Biotest

*From Nature for Life*

# Zutectra®

## Human Hepatitis B Immunoglobulin 500 IU
## Solution for Subcutaneous Injection

Subcutaneous administration

*HBV reinfection prophylaxis after liver transplantation*

Product monograph

PM-UK-ZUT-0005
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# Contents

# Risk of hepatitis B virus reinfection after liver transplantation

Orthotopic liver transplantation (OLT) is a well-established procedure worldwide in patients with liver cirrhosis or hepatocellular carcinoma (HCC) due to chronic hepatitis B virus (HBV) infection. Effective prevention of HBV reinfection of the graft is vital for adequate graft function and patients' long-term survival.[1,2]

According to published studies the gold standard prophylactic treatment for the prevention of HBV is a combination of nucleoside/nucleotide analogues (NA) and hepatitis B immunoglobulin (HBIg).[3] With this combination therapy, the HBV reinfection rate can be reduced to as little as 0.7%, as a recently published retrospective data collection (RDC) has demonstrated.[4]

## The following risk factors at OLT may be important indicators for high risk of HBV reinfection:

- Hepatocellular carcinoma (HCC)[5-8]
- HBV coinfection e.g. human immunodeficiency virus (HIV) and hepatitis D virus (HDV) [5, 11-14]
- HBV-DNA + and/or HBeAg +[5, 9, 10]
- Nephrotoxicity[14-18]
- Poor adherence[5, 19, 20]

## Guidelines from the European Association for the Study of the Liver issued in 2017 state:

EASL 2017

*"... lifelong combination therapy should be given to patients who are at a high risk for HBV recurrence, namely those who are HBV-DNA-positive at the time of liver transplantation, who are HBeAg-positive, have HCC, and HDV or HIV co-infection".*[14]

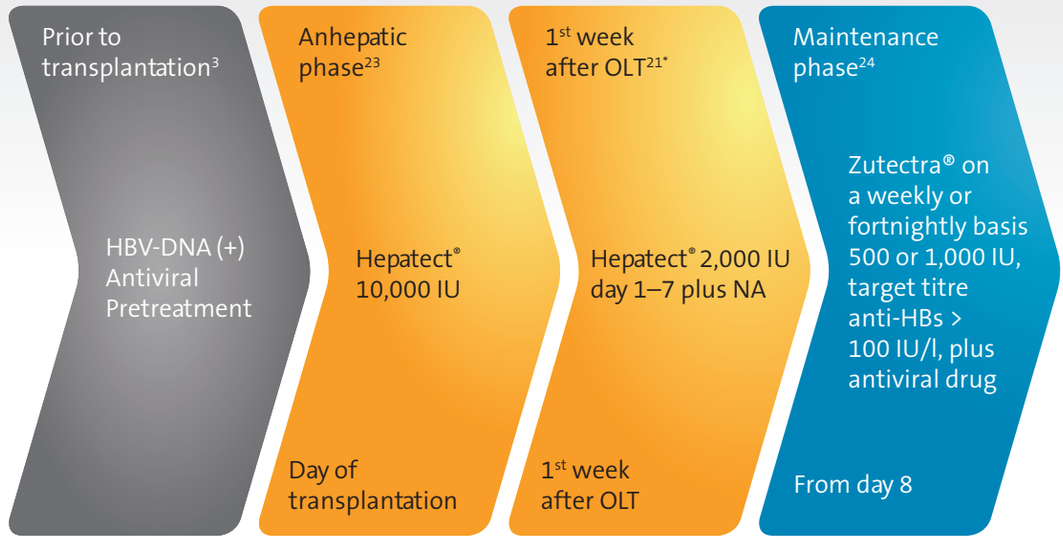
# Measures to help prevent HBV reinfection

Antiviral treatment is usually initiated prior to liver transplantation to reduce the viral load below the detection limit. Following OLT, antiviral treatment is continued, ideally in combination with HBIg. This helps to ensure HBV reinfection prophylaxis at different levels: On the one hand, administration of antiviral drugs aim to prevent replication of the virus. While on the other hand, the anti-HBs antibodies aid prevention of the liver from becoming reinfected by neutralising free HBV particles, stopping them from binding to the HBV receptor on hepatocytes, and inducing antibody-mediated lysis of virus-infected hepatocytes.[5]

HBIg prophylaxis is initiated perioperatively – in the anhepatic phase – by administration of 10,000 international units (IU) HBIg intravenously. Usually, 2,000 IU are administered daily in the first week after OLT. This was demonstrated in the study by Rosenau et al.[21]

The phase of seroconversion is followed by the maintenance phase. In this stage, dosage and administration intervals of HBIg should be adjusted to the individual patient's need, in order to maintain stable levels of anti-HBs in the serum. It is usually sufficient to administer 500 IU subcutaneously either weekly or fortnightly.[22] If intravenous (IV) HBIg is being used, at least 2,000 IU are required per month, however, the average monthly HBIg requirement can vary from 800 – 4,800 IU, depending on the patient.[23] During the maintenance phase, anti-HBs serum levels >100 IU/l are generally considered to be protective.[22]

*Measures to help prevent HBV reinfection*



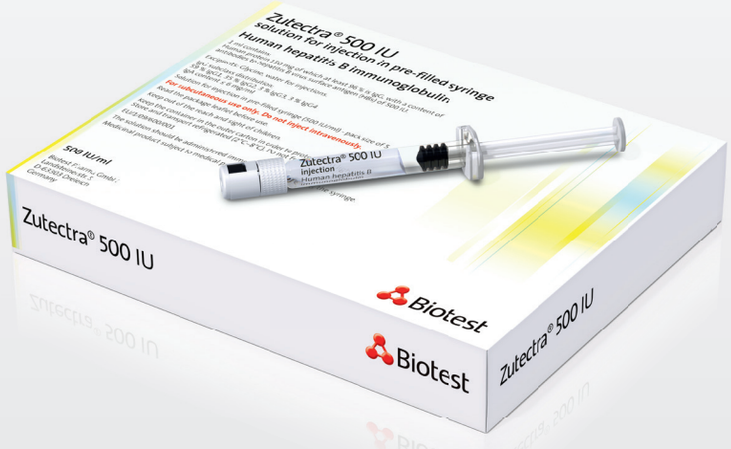

**For more information please refer to the Hepatect® (human hepatitis b immunoglobulin) Summary of Product Characteristics ahead of prescribing.*

