**Table S1: In process specification and testing procedure fixed for pilot and pivotal formulation development and scale up.**

|  |  |  |
| --- | --- | --- |
| **Sr. No** | **Test** | **Specification** |
| **1** | **Description** | White to off-white, round, beveled biconvex, uncoated tablets, both are plain. |
|  | **Identification by uv** | UV absorption spectrum of sample preparation exhibits  maxima and minima, which are at the same wavelengths as  that of standard preparation, as obtained in the assay. |
|  | **Blend uniformity by UV** | (i) Mean of all results is 90.0 % to 110.0 % of target assay.  (ii) RSD of all individual results: Not more than 5.0 % |
|  | **Assay by UV** | Each 225 mg granular powder contains  Not less than 9.50 mg and not more than 11.00 mg  (95.0 % to 110.0 % of labeled amount) |
| 2 | **Average weight of tablets (Weight of 20 tablets/20)** | 225.0 mg ± 3.0 %w/w  (218.0 mg to 232.0 mg) |
| 3 | **Individual weight variation** | Actual average weight (mg) ± 5.0 %w/w. NMT two of tablets should deviate by more than 5.0 % w/w and none should deviates by more than 10.0 % w/w of actual average weight. |
| 4 | **Resistance to crushing (Hardness)** | Target: 4.5 kp  Limit: 3.0 kp to 6.5 kp) |
| 5 | **Thickness** | 4.5 mrn + 0.5 mm  (4.0 mm to 5.0 mm) |
| 6 | **Friability** | NMT 1.0%w/w |
| 7 | **Diameter\*** | 7.9 mm ± 0.2 mm (7.7 mm to 8.1 mm) |

**Table S2: Relative retention time (in h) of the impurities of the alfuzosin**

|  |  |  |  |
| --- | --- | --- | --- |
| Name | Relative retention  time (Approx.) | RRF (relative retention factor) | LOQ (%) limit of quantitation |
| Impurity A | 1.20 | 0.765 | 0.026 |
| Impurity B | 0.53 | 0.664 | 0.026 |
| Impurity D | 0.45 | 0.829 | 0.025 |
| Impurity E | 0.47 | 0.882 | 0.025 |
| Alfuzosin HCL | 1.00 |  |  |

**Table S3: Ratio of rate controlling membrane used for formulation development to evaluate the performance of the rate controlling agent in the drug release rate in pilot formulation**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Experiment No | Mono and di glycerides  Level (%) | Lactose Monohydrate Level (%) | Tablet Wt  Mg | Hardness  (Kp) | Friability  (%) |
| F005 | 30 | 61 | 200 | 4.68 | 0.92 |
| F010 | 35 | 56 | 200 | 4.45 | 0.83 |
| F015 | 30 | 60 | 200 | 4.56 | 0.74 |
| F021 | 46.7 | 45.1 | 225 | 4.6 | 0.84 |
| F022 | 35 | 51 | 200 | 4.36 | 0.63 |
| F025 | 44.4 | 47.1 | 225 | 4.5 | 0.63 |

**Table S4 : Result of in process parameters testing for pivotal and commercial production batch of alfuzosin 10 mg extended release formulation**

