperature not exceeding 30⁰C. |
| **Shelf Life** | 24 months or Expiry of Active Ingredient whichever is earlier. |
| **Pack Format- Sales** | 10 tablets in an Alu-Alu Strip pack. 10 such strips in a printed carton 20 such cartons in a Shipper Box(Shipper E) |
| **Pack Format- P.S.** | 2 tablets in an Alu-Alu Strip pack. 50 such strips along with 50 Nos. Catch-covers in a Corrugated Shipper Box (Shipper H) |
| **Superseded Document No.** | TABMFR019/02 |
| **MFR Review Date** | 19.06.2027 |

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| --- | --- | --- | --- |
| **PREPARED BY** | **APPROVED BY** | | **AUTHORISED BY** |
| Dr. Deepen Pal | Suman Bhowmick | Santanu Roy | Manas Mukherjee |
| Manager-PD | Sr. Manager-Production | Manager- QA | Sr. Manager-QA |
|  |  |  |  |
| Date: | Date: | Date: | Date: |

General Instructions:

**Health and Safety Precautions:**

* Enter and Exit from the production area after following the gowning/ de-gowning process strictly as per the SOP.
* Protect the respiratory organs from active substances. Use face mask, hand gloves and other protective gears if required.
* Store the blend and tablets in well closed PVC containers lined with double polythene sacks.
* Strictly follow personal hygiene requirements as per SOP.

Notes:

1. Manufacturing is to be carried out as per requirements of current GMP.
2. Use clean and dry S.S. Equipments at all stages of manufacturing.
3. Ensure minimum dust generation during Sifting and Milling operations and carry out the said operations near dust extraction systems wherever applicable.
4. All equipments and machineries must be adequately guarded and earthed. The operators must use proper safety equipments like hand gloves, face masks, ear muffs etc. during all operations.
5. Ensure the general cleaning and utensils cleaning are carried out as per respective SOPs and check for cleanliness before use.
6. Ensure that all the machineries and equipments / containers including PLM, Tray Drier, Multimill, Oscillating Granulator, Vibratory Sifter, S.S. Sieves, S.S. Screens, Compression machine and Strip Packing Machine etc. are operated & cleaned as per respective SOPs.
7. Before weighing operations, check cleanliness of balances as per SOP.
8. Discard & destroy all rejected blends and tablets as per SOP.
9. Only QC approved Raw & Packing Materials are to be dispensed / issued by the Material Store for Production.
10. Production should be carried out in controlled environment:
11. Relative Humidity: NMT 55%
12. Temperature: NMT 25⁰C.

**Machineries & Equipments Required**



**\*** XX denotes the Index No. of the machine / equipment as used during Production.

**Batch Formula**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Part** | **Sl.** | **Ingredients** | **Spec** | **Code** | **Qty / Tab** | **UOM** | **Overage** | **Std. Qty.** | **UOM** |
|
| **DRY MIXING** | 1 | Ursodeoxycholic Acid\* | IP | U002 | 150.000 | mg |  | 24.000 | Kg |
| 2 | Sodium Lauryl Sulphate | IP | S016 |  | mg |  | 0.700 | Kg |
| 3 | Avicel/MCC (PH 101) | IP | A027 |  | mg |  | 3.000 | Kg |
| 4 | Sodium Starch Glycollate | IP | D011 |  | mg |  | 1.300 | Kg |
| **PASTE** | 5 | PEG-6000 | IP | P011 |  | mg |  | 0.320 | Kg |
| 6 | Methylene Chloride^ | IP | M020 |  | ml |  | 0.800 | Lt |
| 7 | PVP - K30 | IP | P009 |  | mg |  | 1.100 | Kg |
| 8 | Iso Propyl Alcohol^ | IP | I003 |  | ml |  | 11.200 | Lt |
| **LUBRICATION** | 9 | Sodium Starch Glycollate | IP | D011 |  | mg |  | 0.800 | Kg |
| 10 | Talc | IP | T006 |  | mg |  | 0.500 | Kg |
| 11 | Magnesium Stearate | IP | M004 |  | mg |  | 0.160 | Kg |
| 12 | Colloidal Silicon Dioxide (Aerosil 200) | IP | A025 |  | mg |  | 0.160 | Kg |

\* Calculated on 100% basis

^ Disappears in the course of processing

Adjust the excess qty. of Ursodeoxycholic Acid IP (if required) from the qty. of Avicel (PH 101).