# Zutectra® – HBV reinfection prophylaxis

The development of Zutectra® is based on many years of clinical experience with Hepatect® CP for HBV reinfection prophylaxis in patients after liver transplantation due to an HBV-associated liver disease. Zutectra® is an HBIg preparation that can improve the standard in reinfection prophylaxis – for both patient and physician.[22]

## An HBIg for subcutaneous (SC) injection from post-transplant day 8 or 11 onwards:

- Proven in long-term combination use[4]
- Simple administration by SC injection[22]
- Generally well-tolerated[4]
- Potentially cost effective home therapy[22]
- Supports early switch from IV to SC HBIg[22]



# Zutectra® - Retrospective Data Collection (RDC) on long-term combination therapy[4]

## Study background and objectives:

**Study objective:**

Evaluation of long-term effectiveness and tolerability of combination therapy using IV Hepatect® CP or SC Zutectra® and a nucleoside/nucleotide analogue for prevention of HBV recurrence

**Study design:**

Retrospective, non-interventional, single arm in 20 centres across 5 EU countries

**Primary endpoint:**

HBV-liver transplant patients free of HBV recurrence as assessed by non-detectability of HBsAg and/or HBV-DNA in patients' sera

**Secondary endpoints:**

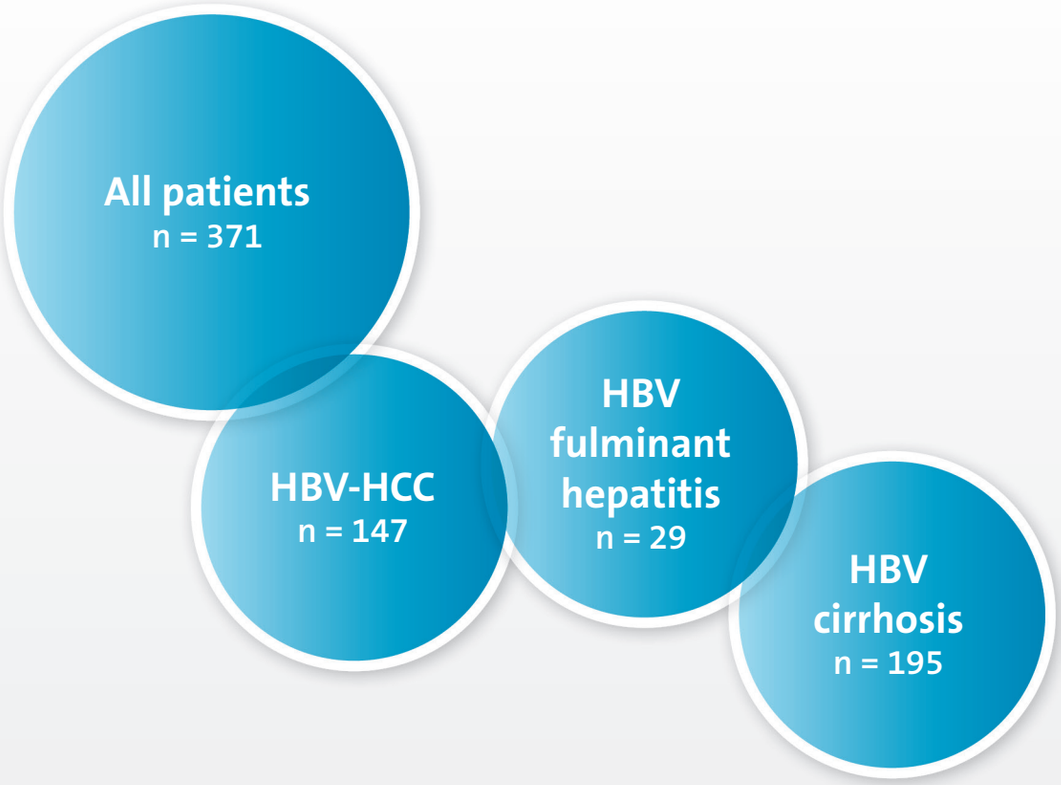
Proportion of patients with HBV recurrence, the time to HBV recurrence, the proportion of patients with HBV-HCC recurrence and serum levels of anti-HBs, HBsAg, and HBV DNA

## Study methodology – inclusion criteria:

- Patients were 18 years or older
- Patients with liver transplantation for fulminant HBV, HBV cirrhosis, or HBV-HCC inside the Milan criteria, or with liver re-transplantation except due to HBV recurrence
- Treatment with any HBIg for at least 1 year from liver transplantation onwards including treatment for at least 6 months with Hepatect® or Zutectra®
- Liver transplantation after the year 2000

## Study parameters:

### Patient cohorts:

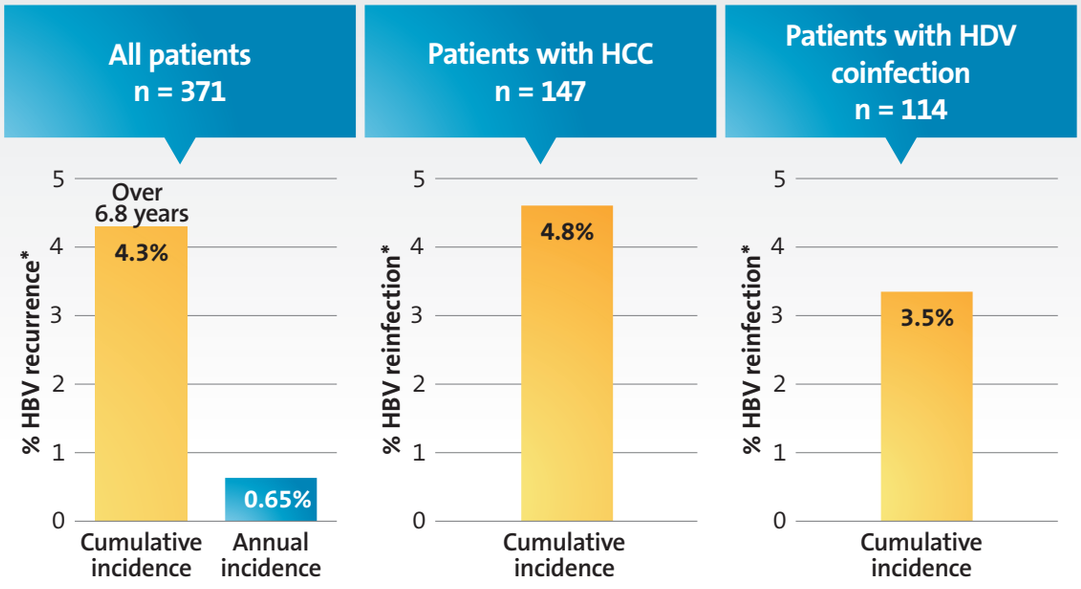



| | |
|---|---|
| Mean follow-up time | 6.8 years |
| Age, mean | 58.5 (10.7) |
| Gender male, n (%) | 257 (77.4%) |
| MELD score, mean (SD) | 18.0 (9.2) |
| Viral coinfection HDV/HCV/HIV, % | 30.7%/10.0%/0% |
| Duration of exposure, mean (SD)<br>Hepatect® (n=299)<br>Zutectra® (n=236)<br>Other HBIg (n=130) | <br>30.8 months<br>36.4 months<br>42.1 months |

