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National Health Care Institute

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2024040834

Date 3 December 2024
Re: GVS advice hepatitis B immunoglobulin (Uman Big®)

Our reference
2024040834

Dear Ms Agema,

The National Health Care Institute advises you on the inclusion of hepatitis B immunoglobulin (HBIG) (Uman Big®) to prevent hepatitis B infection in the Medicine Reimbursement System (GVS). This advice was prompted by your request in the letter of 30 September (CIBG-24-07398).

Uman Big® is indicated for the following indications.

- Prevention of hepatitis B re-infection following liver transplantation in case of hepatitis B-induced liver failure
- In case of accidental exposure to HBsAg-positive material in people who have not been vaccinated;
- In case of persistent hepatitis B infection risk if vaccination against hepatitis B is not possible or has not led to the formation of hepatitis B antibodies;
- In newborn infants born to mothers who are chronic carriers of the hepatitis B virus surface antigen (HBsAg) or who have experienced acute hepatitis B infection during pregnancy;
- In haemodialysis patients, until antibody formation is established after vaccination with a hepatitis B vaccine

Uman BIG® is available as a solution for intramuscular injection in vials of 1 (180 IU) and 3 ml (540 IU).

For the dosage of Uman Big® see the Summary of Product Characteristics[1].

The marketing authorisation holder is asking that the entire registered indication be included in List 1B of the Health Insurance Regulation.

Advice
National Health Care Institute advises you to include the medicinal product in List 1B of the GVS. Inclusion is accompanied by additional costs from the pharmaceutical budget estimated at a maximum of €200,000 in year 3.

We explain the preparation of this advice below.

[1] https://www.geneesmiddeleninformatiebank.nl/smpc/h129963_smpc.pdf

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Substantive assessment

Background
In the Netherlands, active immunisation of high-risk groups against hepatitis B, with a hepatitis B vaccine, is carried out through prevention programmes and in response to high-risk contacts. In some cases, for example when direct protection is desired, passive immunisation with hepatitis B immunoglobulin (HBIG) is indicated, usually combined with or followed by active immunisation[2].

Hepatitis B immunoglobulin (HBIG) was produced by Sanquin Plasma Products (SPP) for the Dutch market and was marketed under the brand name HepBQuin® since 1997. This was an intra-muscular (IM) product. When there were delivery issues with this product, SPP provided a replacement product: HBIG IM (ImmunoHBS®, from manufacturer Kedrion). After the temporary shortage had become permanent, ImmunoHBS® could be ordered and imported with a completed medical certificate[3]. Manufacturer Kedrion has now registered ImmunoHBS® under the brand name Uman Big® in the Netherlands[4]. Therefore, ImmunoHBS® is no longer available through a medical certificate.

Zutectra® and Hepatect CP® are other registered and reimbursed HBIGs. Zutectra® is included in the GVS but is only indicated for the prevention of hepatitis B infection after liver transplantation in case of hepatitis B-induced liver failure. Hepatect CP® is available for inpatient care and just as widely indicated as Uman Big®, but requires intravenous administration in the hospital. For mothers who are hepatitis B carriers and give birth at home, Hepatect CP® is therefore not an appropriate treatment.

Thus, at present, no registered product is included in the GVS for the treatment of newborns whose mother is a hepatitis B carrier. Therefore, according to the National Institute for Public Health and the Environment (RIVM), intramuscular treatment is greatly needed for these mothers who give birth at home.

Previously, it was decided by the Ministry of Health, Welfare and Sport that all immunoglobulins are, in principle, eligible for inclusion in List 1B due to the unique nature of the market and products (letter Farmatec/P 2663949, 24 February 2006). Testing of the interchangeability of immunoglobulins is therefore not required.

Composition and pharmacokinetic properties
The 4 available HBIGs Uman Big®, Zutecta®, Hepatect CP® and HepBQuin® have more or less similar compositions and pharmacokinetic properties. The concentrations vary slightly and the dosage form differs. Human hepatitis B immunoglobulin for intramuscular use is bioavailable in the recipient's circulation with a delay of 2-7 days. It is immediately available when administered intravenously[5]. Human hepatitis B immunoglobulin has a half-life of approximately 3-4 weeks[6]. In short, the pharmacokinetic properties and composition of Uman

2 https://www.farmacotherapeutischkompas.nl/bladeren/preparaatteksten/h/hepatitis_b_immunoglobuline

3 https://www.rivm.nl/sites/default/files/newsletters/101500-2412-253258.html

4 https://www.ema.europa.eu/nl/documents/referral/uman-big-article-29-referral-annex-i-ii-iii_nl.pdf

5 Uman Big®, HepBQuin® (no longer available) and Zutectra® have the same route of administration, namely via an injection. Hepatect CP® is administered intravenously.

6 SmPC Uman Big®, SmPC HepBQuin®, SmPC Zutectra® and SmPC Hepatect CP®

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Big®, HepBQuin® (which is no longer available), Zutectra® and Hepatect CP® are similar.

Based on the previously assessed therapeutic equivalence of HepBquin® with Zutectra® and the comparable pharmacokinetics and composition of HepBquin® and Uman Big®, the National Health Care Institute concludes that Uman Big® has an equal value compared to Zutectra® and Hepatect CP®.

Budget impact analysis
The National Health Care Institute estimates that up to 500 newborns per year will be treated with Uman Big® for the prevention of hepatitis B infection after inclusion in the package. The total costs per patient are €170. This results in possible macro costs of €85,020 in the third year after inclusion.
In addition, Zutectra® may be substituted for by Uman Big® for the prevention of hepatic B re-infection after liver transplantation. The dosage of both medicines is different, both are administered based on HBsAg antibodies. Based on Zutectra®'s claimed IUs (80-90 users per year) for this indication, the maximum additional costs per year due to substitution are estimated at no more than €120,000[7].

Should you need any further information, please do not hesitate to contact us.

Yours sincerely,

Mark Janssen
Chairperson of the Executive Board

[7] GIP Database: Number of users 2019-2023 for ATC code J06BB04: Hepatitis b immunoglobulin