|  |  |  |
| --- | --- | --- |
| *In-process Parameter* | *Exhibit Batch* | *Intended Commercial Production*  *Batches* |
| Description | White to off-white, round, beveled biconvex, uncoated tablets, both are plain. | White to off-white, round, beveled biconvex, uncoated tablets, both are plain. |
| Identification  (By UV) | UV absorption spectrum of sample  Preparation exhibits maxima and minima, which are at the same wavelengths as that of standard preparation, as obtained in the assay. | UV absorption spectrum of sample  Preparation exhibits maxima and minima, which are at the same wavelengths as that of standard preparation, as obtained in the assay. |
| Blend uniformity  (By UV) | (1)103.5% (2) 101.8% (3) 101.5%  (4) 100.8% (5)99.5% (6) 98.6%  (7) 100.4% (8) 98.7% (9) 98.2%  (10) 98.7%  Mean: 100.2%  Min. : 98.2%  Max. : 103.5%  RSD 1.7% | (1)103.5% (2) 101.8% (3) 101.5%  (4) 100.8% (5)99.5% (6) 98.6%  (7) 100.4% (8) 98.7% (9) 98.2%  (10)98.7%  Mean: 100.2%  Min. : 98.2%  Max. : 103.5%  RSD 1.7% |
| ASSAY (BY UV) | Each 225 mg of granular ,powder contains: Alfuzosin hydrochloride  10.08 mg (100.8%) | Each 225 mg of granular ,powder contains: Alfuzosin hydrochloride  10.1 mg (101%) |
| Average weight of tablets (Weight of 20 tablets/20) | 225.0 mg ± 3.0 %w/w  (218.0 mg to 232.0 mg) | 225.0 mg ± 3.0 %w/w  (218.0 mg to 232.0 mg) |
| Individual weight variation | Actual average weight (mg) ± 5.0  %w/w. NMT two of tablets should deviate by more than 5.0 % w/w and  none should deviates by more than  10.0 % w/w of actual average weight. | Actual average weight (mg) ± 5.0  %w/w. NMT two of tablets should deviate by more than 5.0 % w/w and none should deviates by more than 10.0 % w/w of actual average weight. |
| Resistance to crushing (Hardness) | Target: 4.5 kp  Limit: 3.0 kp to 6.5 kp) | Target: 4.5 kp  (Limit: 3.0kp to 6.5 kp) |
| Thickness | 4.5 mrn + 0.5 mm  (4.0 mm to 5.0 mm) | 4.50 mm + 0.50 mm  (4.00 mm to 5.00 mm) |
| Friability | NMT 1.0%w/w | NMT 1.0%w/w |
| Diameter\* | 7.9 mm ± 0.2 mm (7.7 mm to 8.1 mm) | 7.90 mm± 0.20mm (7.70 to 8.10 mm) |

**Table S5: % CDR at each time points of 12 reference tablets UROXATRAL 10 mg extended release tablets at 0.1 N HCL (pH 1.2)**

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Tablet | Time in hours (% cumulative drug release ) | | | | | | | | | | |
| No | 1 | 2 | 3 | 4 | 6 | 8 | 10 | 12 | 16 | 20 | 24 |
| 1 | 16.1 | 22.2 | 28.3 | 33.3 | 41.3 | 48.6 | 55.8 | 64 | 89.7 | 95 | 97.3 |
| 2 | 17.6 | 25.2 | 30.6 | 36 | 41.4 | 49.2 | 55.2 | 62.4 | 85.8 | 89 | 92.7 |
| 3 | 16.3 | 23.7 | 30 | 35.5 | 45.2 | 53.6 | 62.5 | 69.9 | 88.1 | 95.8 | 99.4 |
| 4 | 15.6 | 23 | 29.8 | 36.1 | 46.1 | 58.4 | 71.5 | 82.2 | 96.4 | 102.4 | 102.2 |
| 5 | 14.9 | 23.6 | 29.1 | 34 | 40.3 | 47.6 | 57.4 | 64.7 | 79.2 | 91.8 | 97.2 |
| 6 | 16.8 | 23.8 | 30.3 | 33.7 | 39.6 | 48.2 | 58.2 | 73.2 | 83.6 | 93.5 | 99.8 |
| 7 | 17.6 | 24.9 | 30.1 | 34.7 | 41.3 | 50.3 | 56 | 64.6 | 80.1 | 89.5 | 88.6 |
| 8 | 16.6 | 24 | 27.4 | 34.2 | 43 | 50.2 | 57.8 | 65.5 | 84.6 | 94.9 | 93.8 |
| 9 | 17.7 | 24.6 | 32.4 | 39.8 | 50.5 | 60.5 | 69.6 | 79.9 | 92.4 | 102 | 96.4 |
| 10 | 16.9 | 24.5 | 30.9 | 37.3 | 45.6 | 53.4 | 62.2 | 68.2 | 85 | 96.4 | 91.7 |
| 11 | 16 | 24 | 29.6 | 33.5 | 43 | 51 | 57.9 | 66.5 | 83 | 93.3 | 91.6 |
| 12 | 19.2 | 26.2 | 31.7 | 36.6 | 43.8 | 51.9 | 58.6 | 66.5 | 78.6 | 88 | 89.1 |
| Min | 14.9 | 22.2 | 27.4 | 33.3 | 39.6 | 47.6 | 55.2 | 62.4 | 78.6 | 88 | 88.6 |
| Max | 19.2 | 26.2 | 32.4 | 39.8 | 50.5 | 60.5 | 71.5 | 82.2 | 96.4 | 102.4 | 102.2 |
| Mean | 16.8 | 24.1 | 30 | 35.4 | 43.4 | 51.9 | 60.2 | 69 | 85.5 | 94.3 | 95 |
| RSD | 6.8 | 4.3 | 4.6 | 5.4 | 7.1 | 7.7 | 8.9 | 9.2 | 6.3 | 4.9 | 4.6 |