**RDC, Retrospective Data Collection*

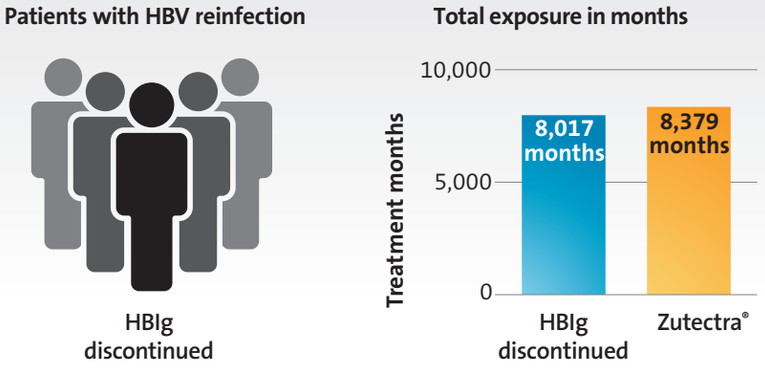
## Results:

### HBV recurrence rate was limited to 0.65% per year with Zutectra®[4]



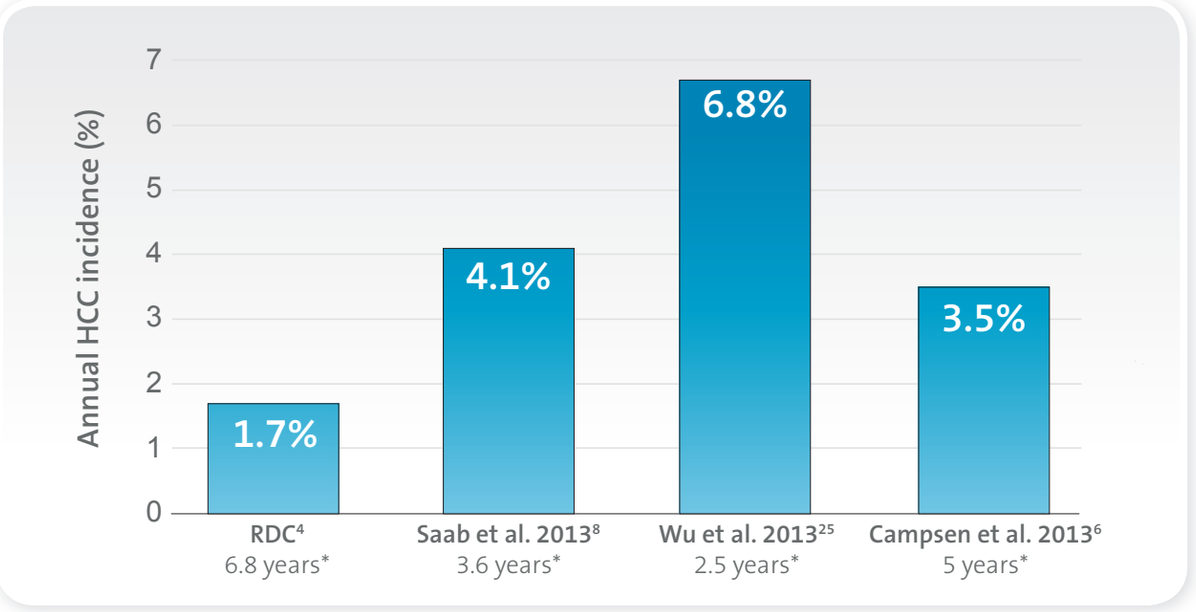

**Patients on LONG-TERM prophylaxis with Zutectra® and NA have a 5-fold lower risk of HBV recurrence compared to patients who stopped using HBIg[4]**

### Zutectra® decreased the risk of HBV recurrence by a factor of 5 vs. patients who discontinued HBIg[4]




**Only one patient with HBV recurrence on Zutectra® was observed. This patient had low anti-HBs titres (18 IU/l)[4]**

## The combination of Zutectra® and a virostatic reduced the recurrence of HCC[4]




**Mean follow-up time*

**The combination of HBIg and a virostatic prevented the recurrence of HCC in more than 90% of patients over 6.8 years[4]**

**Stable trough levels of anti-HBs >100 IU/l** were achieved with Hepatect® and Zutectra® for maintenance therapy over the mean study period of **6.8 years**[4]

### Summary[4]

- Patients on LONG-TERM prophylaxis with Zutectra® and NA have a 5-fold lower risk of HBV recurrence compared to patients who stopped using HBIg
- Only one patient with HBV recurrence under Zutectra® was observed. This patient had low anti-HBs titres (18 IU/l)
- The combination of HBIg and a virostatic prevented the recurrence of HCC in more than 90% of patients over a mean follow-up of 6.8 years

# Zutectra® – Self-administration of HBV reinfection prophylaxis

## Zutectra® allows self-administration by the patient due to its easy and convenient handling[22]

**The SC administration of Zutectra® offers several advantages over IV or intramuscular (IM) injection during the maintenance phase:**

- The small-volume SC administration of 1 ml Zutectra® is easy to perform and very well tolerated[22]
- Following training, patients can self-administer the SC injection on their own[22]
- Personalised titre-based dosing possible[22]

### Zutectra® offers a convenient and cost effective home therapy compared with hospital treatment


**SC administration at home is convenient for patients and reduces staff time[22]**

# Zutectra® – Quality of life[26]

## Significant improvement in the SF-36 parameter $p < 0.0001$[26]

In a study of patients switching from IM or IV administration, they reported with SC administration:

- Fewer adverse events
- More flexibility
- Less support required
- Greater satisfaction
- Less painful

