Annex II

Conditions to the marketing authorisation(s)

<table>
<tr><th>Conditions to the MA</th><th>Due date</th></tr>
<tr><td>The MAH must ensure that the manufacturing processes of the drug substances used for their drug products are reviewed for the potential risk of formation of N-nitrosamines and changed as necessary to minimise nitrosamine contamination as much as possible.</td><td>Within 2 years after Commission Decision</td></tr>
<tr><td>For all N-nitrosamines the MAH must ensure a control strategy is in place in drug substance batches used for their drug products.</td><td>At the time of Commission Decision</td></tr>
<tr><td>For N-nitrosodimethylamine (NDMA) and N nitrosodiethylamine (NDEA) the MAH must introduce the following specifications for the drug substance:

1) Limits for NDMA and NDEA outlined below should be implemented for a transitional period of 2 years:

<table>
<tr><th>Drug substance*</th><th>Max. daily dose (mg)</th><th>NDEA Limit in ng/day</th><th>NDEA Limit in ppm in API</th><th>NDMA Limit in ng/day</th><th>NDMA Limit in ppm in API</th></tr>
<tr><td>Valsartan</td><td>320</td><td>26.5</td><td>0.082</td><td>96.0</td><td>0.300</td></tr>
<tr><td>Losartan</td><td>150</td><td>26.5</td><td>0.177</td><td>96.0</td><td>0.640</td></tr>
<tr><td>Olmesartan</td><td>40</td><td>26.5</td><td>0.663</td><td>96.0</td><td>2.400</td></tr>
<tr><td>Irbesartan</td><td>300</td><td>26.5</td><td>0.088</td><td>96.0</td><td>0.320</td></tr>
<tr><td>Candesartan</td><td>32</td><td>26.5</td><td>0.820</td><td>96.0</td><td>3.000</td></tr>
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* These limits are not applicable for batches where more than one of the above N-nitrosamines has been identified simultaneously; such batches should be rejected.

2) After the transitional period of 2 years, a limit for NDMA and NDEA of maximum 0.03 ppm should be implemented.</td><td>At the time of Commission Decision

Within 2 years after Commission Decision</td></tr>
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