GREEN CROSS

Green Cross Corp. (GCC) is the nation's largest and most trusted manufacturer and supplier of plasma & recombinant products, vaccines, and critical care biopharmaceuticals. GCC dedicates itself to the development and supply of biologicals and special pharmaceuticals essential for people in demand based on the experience and expertise that have accumulated over 40 years.

At GCC facilities, a process for the manufacture of Hepabig® has been developed. This GMP facility is furnished with the newest equipment in manufacturing areas to produce qualified Hepabig® and with precision analyzers and instruments in Quality Control Laboratory.

Headquarter 303 Bojeong-dong, Giheung-gu, Yongin 446-770, Korea.
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Ochang Plant

Hepabig®

Hepatitis B Immune Globulin

Hepabig® is the first step for healthy and happy life

Hepabig® Prescribing Information

Description

Hepabig® is a sterile solution containing Hepatitis B immune globulin (HBIG) which is prepared by Cohn fractionation method from plasma of individuals with high titers of anti-HBs and whose plasma does not show serologic evidence of HBsAg.
Also, donor units found to be negative to anti-HIV 1/2 and anti-HCV are only used in the production of Hepabig®.

Composition

	0.5 ml	1 ml
Hepatitis B Immune globulin, Human	100 I.U.	200 I.U.
Aminoacetic Acid	11.25 mg	22.5 mg
Sodium Chloride	2.5 mg	5.0 mg
Water For Injection	q.s.*	q.s.

* q.s. : Quantum Sufficit

Indications

- For prophylaxis of hepatitis B after exposure to HBsAg, e.g., by accidental "needle-stick" or direct mucous membrane contact by splash, or oral ingestion (pipetting accident) involving HBsAg positive materials such as blood, plasma or serum.
- For prophylaxis of hepatitis B in neonates.

Drug Interactions

- Antibodies present in Hepabig® may interfere with the immune response to live virus vaccines such as measles, mumps and rubella.
- Vaccination with live virus vaccines should be deferred until approximately 3 months after administration of Hepabig®.
- It may be necessary to revaccinate persons who received Hepabig® shortly after live virus Vaccine.
- Hepatitis B vaccine may be administered at the same time, but at a different injection site, without interfering with the immune response.
- No interactions with other products are known.

Storage and Expiry Date

- Store below 10℃ without freezing in hermetic container.
- Maximum Validity : 24 months from the manufacturing date

How supplied

- 0.5 ml / vial X 1, 5, 10
- 1 ml / vial X 1, 10, 50

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HEPABIG

Hepatitis B Immune Globulin

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Every moment of life is filled with joy and happiness

GREEN CROSS

Hepatitis B

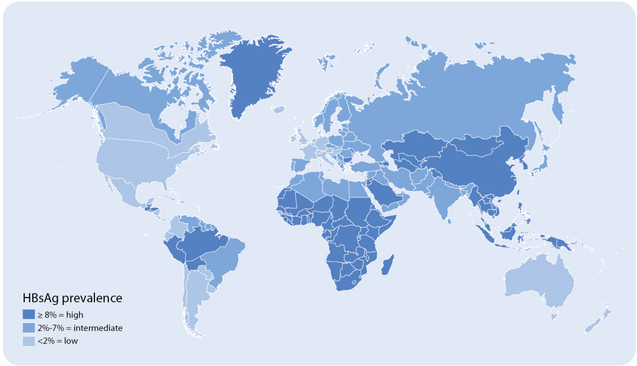
Hepatitis B is a potentially life-threatening liver infection caused by the hepatitis B virus. It is a major global health problem and the most serious type of viral hepatitis. It can cause chronic liver disease and put people at high risk of death by cirrhosis of the liver and liver cancer.

Worldwide, appoximately two billion people have been infected with the hepatitis B virus (HBV), and more than 350 million have chronic (long-term) liver infections.

Symptoms Hepatitis B virus can cause an acute illness with symptoms that last several weeks, including yellowing of the skin and eyes (jaundice), dark urine, extreme fatigue, nausea, vomiting and abdominal pain. It can take several months to a year to recover from the symptoms. HBV can also cause a chronic liver infection that can later develop into cirrhosis of the liver or liver cancer.

