

Supplementary Material

Pharmaceutical Development of Film-coated Mini-tablets with Losartan Potassium for Epidermolysis Bullosa

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Table S1. Composition of mobile phase for purity analysis via HPLC

| Mobile phase | | | |
|------------------|--|-------------------|-------------------|
| buffer | 1.25 mg/mL potassium dihydrogen phosphate and 1.5 mg/mL di-sodium hydrogen phosphate in water (pH approximately 7.0) | | |
| solution A | acetonitrile and buffer (15:85) | | |
| solution B | acetonitrile | | |
| gradient elution | time | solution A | solution B |
| | [min] | [%] | [%] |
| | 0 | 80 | 20 |
| | 10 | 40 | 60 |
| | 11 | 80 | 20 |
| 20 | 80 | 20 | |

Table S2. Flow properties of F 8 and its single components, mean \pm sd, n=3, LP = losartan potassium, SMCC = silicified microcrystalline cellulose

| Material/powder | Hausner ratio | Flowability (Ph.Eur. 10)* |
|-----------------|-----------------|---------------------------|
| F 8 | 1.35 \pm 0.01 | poor |
| LP | 1.50 \pm 0.01 | very poor |
| SMCC 50 | 1.27 \pm 0.02 | passable |

*Rating by mean of Hausner ratio

Table S3. Particle size characterization and Hausner ratio of granules (F 10A, 10B, 10C), mean \pm sd, n=3

| | D ₁₀ [μ m] | D ₅₀ [μ m] | D ₉₀ [μ m] | Hausner ratio | Flowability (Ph. Eur. 10)* |
|------------------------|----------------------------|----------------------------|----------------------------|-----------------|----------------------------|
| F 10A (2 kN/cm) | 59 \pm 1 | 634 \pm 12 | 1135 \pm 4 | 1.41 \pm 0.01 | poor |
| F 10B (4 kN/cm) | 75 \pm 1 | 799 \pm 8 | 1183 \pm 4 | 1.35 \pm 0.02 | poor |
| F 10C (6 kN/cm) | 101 \pm 13 | 832 \pm 12 | 1204 \pm 4 | 1.33 \pm 0.02 | passable |

*Rating by mean of Hausner ratio

Table S4. Purity of the coated mini-tablets (F 10C) stored at 40 °C / 75 % r.h. and 25 °C / 60 % r.h. in different packaging conditions (openly, in polyethylene bags (PE) and in sealed aluminium foil (Alu)). For better overview only results at initial timepoint and after 6 months storage are shown (3rd month timepoint not shown), MT = mini-tablets, ND = not detected, < 0.1 % = impurities detected but not included in calculations

| Coated MT of F 10 C | Purity | 6 months 25 °C / 60 % r.h. | | | 6 months 40 °C / 75 % r.h. | | |
|---------------------------|--------|----------------------------|--------|---------|----------------------------|---------|---------|
| | | Initial | Openly | PE | Alu | Openly | PE |
| 1H Dimer | ND | ND | ND | ND | < 0.1 % | < 0.1 % | < 0.1 % |
| 2H Dimer | ND | ND | ND | ND | ND | ND | < 0.1 % |
| Other single impurities | ND | ND | ND | ND | < 0.1 % | < 0.1 % | ND |
| Sum of unknown impurities | ND | < 0.1 % | 0.10 % | < 0.1 % | 0.11 % | 0.13 % | 0.13 % |
| Sum of total impurities | ND | < 0.1 % | 0.10 % | < 0.1 % | 0.11 % | 0.13 % | 0.13 % |

Table S5. Purity of the coated mini-tablets (F 11) stored at 40 °C / 75 % r.h. and 25 °C / 60 % r.h. in different packaging conditions (openly, in polyethylene bags (PE) and in sealed aluminium foil (Alu)). For better overview only results at initial timepoint and after 6 months storage are shown (3rd month timepoint not shown), MT = mini-tablets, ND = not detected, < 0.1 % = impurities detected but not included in calculations

| Coated MT of F 11 | Purity | 6 months 25 °C / 60 % r.h. | | | 6 months 40 °C / 75 % r.h. | | |
|---------------------------|---------|----------------------------|---------|---------|----------------------------|---------|---------|
| | | Initial | Openly | PE | Alu | Openly | PE |
| 1H Dimer | ND | < 0.1 % | < 0.1 % | < 0.1 % | < 0.1 % | < 0.1 % | < 0.1 % |
| 2H Dimer | ND | < 0.1 % | < 0.1 % | ND | < 0.1 % | < 0.1 % | < 0.1 % |
| Other single impurities | ND | ND | ND | ND | < 0.1 % | < 0.1 % | < 0.1 % |
| Sum of unknown impurities | < 0.1 % | < 0.1 % | < 0.1 % | < 0.1 % | < 0.1 % | 0.10 % | 0.12 % |
| Sum of total impurities | < 0.1 % | < 0.1 % | < 0.1 % | < 0.1 % | < 0.1 % | 0.10 % | 0.12 % |