**Theoretical Batch Weight:**

32.04 Kg

**Calculation:**

Exact quantity of the API based on its Assay Value (s) is to be calculated / checked by QA

1. **When using item of a single AR No.:**

Formula: QC = (Q X 100)/A.

Where,

Qc = Calculated Qty. of Ursoderoxycholic Acid

Q = Theoretical Quantity of Ursoderoxycholic Acid on 100% basis

A = Assay Value of Ursoderoxycholic Acid

Calculated Qty. of Avicel: (27 – QC) Kg

1. **When using Item of 2 different AR Nos.:**

Formula: Q2 = [100Q –Q1A1]/ A2

Where,

Q2 = Calculated Qty. of Ursoderoxycholic Acid of the 2nd lot /AR no.

Q = Theoretical Quantity of Ursoderoxycholic Acid on 100% basis

Q1= Available /Dispensed Qty. of Ursoderoxycholic Acid of the 1st Lot

A1 = Assay Value of 1st lot of Ursoderoxycholic Acid

A2 = Assay Value of 2nd lot of Ursoderoxycholic Acid

Calculated Qty. of Avicel: (27 – Q1 – Q2) Kg

**Note: Assay Values above 100% are considered as 100%**

**Manufacturing Procedure**

**STAGE 1A: DISPENSING**

1.1 Dispense the materials under dispensing booth at the Material Store and get counter checked by the production / QA personnel.

1.2 Dispense all the ingredients in polythene sacks/suitable containers.

1.3 Tie the tags or write on the sacks with a marker pen all the relevant information about the raw material.

1.4 Weigh/ Measure all the excipients before weighing of active ingredients.

1.5 Weigh / Measure all the ingredients as per the Production Order issued by the Production Dept.

1.6 The Quantity of the API, Ursoderoxycholic Acid is to be calculated on 100% Assay basis by QA and it is to be noted on the Production Order and duly signed by the QA personnel. The difference in weight is to be adjusted with Avicel.

**STAGE 1B: COUNTER-CHECKING AT PRODUCTION**

* 1. Transfer the materials kept at the R.M. Hold Area to the Charge Area.
  2. Counter-check the dispensed quantity of all the items.

**STAGE 2: SIFTING** [Ref SOP No. DMSTAB004]

2.1 Counter check the weights of all ingredients before using in` the batch.

2.2 Transfer requisite quantities of Item Nos. 1-4 to the Sifting area.

2.4 Sift the materials by a Vibratory Sifter fitted with 30# mesh.

2.5 Note down the size and no. used, as well as the integrity of the sieve before and after pulverizing / sifting of the materials.

2.6 Record the observations in Table.

**STAGE 3: DRY MIXING** [Ref SOP No. DMSTAB001]

3.1 Load the sifted materials into the planetary mixer and mix at high speed mode for 15 mins.

3.2 Record the observation in table.

**STAGE 4: BINDER PREPARATION** [Ref SOP No. DMSTAB009 & 016]

* 1. In a clean dry 45 lts. S. S. Vessel, take Isopropyl alcohol add P.V.P.-K30 and stir for 30 minutes or until the solution is clear. (Solution-1)
  2. In another clean dry 2 Lts S.S Mug take Methylene Chloride, add P.E.G.-6000 and stir for 15 mins. (Solution-2)
  3. Cover the S. S. vessels with lids & affix the tags Solution-1 & Solution-2 respectively.

**STAGE 5: WET MIXING** [Ref SOP No. DMSTAB001]

5.1 Add the Solutions 2 & 1 respectively to the dry mix blend of Stage 3 in the PLM and mix properly to get good lumps & granules.

**STAGE 6: DRYING** [Ref SOP No. DMSTAB011]

6.1 Load the wet mass in the S.S. trays of the Tray drier homogenously

6.2 Air-dry the mass for 8 to 10 hrs.

6.3 Dry further 30 to 45 minutes at 45°C if required.

**STAGE: 7 SIZE REDUCTION** [Ref SOP No. DMSTAB003]

7.1 Transfer the material from stage 6 to the milling area.

7.2 Mill the material using an Oscillating Granulator through 12# sieve.

7.3 Collect the granules in polythene sacks placed in PVC containers & record the weight.

**STAGE: 8 LUBRICANT SIFTING** [Ref SOP No. DMSTAB004]

8.1 Counter check the weights of all ingredients before using in the batch.

8.2 Sift SSG, Talc, Magnesium Stearate and Aerosil-200 through 60# sieve.

8.3Record the sieve size used, as well as the integrity of the sieve before and after sifting of individual material.