**Table S6: % CDR of at each time points of 12 test tablets of final alfuzosin 10 mg extended release tablets formulation at 0.1N HCL (pH 1.2)**

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Tablet | Time in hours (% cumulative drug release ) | | | | | | | | | | |
| No | 1 | 2 | 3 | 4 | 6 | 8 | 10 | 12 | 16 | 20 | 24 |
| 1 | 18.3 | 25.8 | 32.2 | 36.3 | 45.8 | 50.2 | 54.8 | 58.5 | 65.5 | 72.4 | 75.9 |
| 2 | 20.1 | 27.3 | 33.2 | 37.5 | 45.4 | 52.3 | 57.2 | 61.2 | 69.5 | 73.8 | 77.6 |
| 3 | 18.9 | 27 | 33 | 37 | 44.8 | 50.8 | 56.2 | 60.6 | 68.6 | 74.7 | 78.5 |
| 4 | 18.6 | 26.9 | 32.5 | 38.5 | 44.4 | 50.8 | 55.3 | 59.4 | 68 | 72.3 | 76.4 |
| 5 | 17.8 | 26 | 31.4 | 34.9 | 42.6 | 48.2 | 52.8 | 56.8 | 64.8 | 70.2 | 75 |
| 6 | 17.6 | 25.7 | 31 | 35.1 | 42.9 | 48.4 | 53.2 | 57.4 | 64.7 | 70.6 | 74.6 |
| 7 | 19.1 | 26.7 | 32.4 | 37.6 | 45.2 | 51.3 | 56.9 | 60.5 | 65.2 | 70.3 | 75.5 |
| 8 | 18.5 | 26 | 31.9 | 35.9 | 44.1 | 49.5 | 54 | 58.1 | 65.2 | 71.9 | 75.7 |
| 9 | 19.4 | 26.7 | 31.9 | 36.5 | 44.3 | 49.7 | 54.6 | 59 | 65.4 | 72.2 | 75.5 |
| 10 | 19.2 | 26.9 | 32.4 | 36.7 | 44.1 | 49.7 | 54.5 | 58.9 | 66.1 | 71.9 | 75.8 |
| 11 | 18.8 | 26.8 | 32.3 | 36.7 | 44.6 | 49.8 | 53.8 | 59.1 | 66.7 | 72.8 | 77.2 |
| 12 | 19.1 | 27 | 32.8 | 36.8 | 44.1 | 50.5 | 54.7 | 60 | 66.6 | 72.3 | 77.8 |
| Min | 17.6 | 25.7 | 31 | 34.9 | 42.6 | 48.2 | 52.8 | 57.4 | 64.7 | 70.2 | 74.6 |
| Max | 20.1 | 27.3 | 33.2 | 38.5 | 45.8 | 52.3 | 57.2 | 61.2 | 69.5 | 74.7 | 78.5 |
| Mean | 18.8 | 26.6 | 32.3 | 36.6 | 44.4 | 50.1 | 54.8 | 59.1 | 66.4 | 72.1 | 76.3 |
| RSD | 3.7 | 2 | 2 | 2.8 | 2.1 | 2.3 | 2.5 | 2.2 | 2.4 | 1.8 | 1.6 |

**Table S7: % CDR of at each time points of 12 reference tablets Uroxatral (alfuzosin 10mg) extended release tablets formulation at pH 4.7**