- 78 OLT patients dosed with IV or IM HBIg were converted to SC Zutectra® (mean 8 years post-Tx)[26]
- Quality of life was based on validated questionnaires (SF-36 Health Survey at conversion and at a mean time of 6 months after conversion)[26]

## By switching to self-administration with Zutectra® by SC injection, patients can gain greater independence in their personal life:

- Injections can be given at any time of day, at times convenient to them[22]
- Fewer clinic appointments, requiring less travel time and lower transportation costs[22]
- Less time spent away from home or work[22]
- More flexible leisure time (e.g. ability to travel)[22]
- Significant improvement in quality of life[26]

# ZEUS – Study on early use of Zutectra® after liver transplantation

## The results of the Zutectra® Early Use Study (ZEUS) — an open, prospective, single arm phase III trial — demonstrate that the option to switch early from IV to SC administration of HBIg is manageable in patients receiving a liver transplant for HBV-associated liver failure[22]

**Study population:**

- 49 patients (41/49 male, 83.7 %) after liver transplantation, 45 of these patients (91.8 %) due to HBV-induced liver cirrhosis
- Mean age: 52 years
- Time to switch to Zutectra®: 8–11 days after transplantation = 37 patients, 15–18 days after transplantation = 12 patients

At the time of OLT, all patients were HBV-DNA-negative; when switched to SC HBIg, all patients were also HBsAg-negative. During the study, the patients received additional antiviral therapy as well.

**Dose regimen:**

- Weekly or fortnightly administration of 500 – 1,500 IU (based on anti-HBs serum levels)*

**Primary outcome measure:**

- Failure rate by month 6 (anti-HBs serum level ≤ 100 IU /l) or HBV reinfection after 6 months despite anti-HBs serum level ≥ 100 IU /l

## Results:

**Dosage:**

- In most patients, administration of 500 IU on a weekly or fortnightly basis was sufficient
- Overall, only a few dose adjustments were needed

*ZEUS - study on early use of Zutectra® after OLT Zutectra® dosage[22]*

| | | Beginning of study | End of study |
|---|---|---|---|
| Once per week (n = 20) | 500 IU | 19 | 15 |
| | 1,000 IU | 1 | 5 |
| Once every 2 weeks (n = 29) | 500 IU | 22 | 20 |
| | 1,000 IU | 5 | 8 |
| | 1,500 IU | 2 | 1 |

**500-1000 IU is the recommended dose as per the Zutectra® SmPC, however, 1500 IU can be used in exceptional cases*

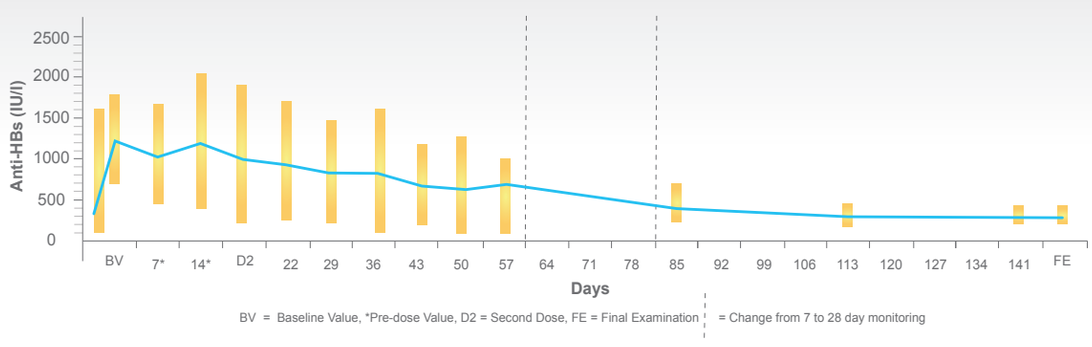
## Easy to use[22]

After 14 weeks, all patients (n = 49) administered Zutectra® themselves or had a caregiver perform the injection. 100% of patients were satisfied with their treatment. After 16 weeks 100% rated the injection as convenient. According to the patient diary, compliance was 100% during the entire study period.

**Efficacy:**

- All patients had HBIg serum levels > 100 IU/l and remained HBsAg-negative during the entire study
- The anti-HBs levels reached their maximum values after the second administration and eventually plateaued at an average of approximately 290 IU/l
- At the end of the study, all patients (n = 49) remained HBV-DNA-negative

*Anti-HBs levels during the ZEUS study (mean ± standard deviation)*




## Summary[22]

- The combination of Zutectra® and an antiviral drug may effectively protect patients from HBV reinfection
- Switching early to Zutectra®, one week after liver transplantation, allows patient-friendly prophylaxis and helps achieve sufficient HBIg levels

# Prospective clinical trials on the efficacy and tolerability of Zutectra®

## Yahyazadeh A et al. 2011[27] – An open, prospective, single-arm phase III study investigating the efficacy, safety and self-administration of weekly Zutectra®

**Study population:**

- 23 male and female patients after receiving a liver transplant for HBV-associated liver failure
- The median age was 51 years, the mean weight was 75 kg
- The mean time between transplantation to the first Zutectra® dose was 5.1 years

**Dose regimen:**

- Weight-dependent weekly dose of 500 – 1,000 IU
- About 2 – 3 weeks after the last dose of long-term prophylaxis with intravenous HBIg (Hepatect® CP, Biotest), the patients were switched to subcutaneously administered Zutectra®

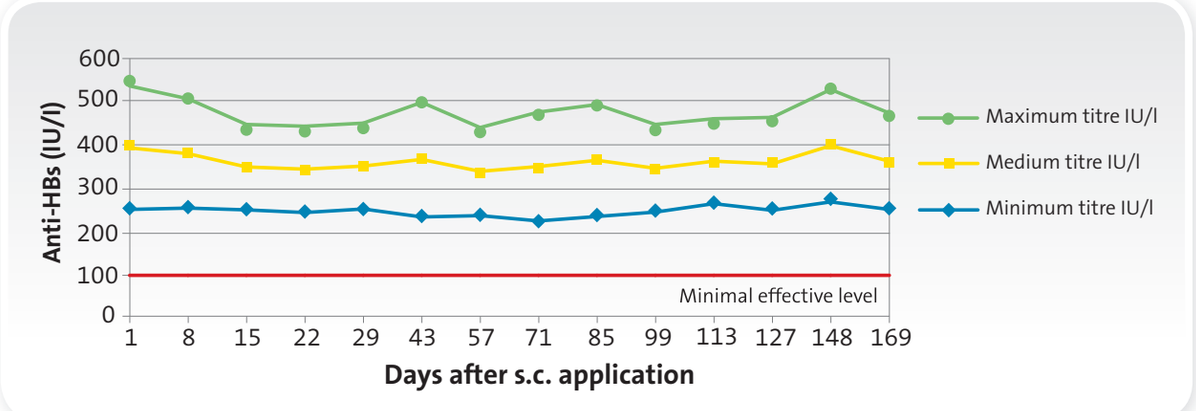
**Primary outcome measure:**

- Anti-HBs serum levels ≥ 100 IU/l at each sample time point during the study period of 18 weeks (optional 24 weeks)