8.4Check for the residue if any from each material for appearance and quantity.

8.5Record the observations in table.

**STAGE: 9 LUBRICATION** [Ref SOP No. DMSTAB001]

9.1Transfer the sized granules from stage 8 to the mixing area.

9.2 Load the dried sifted granules into the planetary mixer.

9.3 Add Sodium Starch Glycollate & Aerosil 200 and mix for 6 mins at slow speed mode.

9.4 Add Talcum & Magnesium stearate and mix for 3 mins at slow speed.

**STAGE 10: Weighing Record of Lubricated Granules**

10.1 Unload the final mixed granules in double poly lined tightly closed container.

10.2 Record the observations in table.

**STAGE: 11 TABLET COMPRESSION** [Ref SOP No. DMSTAB005]

11.1 Transfer the blended materials to the compression room.

11.2 Set & operate the compression machine as in following table.

11.3 Carry out initial checking as in following table.

11.4 Carry out the following in-process controls as per the given frequency & Record.

11.4.1 Weight of 10 tablets (5 from each station) every 30 mins.

11.4.2 Thickness of 10 tablets (5 from each station) every 2 hours

11.4.3 Hardness of 6 tablets (3 from each station) every 2 hours.

11.4.4 Appearance of one round of tablets every 2 hour.

11.4.5 Disintegration time of 12 tablets (6 from each station) every 4 hour.

11.4.6 Friability of 33 tablets once in a day.

11.4.7 Wt. variation test as per IP on 20 tablets every 4 hour.

11.4.8 Check for spots on tablets from lubrication oil every 30 mins.

11.4.9 Collect the tablets in double polythene sack lined containers.

11.4.10 Compress tablet with 33 stn Rotary Compression m/c with flat circular punch.

11.4.11 Record the weight of compressed tablets in table

**Compression Specifications**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Sl.** | **Tablet Parameter** | **Standard** | **No. of tabs** | **In-Process Frequency** |
| 1 | Description | White Circular flat bevelled edged tablet with bisecting mark on one side | All Stations | 2 hrs/ continuous |
| 2 | Oil Spot | The tablets should be free of oil spots | All Stations | 2 hrs/ continuous |
| 3 | Avg. Tab Weight | 200 mg ± 2% | 20 | NMT 30 min |
| 4 | Wt. of 20 tabs | 4 gm ± 2% | 20 | NMT 30 min |
| 5 | Thickness | 3.45 - 3.70 mm | 1 0 | 2 hrs |
| 6 | Hardness | 5-10 Kgf | 3 | 2 hrs |
| 7 | Disintegration Time | NMT 15 minutes | 6 | 4 hrs |
| 8 | Friability | NMT 1% w/w | 33 | Daily |
| 9 | Weight Variation | NMT 7.5% | 20 | 4 hrs |
| 10 | Punch Details | 7.95 mm dia, BB tooling, flat, circular, bevelled edged | \_ | \_ |

First two/ three rounds of tablets from both sides to be discarded when the m/c is set up for the production

after change over cleaning.

Expected Yield: NLT 98% after compression.

**Hold Time Limits**

|  |  |  |
| --- | --- | --- |
| Sl | Manufacturing Status | Hold Time |
| 1 | Compressed Tabs | 14 days |

**Packing**

Pack the tablets using a 8 Track Strip Pack Machine as per Packaging Instruction No. PI-TAB-019.

**Standard Pack Format:**

|  |
| --- |
| **Sales Pack:** **10 tabs packed in Alu-Alu Strips. 10 Strips in each Carton. 20 Cartons packed in each**  **Shipper Box.**  **P.S. Pack:** **2 tabs packed in Alu-Alu Strips. 50 Strips + 50 nos. Box Type Catch Covers in each**  **Shipper Box.** |

**Revision History**

|  |  |  |  |
| --- | --- | --- | --- |
| **Sl.** | **Version No./ date** | **Superseded Document No.** | **Reason for change** |
| 1. | 02/30.03.2021 | TABMFR019/01 | Change of format and details |
| 2. | 03/ | TABMFR019/02 | Change in the limit of tablet hardness and thickness as per APQR. |