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Tablet | Time in h (% cumulative drug release ) | | | | | | | | | | |
| No | 1 | 2 | 3 | 4 | 6 | 8 | 10 | 12 | 16 | 20 | 24 |
| 1 | 19 | 25.1 | 29.6 | 35.8 | 39.7 | 54.4 | 58 | 65.5 | 78.8 | 87.7 | 90.7 |
| 2 | 18 | 25.1 | 29.6 | 35.8 | 40.3 | 54.4 | 58 | 65.5 | 77.6 | 87.8 | 90.2 |
| 3 | 18 | 25.2 | 28.1 | 35.3 | 43.2 | 52.9 | 63 | 69.7 | 78.2 | 85.5 | 89.9 |
| 4 | 18 | 22.8 | 29.2 | 35.3 | 43.1 | 52.8 | 63.2 | 66.5 | 78.6 | 85.6 | 89 |
| 5 | 16.8 | 22.9 | 30.1 | 35.2 | 43 | 52.7 | 59.6 | 66.3 | 78.6 | 84.8 | 89.2 |
| 6 | 16.9 | 24 | 29.9 | 36.4 | 46.2 | 51.8 | 59.5 | 66.7 | 78.8 | 84 | 88.1 |
| 7 | 17.5 | 23.7 | 31.2 | 36.5 | 45.2 | 55.1 | 58.2 | 65.4 | 76.8 | 85.1 | 89.8 |
| 8 | 17.5 | 23.3 | 30.4 | 33.7 | 43.6 | 52.4 | 58.4 | 70.4 | 83.2 | 85.5 | 89.8 |
| 9 | 17.5 | 22.3 | 27.6 | 36.3 | 42.1 | 53.1 | 62.6 | 69.3 | 81.9 | 84.4 | 89.2 |
| 10 | 16.7 | 25 | 29.8 | 36.1 | 42.9 | 53.7 | 62.7 | 66.2 | 79.8 | 86.4 | 91.1 |
| 11 | 16.7 | 25 | 30.1 | 35.3 | 42.7 | 53.6 | 62.8 | 68.3 | 78.3 | 85.8 | 91.1 |
| 12 | 19 | 24.6 | 31.1 | 34.7 | 44.7 | 55.2 | 59.3 | 67.9 | 76.8 | 85.3 | 90.3 |
| Min | 16.7 | 22.8 | 27.6 | 33.7 | 39.7 | 51.8 | 58 | 65.4 | 76.8 | 84 | 88.1 |
| Max | 19 | 25.2 | 31.2 | 36.5 | 46.2 | 55.2 | 63.2 | 70.4 | 83.2 | 87.8 | 91.1 |
| Mean | 17.6 | 24.1 | 29.7 | 35.5 | 43.1 | 53.5 | 60.4 | 67.3 | 79 | 85.7 | 89.9 |
| RSD | 4.6 | 4.4 | 3.6 | 2.3 | 4.3 | 2 | 3.6 | 2.6 | 2.4 | 1.4 | 1 |

**Table S8: % CDR of at each time points of 12 test tablets of final alfuzosin 10 mg extended release tablets formulation batch at pH 4.7**

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Tablet | Time in h (% cumulative drug release ) | | | | | | | | | | |
| No | 1 | 2 | 3 | 4 | 6 | 8 | 10 | 12 | 16 | 20 | 24 |
| 1 | 17.9 | 25.8 | 31.2 | 36.2 | 42.8 | 50.1 | 55.8 | 59.9 | 68.3 | 74 | 17.9 |
| 2 | 18.8 | 26.4 | 31.6 | 36.6 | 44.5 | 51.2 | 56.5 | 61.7 | 69.9 | 78.2 | 18.8 |
| 3 | 17.9 | 25.8 | 31.6 | 36.2 | 44.3 | 50.6 | 55.9 | 60.7 | 68.9 | 75.4 | 97.9 |
| 4 | 18.2 | 24.8 | 32.2 | 35.2 | 42.9 | 51 | 56 | 59.8 | 67.1 | 75 | 98.2 |
| 5 | 18.9 | 24.8 | 30.3 | 35.1 | 42.8 | 49.7 | 54.6 | 59.3 | 67.7 | 75 | 98.9 |
| 6 | 17.3 | 27.4 | 32.6 | 37.7 | 46.2 | 52.7 | 58.4 | 63.3 | 71.8 | 78.8 | 97.3 |
| 7 | 19.1 | 26.7 | 32.4 | 37.5 | 43.3 | 51.3 | 57 | 61.8 | 70.4 | 77.3 | 99.1 |
| 8 | 18.2 | 25.7 | 31.4 | 35.9 | 42.8 | 49.6 | 54.9 | 59.4 | 68.5 | 74.9 | 98.2 |
| 9 | 18.7 | 26.3 | 31.8 | 37.1 | 44.8 | 51.1 | 57.6 | 62.1 | 70.8 | 77.1 | 98.7 |
| 10 | 18.9 | 26.4 | 32.3 | 37.3 | 45.8 | 51.4 | 57.3 | 62.1 | 71 | 77.2 | 98.9 |
| 11 | 18.4 | 26.2 | 32.3 | 36.9 | 44.6 | 50.6 | 56.5 | 61.4 | 70 | 77.3 | 98.4 |
| 12 | 19.7 | 26.7 | 32.6 | 37.7 | 45.7 | 52.2 | 58.2 | 63.5 | 72.2 | 79.9 | 99.7 |
| Min | 17.3 | 24.8 | 30.3 | 35.1 | 42.8 | 49.6 | 54.6 | 59.3 | 67.1 | 74 | 97.3 |
| Max | 19.7 | 27.4 | 32.6 | 37.7 | 46.2 | 52.7 | 58.4 | 63.5 | 72.2 | 79.9 | 99.7 |
| Mean | 18.5 | 26.1 | 31.9 | 36.6 | 44.2 | 51 | 56.6 | 61.3 | 69.7 | 76.7 | 98.5 |
| RSD | 3.5 | 2.9 | 2.1 | 2.5 | 2.9 | 1.8 | 2.1 | 2.3 | 2.3 | 2.4 | 3.5 |

