# Procedural steps taken and scientific information after the authorisation
# Changes made after 01/10/2002

**Hexavac**

**For procedures finalised before 01/10/2002, please refer to module 8A**

**MAJOR CHANGES[1]**

| No | Scope | Opinion issued on | Commission Decision Issued/ amended on | Product Information affected[2] | Summary |
|---|---|---|---|---|---|
| Z/0028 | Article 18 Review<br><br>Further to the request from the European Commission to the CHMP to issue an opinion on measures necessary to ensure the safe and effective use of Hexavac further to the CHMP review on Hepatitis short and long-term protection afforded by recombinant Hepatits B vaccines. | 15/09/2005 | 17/11/2005 | | Please refer to the scientific conclusions: Hexavac-H-298-Z-28 |
| II/0026 | Change(s) to the test method(s) and/or specifications for the active substance | 27/07/2005 | 05/08/2005 | | |
| II/0024 | Change(s) to the manufacturing process for the active substance | 27/07/2005 | 05/08/2005 | | |
| II/0022 | Change(s) to the test method(s) and/or specifications for the active substance | 21/04/2005 | 28/04/2005 | | |
| II/0019 | Change(s) to the manufacturing process for the active substance | 21/10/2004 | 28/10/2004 | | |
| A18/0029 | Article 18 Review | 21/04/2005 | 19/09/2005 | | Please refer to the scientific conclusions: Hexavac-H-298-A18-655 |



[1] Major changes e.g. Type II variations, Annex II applications, Renewals and Annual Reassessments
[2] SPC (Summary of Product Characteristics), Labelling, PL (Package Leaflet)

| No | Scope | Opinion issued on | Commission Decision Issued/ amended on | Product Information affected[2] | Summary |
|---|---|---|---|---|---|
| | Further to the request from the European Commission to the CHMP to issue an opinion on the safety profile, especially considering the occurrence of Sudden Unexpected Deaths after administration of Hexavac in the second year of life. | | | | |
| II/0017 | Update of Summary of Product Characteristics and Package Leaflet<br><br>Update of sections 4.2, 4.4, 4.5 and 4.8 of the SPC regarding boosting following assessment of the follow-up measure "Progress report on Active Surveillance to detect cases of invasive Hib disease in infants immunised with Hexavac in Germany", concomitant administration of Hexavac with Prevenar and to add "Haemophilus influenzae" in the second paragraph of section 4.8, due to previous omission, and other minor changes. | 20/11/2003 | 29/01/2004 | SPC, PL | Based on the submitted data, and following assessment of the follow-up measure "Progress report on Active Surveillance to detect cases of invasive Hib disease in infants immunised with Hexavac in Germany, the CHMP agreed that the MAH should clarify in section 4.2 (Posology and method of administration) that a booster dose must be given between 12 and 18 months of age, according to official recommendations.<br><br>Additionally, based on the assessment of the clinical trial data submitted, the CHMP agreed that sections 4.4 (Special warnings and special precautions for use), 4.5 (Interaction with other medicinal products and other forms of interaction) and 4.8 (Undesirable effects) should be updated to include information on co-administration with Prevenar.<br><br>Furthermore, section 4.8 was updated to include "Haemophilus influenzae" in the second paragraph, due to previous omission.<br><br>The Package Leaflet was updated accordingly. |
| II/0014 | Change(s) to shelf-life or storage conditions | 17/10/2002 | 14/01/2003 | SPC | |
| II/0013 | Update of Summary of Product Characteristics and Package Leaflet | 17/10/2002 | 14/01/2003 | SPC, PL | Based on the submitted data, and following assessment of the first PSUR covering the period from 02.10.2000 to 22.04.2001, the |

| No | Scope | Opinion issued on | Commission Decision Issued/ amended on | Product Information affected[2] | Summary |
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| | Update of section 4.8 of the SPC following the review of the first PSUR to include the "hypotonic-hyporesponsive episode". Other amendments were also made to section 4.8 according to post marketing experience. | | | | CHMP agreed that the MAH should update section 4.8 (Undesirable effects) on hypotonic-hyporesponsive episode.<br><br>Additionally, taking into consideration the post marketing experience, section 4.8 was also updated to include 1) commonly, oedema, pruritus, urticaria; 2) rarely, prolonged or abnormal crying; and 3) very rarely, allergic reaction, chills, fatigue, hypotonic-hyporesponsive episode, malaise, oedema, pallor, swelling or oedema of the entire limb(s), transient local lymph node swelling, convulsions (febrile and non febrile), encephalitis, encephalopathy with acute brain oedema, eyes rolling, Guillain Barré Syndrome, hypotonia, neuritis, abdominal pain, meteorism, nausea, petechiae, purpura, purpura thrombocytopenic, thrombocytopenia, agitation, sleep disorder, dyspnoea or Stridor inspiratory, angioedema, erythema, pruritus, rash, urticaria and flushing.<br><br>The Package Leaflet was updated accordingly and the local representatives list was reviewed. |
| II/0002 | Update of or change(s) to the pharmaceutical documentation | 17/02/2005 | 24/02/2005 | | |
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**MINOR CHANGES**[3]

| No | Scope | Product Information affected[2] | Date[4] |
|---|---|---|---|
| IA/0025 | 43_a_01_ Add./replacement/del. of measuring or administration device - addition or replacement | SPC, Labelling, PL | 26/04/2005 |
| IA/0023 | 01_Change in the name and/or address of the marketing authorisation holder<br>04_Change in name and/or address of a manuf. of the active substance (no Ph. Eur. cert. avail.)<br>05_Change in the name and/or address of a manufacturer of the finished product | SPC, Labelling, PL | 29/03/2005 |
| N/0020 | Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification) | PL | 04/08/2004 |
| IA/0018 | 07_a_Replacement/add. of manufacturing site: Secondary packaging site | | 14/07/2004 |
| I/0016 | Change in specification of starting material/intermediate used in manuf. of the active substance | | 08/08/2003 |
| I/0015 | Change in specification of starting material/intermediate used in manuf. of the active substance | | 24/07/2003 |
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[3] Minor changes e.g. Type I variations and Notifications
[4] Date of entry into force of the change