### Results:

- The anti-HBs serum concentration remained stable in the range of 350 – 400 IU/l
- No patient developed an HBV reinfection (i.e. all remained HBsAg-negative)
- Laboratory assays and regular physical check-ups showed no clinically relevant changes
- Good patient compliance: By the end of the study, 96 % of the patients (n = 22) were self-administering at home

*Anti-HBs-titre time curve over 24 weeks*



## Di Costanzo GG et al. 2013[28] – Study to evaluate the safety, efficacy and tolerability of weekly self-administration of Zutectra®

**Study population:**

- 135 male and female patients after receiving a liver transplant for HBV-associated liver failure
- The median age was 57 years (34 – 78 years), the mean weight was 75 kg (50 – 117 kg). Time from transplantation to first Zutectra® administration was < 5 years in 33/135 patients, 5–10 years in 61/135 patients and > 10 years in 41/135 patients

**Dose regimen:**

- Weight-dependent weekly administration of 500 – 1,000 IU
- 2 – 3 weeks after the last dose of long-term prophylaxis with intravenous HBIg (Hepatect® CP, Biotest), the patients were switched to subcutaneously administered Zutectra®

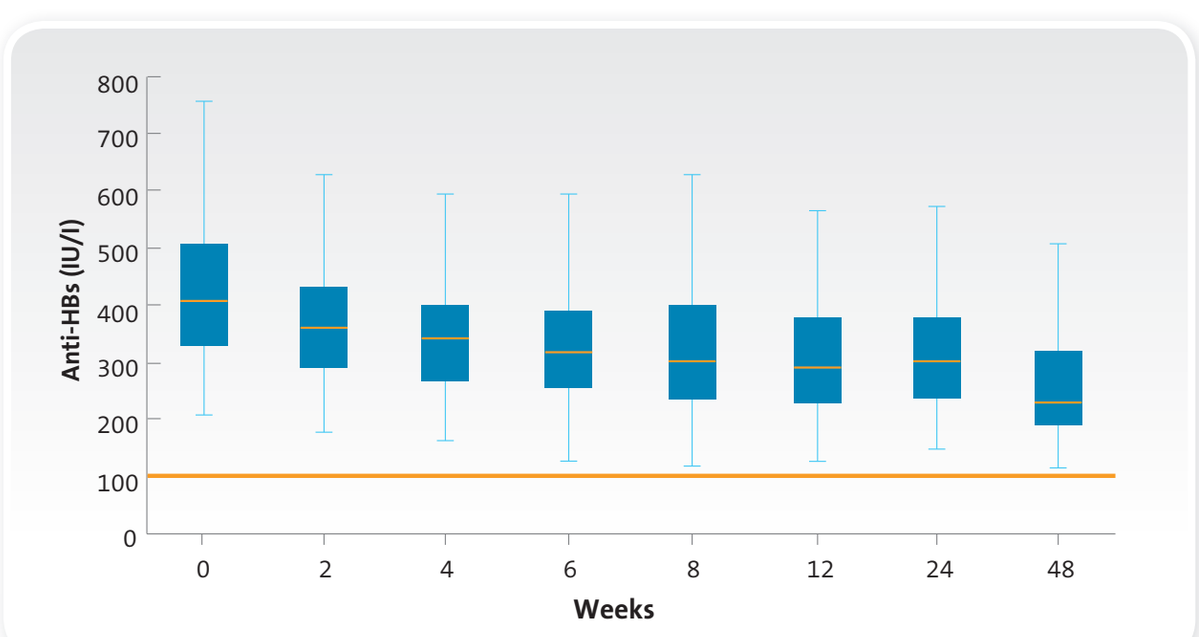
**Primary outcome measure:**

- Anti-HBs serum levels ≥ 100 IU/l during the study period of 48 weeks

### Results:

- At the end of the trial, the median anti-HBs serum concentration was 232 IU/l (115 – 566 IU/l)
- 98 % of the patients showed an anti-HBs level significantly above the threshold (> 150 IU/l)
- No changes in safety-relevant laboratory parameters or any therapy discontinuations related to adverse events were observed

*Anti-HBs-titre curve over 48 weeks*



## Klein CG et al. 2013[29] – Observational study on compliance, efficacy and tolerability of the self-administration of Zutectra®

**Study population:**

- 61 male and female patients after receiving a liver transplant for HBV-associated liver failure
- The median age was 57 years (26 – 75 years), the mean Body Mass Index was 26.4 (± 4.5)
- The median time from transplantation to study initiation was 5.7 years (0.2 – 19 years)

**Dose regimen:**

- Weight-dependent dose of 500 – 1,000 IU administered weekly or every two weeks
- After long-term prophylaxis with intravenous HBIg (Hepatect® CP, Biotest), the patients were switched to subcutaneously administered Zutectra®