**Table S9: % CDR of at each time points of 12 reference tablets Uroxatral (alfuzosin 10mg) extended release tablets formulation at pH 6.8**

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Tablet | Time in h (% cumulative drug release ) | | | | | | | | | | |
| No | 1 | 2 | 3 | 4 | 6 | 8 | 10 | 12 | 16 | 20 | 24 |
| 1 | 18.7 | 21.5 | 27.4 | 32.1 | 38.8 | 45.7 | 52 | 56.9 | 70.6 | 80.3 | 87.2 |
| 2 | 18.5 | 20.4 | 24.8 | 28.9 | 35.8 | 41.5 | 46 | 51.1 | 64.8 | 73.7 | 79.8 |
| 3 | 17.6 | 20 | 25 | 29.5 | 38.9 | 46 | 52.3 | 57.9 | 72.5 | 82.2 | 86 |
| 4 | 19.3 | 22.4 | 29.5 | 34.1 | 41.4 | 49.5 | 54.4 | 60.6 | 74.1 | 82.7 | 86.2 |
| 5 | 16.9 | 19.8 | 25.4 | 28.7 | 35.1 | 41.1 | 45.7 | 51.2 | 64.7 | 73 | 78.8 |
| 6 | 18 | 20.6 | 25.2 | 29.2 | 35.4 | 41.6 | 46.3 | 53.2 | 66.7 | 77.7 | 85.2 |
| 7 | 15.7 | 20.4 | 25.5 | 30 | 34.6 | 40.5 | 47 | 52.4 | 62.4 | 71.6 | 79.3 |
| 8 | 14.9 | 21 | 25.7 | 29.9 | 35.1 | 41.6 | 47.9 | 53.9 | 65.1 | 74.9 | 81.1 |
| 9 | 15.3 | 21.4 | 26.3 | 32 | 39.8 | 47.4 | 55.1 | 62 | 77.9 | 87 | 90.2 |
| 10 | 14.9 | 23.4 | 25.1 | 29.4 | 35.4 | 41.1 | 46.7 | 53 | 623 | 72.6 | 81.1 |
| 11 | 16 | 23.4 | 28 | 32.5 | 38.3 | 45.2 | 50.4 | 55.4 | 65.5 | 74 | 80.3 |
| 12 | 15.5 | 21.4 | 25.5 | 29.7 | 35.7 | 41.7 | 47.2 | 52.8 | 63 | 73.8 | 81 |
| Min | 14.9 | 19.8 | 24.8 | 28.7 | 34.6 | 40.5 | 45.7 | 51.1 | 62.3 | 71.6 | 78.8 |
| Max | 19.3 | 23.4 | 28 | 34.1 | 41.4 | 49.5 | 55.1 | 62 | 77.9 | 87 | 90.2 |
| Mean | 16.8 | 21.3 | 26.1 | 30.5 | 37 | 43.6 | 49.3 | 55 | 67.5 | 77 | 83 |
| RSD | 9.5 | 5.7 | 5.5 | 5.7 | 6.1 | 6.9 | 6.9 | 6.5 | 7.5 | 6.4 | 4.5 |

