Demonstration of Pharmacokinetic and Pharmacodynamic Comparability in Healthy Volunteers for B12019, a Proposed Pegfilgrastim Biosimilar

K. Roth1 | H. Wessels1 | D. Lehnick2 | K. Jacob1 | R. Jankowsky1

• To demonstrate pharmacokinetic (PK) comparability of B12019 to the reference product Neulasta® based on the
• Primary PK parameters: AUC0-last and Cmax
• Days 6, 7, 8, 10, 12, 15, 18, 22, 29 and on day 43 in each period (10 samples)
• Randomised, double-blind, two-stage, two-way crossover, with sequential subcutaneous (s.c.) administration of

Study design:
• To demonstrate pharmacokinetic (PK) comparability of B12019 to the reference product Neulasta® based on the
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• Days 6, 7, 8, 10, 12, 15, 18, 22, 29 and on day 43 in each period (10 samples)
• Randomised, double-blind, two-stage, two-way crossover, with sequential subcutaneous (s.c.) administration of

Results: Pharmacokinetics:
• According to the predefined decision rules, no stage 2 was performed
• There was no relevant difference in the exposure of pegfilgrastim after administration of B12019 and Neulasta®
• Geometric mean ratio of AUEC0-last and Cmax for B12019 and Neulasta® was 94.32% and 95.23%, respectively (see Table 2).
• The secondary PK parameters showed similar descriptive statistics across treatments (see Table 3).

Table 2. Summary of the statistical analysis of pegfilgrastim (model-based PK set, N =167)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Randomized set</th>
<th>PD set</th>
<th>Model-based PD set</th>
</tr>
</thead>
<tbody>
<tr>
<td>PK set</td>
<td>84</td>
<td>85</td>
<td>84</td>
</tr>
<tr>
<td>PD set</td>
<td>84</td>
<td>83</td>
<td>87</td>
</tr>
<tr>
<td>PD set</td>
<td>79</td>
<td>82</td>
<td>81</td>
</tr>
<tr>
<td>PD set</td>
<td>79</td>
<td>82</td>
<td>81</td>
</tr>
</tbody>
</table>

Table 3. Summary of the secondary PK parameters of pegfilgrastim (PK set, N=102)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>B12019</th>
<th>Neulasta®</th>
<th>B12019/Neulasta®</th>
</tr>
</thead>
<tbody>
<tr>
<td>tmax [h]</td>
<td>12.48±6.39</td>
<td>12.14±6.39</td>
<td>1.02 (0.81–1.26)</td>
</tr>
<tr>
<td>t1/2 [h]</td>
<td>5.31±2.51</td>
<td>5.31±2.51</td>
<td>1.00 (0.81–1.26)</td>
</tr>
</tbody>
</table>

Statistical evaluation:
• Primary PK parameter: AUC0-last (expressed as percentage of Neulasta®)
• Secondary PK parameters: Cmax, tmax, t1/2, and allometric exponents

Clinical evaluation:
• Safety: No relevant difference in ANC after administration of B12019 and Neulasta®. Geometric mean ratio of AUEC0-last and Cmax for B12019 and Neulasta® was 94.32% and 95.23%, respectively (see Table 2).
• The secondary PK parameters showed similar descriptive statistics across treatments (see Table 3).

Immunogenicity:
• No antibodies against the filgrastim moiety or neutralising antibodies were detected for B12019 and Neulasta®.

Conclusion:
• The study demonstrated PK and PD comparability of B12019 and EU-authorised Neulasta®.
• No antibodies against the filgrastim moiety or neutralising antibodies were detected for B12019 and Neulasta®.