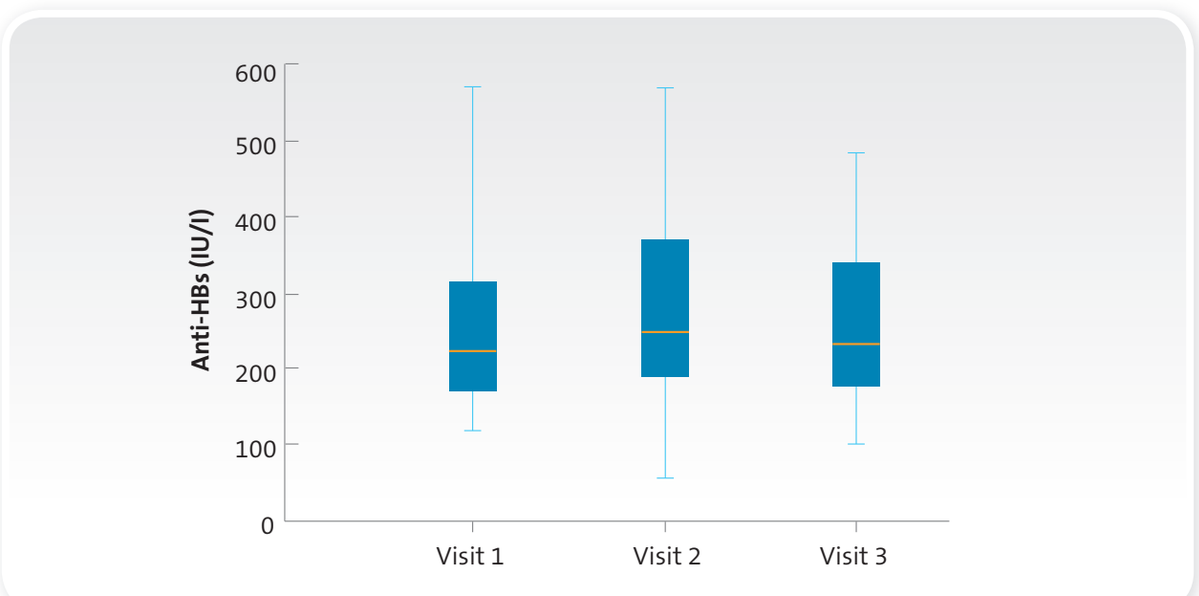
**Primary outcome measure:**

- Sufficient compliance to ensure anti-HBs serum levels ≥ 100 IU/l over the 18-week study period

## Results:

- At the end of the study, the mean anti-HBs serum concentration was 255 IU/l
- In 93 % of the patients, compliance was sufficient to ensure protective anti-HBs levels > 100 IU/l
- No patient was reinfected
- 961 of a total of 1,006 injections (95.5 %) took place at home, 96.1 % of these by the patients themselves, the others by relatives

*Anti-HBs-titre time curve over 18 weeks*



# Zutectra® – Product profile

*Zutectra® - Product profile*[24]

| | |
|---|---|
| Quantity of immunoglobulin G (IgG): | Human protein 150 mg/ml of which at least 96% is IgG |
| Quantity of IgG anti-HBs: | 500 IU/ml |
| Distribution of IgG subclasses: | IgG 1 59%<br>IgG 2 35%<br>IgG 3 3%<br>IgG 4 3% |
| Excipient: | Glycine |
| Route of administration: | Syringe with 1 ml (500 IU) for SC injection |
| Shelf life: | 24 months at 2°C – 8°C (refrigerated) |

**Indication and dosage:**[24]

Zutectra® is approved for the prevention of hepatitis B virus (HBV) reinfection in HBsAg and HBV-DNA negative adult patients at least one week after liver transplantation for hepatitis B induced liver failure. HBV-DNA negative status should be confirmed within the last 3 months prior to OLT. Patients should be HBsAg-negative before treatment starts. The concomitant use of adequate virostatic agents should be considered as standard of hepatitis B reinfection prophylaxis.

In HBV-DNA-negative adults, Zutectra® is subcutaneously administered after liver transplantation, on a once weekly or fortnightly basis guided by anti-HBs trough serum levels.

Prior to initiation of subcutaneous treatment with Zutectra® anti-HBs serum levels should be adjusted to levels of 300 – 500 IU/l or above, using an intravenous hepatitis B immunoglobulin in order to ensure adequate anti-HBs coverage during the switch from intravenous to subcutaneous administration. Antibody levels >100 IU/l should be maintained in HBsAg- and HBV-DNA-negative patients.

The administered subcutaneous dose may be individually adapted, from 500 IU up to 1,000 IU (in exceptional cases up to 1,500 IU) on a weekly or fortnightly basis, guided by anti-HBs serum concentrations and at the discretion of the physician in charge. Antibody levels > 100 IU/l should be maintained.

The pre-filled Zutectra® syringe should be warmed to room temperature (approx. 23 °C – 27 °C) before use. Detailed instructions on how to inject Zutectra® subcutaneously can be found in the package leaflet.

# Undesirable effects[24]

**Summary**

Most adverse drug reactions (ADRs) were mild to moderate in nature. In isolated cases human normal immunoglobulins may cause an anaphylactic shock.

| MedDRA System Organ Class | Adverse reactions | Frequency |
|---|---|---|
| Nervous system disorders | Headache | Uncommon |
| Gastrointestinal disorders | Upper abdominal pain | Uncommon |
| General disorders and administration site conditions | Injection site reactions like pain, urticaria Common at injection site, haematoma and erythema | Common |

**Adverse reactions observed with human immunoglobulin preparations**

| With normal immunoglobulins the following ADRs may occur occasionally | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Chills | Headache | Dizziness | Fever | Vomiting | Allergic | Nausea | Arthralgia | Low blood pressure | Moderate Low back pain |

| Local reactions at injection sites | | | | | | | |
|---|---|---|---|---|---|---|---|
| Swelling | Soreness | Redness | Induration | Local heat | Itching | Bruising | Rash |

**Rarely human normal immunoglobulins may cause a sudden fall in blood pressure and, in isolated cases, anaphylactic shock, even when the patient has shown no hypersensitivity to previous administration.**

Please refer to the Zutectra® Summary of Product Characteristics for further information.

# Pharmacokinetic properties[24]

## Distribution

Zutectra is slowly absorbed into the recipient's circulation and reaches a maximum after a delay of 27 days.

## Biotransformation

IgG and IgGcomplexes are broken down in the reticuloendothelial system.

## Elimination

Zutectra has a half-life of about 34 weeks. This half-life may vary from patient to patient.