**Table S10: % CDR of at each time points of 12 reference tablets (alfuzosin 10mg) extended release tablets formulation at pH 6.8**

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Tablet | Time in h (% cumulative drug release ) | | | | | | | | | | |
| No | 1 | 2 | 3 | 4 | 6 | 8 | 10 | 12 | 16 | 20 | 24 |
| 1 | 16.6 | 23.6 | 29.6 | 34.4 | 42.3 | 48.5 | 54.4 | 59.1 | 68.2 | 74.6 | 96.6 |
| 2 | 16.9 | 24 | 29.5 | 33.9 | 42 | 48.7 | 54 | 59.5 | 68.8 | 76.8 | 96.9 |
| 3 | 16.6 | 23.8 | 29 | 34.1 | 41.6 | 47.6 | 53.8 | 58 | 66.9 | 74.1 | 96.6 |
| 4 | 17.2 | 24.4 | 34.3 | 34.3 | 40.8 | 47.3 | 53.4 | 57.3 | 67 | 73 | 97.2 |
| 5 | 16.9 | 24 | 29.1 | 33.6 | 41.1 | 48.1 | 53.2 | 57.9 | 65.5 | 72.3 | 96.9 |
| 6 | 16.7 | 23.7 | 29 | 34.1 | 41.3 | 48.3 | 53.3 | 58.3 | 66.2 | 74.8 | 96.7 |
| 7 | 16.8 | 23.6 | 29.5 | 33.9 | 40.8 | 47.9 | 53.2 | 58.5 | 67.4 | 74.7 | 96.8 |
| 8 | 16.8 | 24.1 | 29.6 | 33.9 | 41.2 | 48.2 | 53.7 | 58.4 | 67.2 | 74.8 | 96.8 |
| 9 | 17.1 | 23.8 | 30 | 34 | 41.9 | 48.1 | 53.6 | 58.6 | 67.7 | 74.4 | 97.1 |
| 10 | 16.8 | 24.6 | 29.5 | 34 | 41.6 | 47.3 | 533 | 58.2 | 67.6 | 73.8 | 96.8 |
| 11 | 16.9 | 23.7 | 29.6 | 34 | 41.5 | 47.6 | 53.2 | 58.2 | 66.6 | 73.6 | 96.9 |
| 12 | 17 | 23.9 | 29.4 | 34.1 | 41.6 | 47.5 | 53.3 | 58 | 66.8 | 74.9 | 97 |
| Min | 16.6 | 23.6 | 29 | 33.6 | 40.8 | 47.3 | 53.2 | 57.3 | 65.5 | 72.3 | 96.6 |
| Max | 19.3 | 23.4 | 28 | 34.1 | 41.4 | 49.5 | 55.1 | 62 | 77.9 | 87 | 99.3 |
| Mean | 16.9 | 23.9 | 29.8 | 34 | 41.5 | 47.9 | 53.5 | 58.3 | 67.2 | 74.3 | 96.9 |
| RSD | 1.1 | 1.3 | 4.8 | 0.6 | 1.1 | 1 | 0.7 | 1 | 1.3 | 1.5 | 1.0 |

**Table S11: Freeze and Thaw Stability of QC samples of Alfuzosin in Human Plasma (I to 4 and 6 Cycles)**

|  |  |  |  |
| --- | --- | --- | --- |
| AFTER ONE CYCLE | HIGH  25ng/ml | MEDIUM  2 ng/mL | LOW  0.15ng /ml |
|  |
| MEAN | 25.47 | 2.049 | 0.1446 |
| %CHANGE | 1.9 | 2.5 | -3.6 |
| Room temperature after 25hrs |  |  |  |
| NOMINAL value ng/ml | 25 | 2 | 0.15 |
| %CHANGE | 1.7 | 3.2 | 5 |
| Refrigerator stability 4°C ±6°C after 71 Hours |  |  |  |
| NOMINAL value ng/ml | 25 | 2 | 0.15 |
| %CHANGE | -8.9 | -8.3 | -10.8 |
| Stock solution stability |  |  |  |
| Refrigerator () % change | 0.6 | .70 | 1.2 |
| Room temperature | 2.3 | 2.9 | 3.1 |