Hepatitis B is endemic in China and other parts of Asia. Most people in the region become infected with HBV during childhood. In these regions, 8% to 10% of the adult population are chronically infected. Liver cancer caused by HBV is one of the top three causes of death from cancer in men, and a major cause of cancer in women.

FIGURE 1. Geographic distribution of chronic hepatitis B virus (HBV) Infection - worldwide , 2006"



For multiple countries, estimates of prevalence of hepatitis B surface antigen (HBsAg), a marker of chronic HBV infection, are based on limited data and might not reflect current prevalence in countries that have implemented childhood hepatitis B vaccination. In addition, HBsAg Prevalence might vary within countries by subpopulation and locality. Source: CDC, Travelers' health: 2012 yellow book, Atlanta, GA: US department of Health and Human Services, CDC.

Common modes of transmission

- Perinatal (from mother to baby at birth)
- Early childhood infections (interpersonal contact with infected household)
- Unsafe injection practice
- Blood transfusions
- Sexual contact

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Hepabig® (Hepatitis B Immune Globulin, Human)

Hepabig® is a sterile solution containing Hepatitis B immune globulin (HBIG) which is prepared by Cohn fractionation method from plasma of individual with high titers of anti-HBs and whose plasma does not show serologic evidence of HBsAg.

- For prophylaxis of hepatitis B after exposure to HBsAG,e.g., by accidental "needle-stick" or direct mucous membrane contact.
- For prophylaxis of hepatitis B in neonate

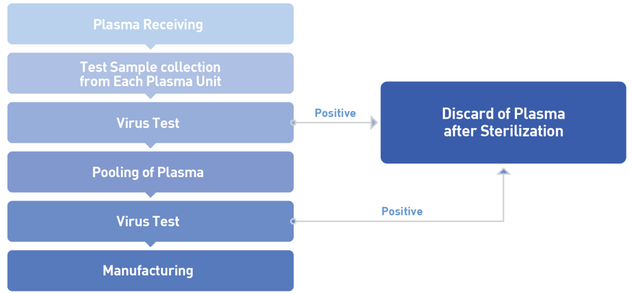
Your Safety Matters to Us

Qualified Donors.

Plasma used for manufacture of Hepabig® is collected from eligible donors obtained from FDA licensed centers located in the U.S.A.

Thorough Plasma Screen

In order to assure the safety, Green Cross Corp. retests all receiving plasma units from plasma suppliers in accordance with International Regulations. Tests are performed by using sensitive diagnostic kits (HIV Ag/Ab, HBsAg, Anti-HCV by EIA and HCV-RNA, HAV-RNA, HIV-RNA, HBV-DNA by NAT) prior to manufacturing as follows :



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Virus Inactivation Validation on Fraction III Precipitation and Pasteurization

To ensure the safety of Hepabig® the virus inactivation study was performed on 2 steps (fraction III precipitation and pasteurization) of manufacturing process. The residual virus titers were determined by infectivity assay. Minimum detectable levels were given by cytotoxicity test and interference test.

The viruses used in study are described in following table :

Virus	Genotype	Lipid envelope	Resistance
Human Immunodeficiency Virus (HIV-1)	ss-RNA	Lipid envelope	Low
Bovine Herpes Virus (BHV)	ds-DNA	Lipid envelope	Medium
Bovine viral diarrhea virus (BVDV)	ss-RNA	Lipid envelope	Medium
Porcine Parvovirus (PPV)	ss-DNA	Non Lipid envelope	High
Hepatitis A Virus (HAV)	ss-RNA	Non Lipid envelope	Medium-High

The Log clearance values from the study are summarized in following table :

Process Step	Lipid enveloped			Non enveloped	
	HIV-1	BHV	BVDV	HAV	PPV
Fraction III Precipitation	≥ 4.71	≥ 6.22	≥ 4.21	≥ 4.11	3.53
Heat treatment (Pasteurization)	≥ 5.75	≥ 5.71	≥ 4.07	≥ 4.17	3.17
Cumulative LRF*	≥ 10.46	≥ 11.93	≥ 8.28	≥ 8.28	6.70

* LRF : Log Reduction Factor (Virus Reduction Factor)

As shown above,
it is clearly indicated that fraction III
precipitation and pasteurization steps in manufacturing
process for Hepabig® are effective
in inactivating & removing the potential viral contaminants.