# Production and virus safety

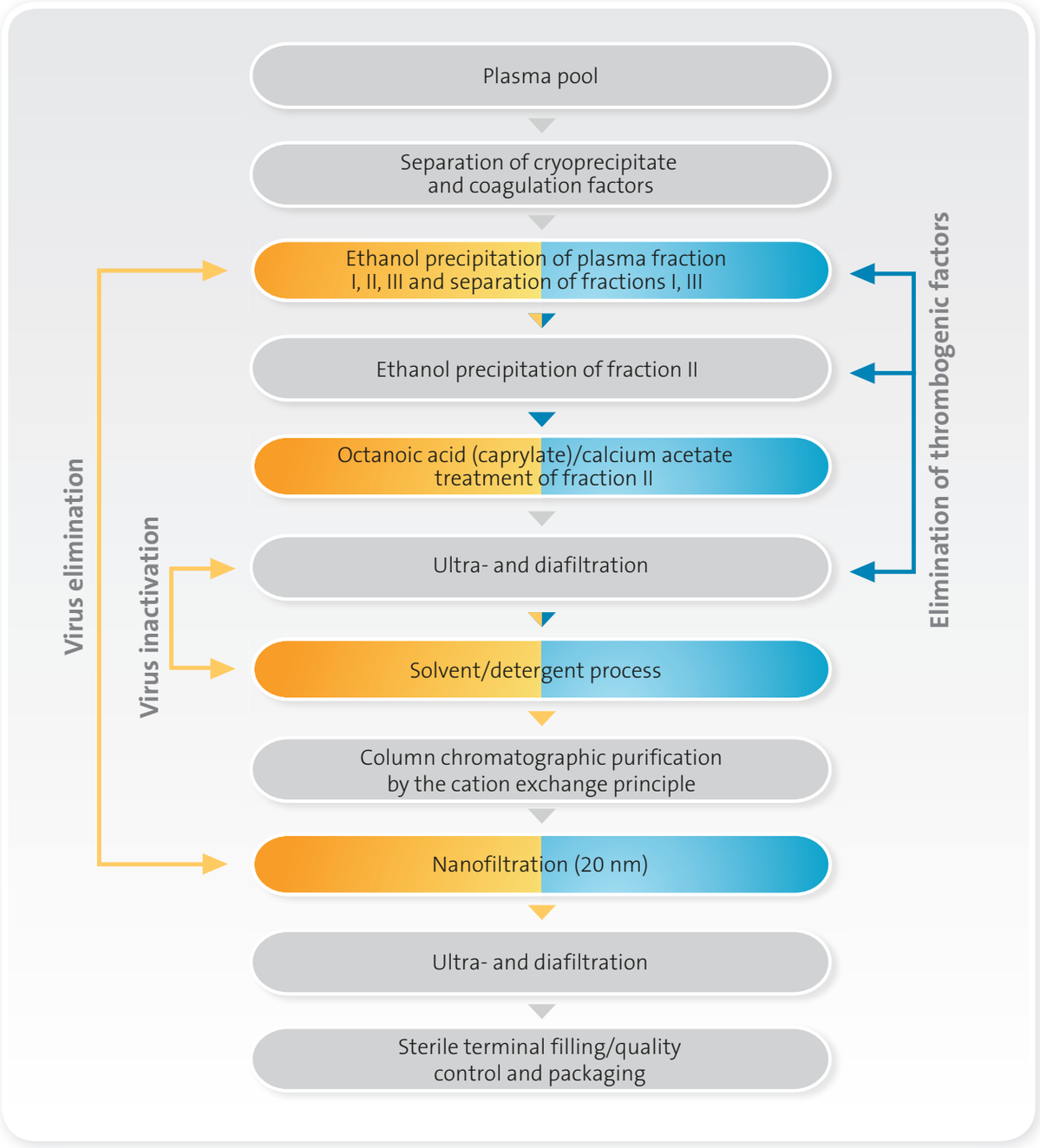
Zutectra® is a subcutaneously administered hepatitis B immunoglobulin for prophylaxis against HBV reinfection of the graft after liver transplantation. It is produced from the plasma of healthy donors and contains a standardised anti-HBs antibody titre of 500 IU/ml.

The manufacturing of Zutectra® is based on the Hepatect® CP manufacturing process. All process steps — from plasma donation to documentation of use — are subject to stringent safety and quality management according to the guidelines of the European Medicines Agency (EMA).[30]

Biotest ensures strict compliance with the standards of the Plasma Protein Therapeutic Association (PPTA) that go beyond regulatory requirements. In recognition of that, Biotest has been entitled to use the PPTA's QSEAL seal of quality and is re-certified at regular intervals.[31]

# Safety steps in plasma fractionation

*Zutectra® manufacturing process*[30,31]



# References


1. Samuel D. Digestive and Liver Dis, 2009; 41 S: 185–189
2. Mas A. Digestive and Liver Dis, 2009; 41 S: 191–194
3. Cholongitas E. and Papatheodoridis GV. Gastroenterol, 2013; 19 (48): 9189-97
4. Beckebaum, S et al. Ann Transplant 2018; 23: 789-801
5. Roche B, et al. Transplantation. 2015; 99(7): 1321-34
6. Campsen J, et al. Liver Transpl. 2013; 19(9): 1020-29
7. Dugam M, et al. Transplantation Proc. 2015; 47(6): 1939-44
8. Saab S, et al. Liver Transpl. 2009; 15(11): 1525-34
9. Roche B. Samuel D. Semin Liver Dis. 2012; 32(3): 245-55
10. Lin L Y, et al. J Med Virol. 2010; 82(9): 1494-500
11. Heidrich B, et al. Hepatology. 2014; 60(1): 87-97
12. Terrault NA, et al. Liver Transpl. 2006; 12(5):801(7)
13. Triantos C, et al. Aliment Pharmacol Ther. 2012; 35(6): 663-673
14. European Association for the Study of the Liver management of hepatitis B virus infection. J Hepatol. 2017; 67(2):370-398
15. Maggi P, et al. J Antimicrob Chemother. 2014; 70: 1150–54
16. Deray G, et al. Advances in Hepatology. 2015; http://dx.doi org/10.1155/2015/596829
17. Izzedine H, et al. Kidney Int. 2004; 66(3): 1153-8
18. Lampertico P, et al. Aliment Pharmacol Ther. 2016; 44: 16–34
19. Buti M, et al. Transplantation. 2007; 84(5): 650-4
20. Lieveld FL, et al. Ann Hepatol. 2013; 13(3): 380-91
21. Rosenau J, et al. J Hepatol. 2001; 34(6): 895-902
22. De Simone P, et al. Transplantation. 2016; 100(7): 1507-12
23. Rosenau J, et al. J Hepatol. 2007; 46: 635-644
24. Zutectra Summary of Product Characteristics
25. Wu TJ, et al. Ann Surg Oncol. 2013; 20(11): 3582–90
26. Volpes R et al, Transplant Int, 2015; 4: 235
27. Yahyazadeh A, et al. Transplant Int, 2011; 24: 441–450
28. Di Costanzo GG, et al. Am J Transplant, 2013; 13(2): 348-352
29. Klein CG, et al. Ann Transplant, 2013; 18: 677-684
30. UK Data on file REF 00240 2.3 S Drug Substance Overview of Manufacturing Process for Zutectra
31. Independent seal of Quality Standards of Excellence, Assurance and Leadership granted by the Plasma Protein Therapeutics Association