Table S12: IR peak assignment for both test and reference alfuzosin

|  |  |  |
| --- | --- | --- |
| Frequency (1/cm) | | Assignment |
| Reference | Test |
| 3371.57 | 3369.64 | -N-H aromatic stretching (primary amine) |
| 3138.18 | 3068.75,3049.46 | *=C-H aromatic stretching* |
| 2935.66 | 2933.73 | *-C-H stretching* |
| 1654.92, 1631.78 | 1670.35, 1631.78 | -C=O stretching (Secondary amide) |
| 1087.85 | 1087.85 | -C-O stretching (5 member ring) |

**Table S13: Proton NMR peak assignment**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Chemical Shift (δ ppm) | | Multiplicity | No of protons | Assignment |
| Reference | Test |  |  |  |
| 11.93 | 11.96 | Singlet | 1 | 13 |
| 8.89-8.49 | 8.89-8.48 | Singlet | 2 | 28 |
| 7.90 | 7.89 | Triplet | 2 | 10 |
| 7.75-7.63 | 7.76--7.65 | Doublet | 2 | 5,8 |
| 4.21-4.17 | 4.21-4.17 | Multiplet | 1 | 15 |
| 3.86-3.82 | 3.86-3.83 | Doublet | 6 | 23, 25 |
| 3.76-3.65 | 3.76--3.65 | Multiplet | 3 | 12 |
| 3.34 | 3.33 | Singlet | 3 | 21 |
| 3.16-3.11 | 3.16-3.12 | Quartrate | 2 | 18 |
| 2.07-1.74 | 2.07-1.75 | Multiplet | 6 | 11,16 and 17 |

Table S14: 13C NMR Chemical shift Assignment for alfuzosin test and standard drug

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Chemical Shift (Delta ppm) | | No of carbon | Chemical Shift (Delta ppm) | | No of carbon |
| Reference drug | Test drug |  | Reference drug | Test drug |  |
| 172.5 | 172.46 | 14 | 77.71 | 77.69 | 15 |
| 161.04 | 161.03 | 2 | 68.52 | 68.49 | 18 |
| 155.08 | 155.07 | 4 | 56.26 | 56.25 | 23 |
| 151.77 | 151.75 | 26 | 56.03 | 56.01 | 25 |
| 146.58 | 146.56 | 6 | 47.23 | 47.21 | 12 |
| 136.27 | 136.26 | 7 | 35.94 | 35.92 | 10 |
| 105.05 | 105.07 | 8 | 35.68 | 35.66 | 21 |
| 101.51 | 101.5 | 27 | 29.93 | 29.88 | 16 |
| 99.25 | 99.26 | 5 | 26.96 | 26.93 | 11 |
|  | | 15 | 24.95 | 24.92 | 17 |

Table S15: Molecular ion peaks of Alfuzosin test and reference drugs

|  |  |
| --- | --- |
| Batch | Molecular Ion Peak (M + 1) |
| Reference drug | 390.00 |
| Test drug | 390.00 |

**Figure S1: Description of Large scale manufacturing process**

**A schematic diagram of manufacturing alfuzosin hydrochloride extended release tablets 10mg**

**Raw materials**

**In process**

**Analysis**

Alfuzosin Hydrochloride , Lactose Monohydrate, NF, Mono and Di Glycerides, NF, Magnesium Stearate, NF and Talc, NF

**Shifting**

**Dispensing**

Colloidal Silicon Dioxide, NF

Opacode black S-1-27794

Isopropyl Alcohol

**Dry mixing** (Jacketed rapid Mixer granulator)

Alfuzosin Hydrochloride , Lactose Monohydrate, NF, Mono and Di Glycerides, NF,

**Hot Melt granulation**

**Milling** (Oscillating Granulator equipped with

1. 2 I mm screen)

Colloidal silica (Aerosol 200)

**In-Process analysis**

Description

Identification

Assay

Blend unifonnity

**Blending** (Conta Blender)

Talc NF

**Lubrication** (Conta Blender)

Magnesium Stearate, NF

**In-Process Checks**

• Description

• Average weight Of tablets

• Individual weight variation

• Thickness

• Hardness • Friability

**Compression (Compression machine)**

**In-Process Checks**

Description

**Metal detection**

**(Metal Detector)**

**Tablet Imprinting**

**Acceptance Quality Level (AQL) test**

**Finished Product Analysis**

As per finished product specification

**Visual Inspection (Visual inspection Belt)**

**Packaging**