# Prescribing Information

Abbreviated Prescribing Information

**Zutectra® 500 IU Human hepatitis B immunoglobulin for subcutaneous injection in pre-filled syringe. Please consult full Summary of Product Characteristics (SmPC) before prescribing.**
Zutectra is a solution for subcutaneous injection of human hepatitis B immunoglobulin 500 IU/ml. Each 1ml pre-filled syringe contains 150 mg/ml human protein of which at least 96% of human protein is IgG.
**Indications and dosing:** Prevention of hepatitis B virus (HBV) re-infection in HBsAg and HBV-DNA negative adult patients at least one week after liver transplantation for hepatitis B induced liver failure. HBV-DNA negative status should be confirmed within the last 3 months prior to OLT. Patients should be HBsAg negative before treatment start. The concomitant use of adequate virostatic agents should be considered as standard of hepatitis B re-infection prophylaxis.
**Dose:** Prior to initiation of subcutaneous treatment with Zutectra, anti-HBs serum levels should be stabilised with an intravenous hepatitis B immunoglobulin at or above 300-500 IU/l to ensure anti-HBs coverage during dosing transition. At least 1 week after liver transplantation, in HBV-DNA negative adults, subcutaneous injections may be given weekly or fortnightly according to serum anti-HBs trough levels. Antibody levels >100 IU/l should be maintained in HBsAg and HBV-DNA negative patients. Dose to be individualised from 500 IU up to 1,000 IU (1,500 IU in exceptional cases). Patients must be monitored for serum anti-HBs antibody levels regularly, at least every 2-4 weeks and at discretion of physician for at least 6 months.
**Contraindications and precautions:** Hypersensitivity to any components or human immunoglobulins. Zutectra must not be administered intravascularly. If recipient is a carrier of HBsAg there is no benefit in use of this medicine and no data about efficacy in post-exposure prophylaxis is available. Rarely a fall in blood pressure with anaphylactic reaction can occur. These can often be avoided by initially injecting slowly, to ensure patient is not sensitive to human normal immunoglobulin and carefully monitoring for symptoms during and for at least 20 minutes after first injection (1 hour for those at higher risk).

**Refer to SmPC for all special warnings and precautions. Undesirable effects:** Common: Injection site reactions (pain, urticaria at injection site, haematoma and erythema). Rarely normal human immunoglobulins can result in sudden drop in blood pressure and in isolated cases may cause an anaphylactic shock.
**Please refer to SmPC for further details.**
**Shelf life:** 2 years. Store and transport refrigerated (2 to 8°C). Do not freeze.
**NHS list price:** £1,500 per pack of 5 x 1 ml pre-filled syringes.
**Legal category: POM. MA number:** Zutectra® EU/1/09/600/001.
**MA holder:** Biotest Pharma GmbH. Landsteinerstrasse 5, 63303 Dreieich, Germany.

**Revision of prescribing information:** March 2018.

**Further information can be obtained from Biotest (UK) Ltd**. First Floor,
Park Point, 17 High Street, Longbridge, Birmingham, West Midlands B31 2UQ.
Phone: +44 (0) 121 733 3393 Fax: +44 (0) 121 7333 3066.
email: **medicinesinformation.uk@biotest.com**
website: **www.biotestuk.com**

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard or search MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to Biotest (UK) Ltd. on **0121 733 3393** or **medicinesinformation.uk@biotest.com**

Abbreviated Prescribing Information

**Hepatect® CP 50 IU/ml Human hepatitis B immunoglobulin solution for intravenous infusion.**
**Please consult full Summary of Product Characteristics (SmPC) before prescribing.**
Hepatect CP is a solution for intravenous infusion of human hepatitis B immunoglobulin containing 50 g/l human protein. Each 2 ml vial contains 100 IU, 10 ml vial 500 IU; 40 ml vial 2000 IU and 100 ml vial 5000 IU. In all cases at least 96% of human protein is IgG, with a content of antibodies to hepatitis B virus surface antigen (HBs) of 50 IU/ml.
**Indications and dosing:** Prevention of hepatitis B virus re-infection after liver transplantation for hepatitis B induced liver failure; dose (adults): 10,000 IU on day of transplantation, peri-operatively then 2,000 – 10,000 IU/day for 7 days and as necessary to maintain antibody levels above 100-150 IU/l in HBV-DNA negative patients and above 500 IU/l in HBV-DNA positive; dose (children): dose should be adjusted according to body surface area, on the basis of 10,000 IU/1.73 m2. Immunoprophylaxis of hepatitis B; in case of accidental exposure in non-immunised subjects (including persons whose vaccination is incomplete or status unknown), dose: at least 500 IU preferably within 24-72 hours after exposure; in haemodialysed patients, indicated until vaccination has become effective, dose: 8-12 IU/kg, max 500 IU, every 2 months until seroconversion after vaccination; in the newborn of a hepatitis B virus carrier-mother, dose: 30-100 IU/kg at or as soon after birth until seroconversion after vaccination; in subjects who did not show an immune response (no measurable hepatitis B antibodies) after vaccination and for whom a continuous prevention is necessary due to the continuous risk of being infected with hepatitis B, dose: 500 IU to adults and 8 IU/kg to children every 2 months. Minimum protective antibody titre is 10 mIU/mL. Hepatect CP should be infused intravenously at 0.1 ml/kg/hr for 10 minutes and gradually increased to max 1ml/kg/hr, if well tolerated.
**Contraindications and precautions:** Hypersensitivity to any components or human immunoglobulins. Caution recommended in patients with thrombotic risk factors and those deficient in IgA. Patients should be monitored for serum anti-HBs regularly and monitored during infusion period for severe reactions related to infusion rate.

**Refer to SmPC for all special warnings and precautions. Undesirable effects:** Rare: Hypersensitivity, headache, tachycardia, hypotension, nausea, vomiting, skin reaction, erythema, itching, pruritus, fever, malaise and chill. Very rare: Anaphylactic shock and arthralgia.
**Please refer to SmPC for further details.**
**Shelf life:** 2 years. Store at 2 to 8°C. Do not freeze.
**NHS list price:** £0.55/IU (available in 100 IU, 500 IU, 2000 IU or 5000 IU vials).
**Legal category: POM. MA number:** Hepatect® CP PL04500/0006.
**MA holder:** Biotest Pharma GmbH. Landsteinerstrasse 5, 63303 Dreieich, Germany.

**Revision of prescribing information:** April 2018.

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Biotest

*From Nature for Life*

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