SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICAL PRODUCT

BIMMUGEN

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

HBsAg 10.µg per 0.5 ml

3. PHARMACEUTICAL FORM

Injection, Suspension

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

1) Prevention of Hepatitis B virus infection.
2) Prevention of vertical transmission of Hepatitis B virus infection.
   (should be administered in combination with Hepatitis B immunoglobulin)
3) Protection of transmission of Hepatitis B virus infection after acute exposure to blood
   containing HBsAg. (should be administered in combination with Hepatitis B immunoglobulin)

4.2 Posology and method of administration

1) Ordinarily, two doses of 0.5 ml of BIMMUGEN should be administered subcutaneously or intramuscularly at intervals of four weeks. A third dose of 0.5 ml should be given 20 to 24 weeks after the first inoculation in the same manner.

For children under 10 years old, three doses of 0.25 ml of BIMMUGEN each should be injected subcutaneously at same intervals.

A boosting dose is recommended for persons who were not actively immunized.

2) Dosage for infants born to HBsAg positive mothers (In combination with hepatitis B immunoglobulin)

Infants born to HBsAg positive mothers are at high risk of becoming chronic carriers of hepatitis B virus infection.
The recommended dosage for infants born to HBsAg positive mothers is as follows.

Administer the initial dose of 0.5~ 1.0 ml of hepatitis B immunoglobulin intramuscularly within 5 days after birth, preferably within 48hrs. Maintenance therapy is conducted using 0.16~ 0.24 ml/kg of hepatitis B immunoglobulin.

Ordinarily, the first dose of BIMMUGEN 0.25 ml should be given subcutaneously within 2 to 3 months after birth, and second and third doses of 0.25 ml should be given in the same manner, one and three months after the first dose, respectively.
If not actively immunized, it is recommended that additional doses of BIMMUGEN should be administered.

3) Acute exposure to blood containing HBsAg
(In combination with hepatitis B immunoglobulin)
Hepatitis B immunoglobulin of 5 to 10 ml should be given as soon as possible after exposure, preferably within 48hrs by intramuscular injection to adult. If necessary, increase the dose or readminister the same dose. Administer 0.16~0.24 ml/kg of hepatitis B immunoglobulin to children.

Ordinarily, the first dose of BIMMUGEN 0.5 ml should be given subcutaneously or intramuscularly to adults within 7 days after exposure, and second and third doses of 0.5 ml should be given in the same manner, one, and three to six months after the first dose, respectively.

For children under 10 years old, three doses of 0.25 ml of BIMMUGEN each should be given subcutaneously at same intervals.
If not actively immunized, it is recommended that additional doses of BIMMUGEN should be administered.

4.3 Contraindication

Do not inoculate the vaccine to persons or potential patients recognized as having disorders or abnormalities falling under anyone of the following categories by physical checks or auscultation. As an exception, however, inoculation can be made to those who may be infected with hepatitis B and who have no risk of incurring appreciable disorders due to the inoculation.
1) Patients with fever or considerable malnutrition.
2) Patients who are affected by cardiovascular, renal or hepatic disorders and whose symptoms are in acute, aggravating or active states.
3) Persons in whom some allergies due to ingredients of the vaccine may clearly be expected.
4) Persons who have clearly experienced abnormal side effects due to inoculation of this preparation.
5) Persons who have manifested convulsive symptoms within one year before inoculation.
6) Pregnant women.
7) Other persons who were deemed unqualified for the inoculation, in addition to the above.

4.4 Special warnings and precautions for use

(Precautions for inoculation)
1) Sterilize apparatus for injection by dry heating, autoclaving, boiling, exposure to ethylene oxide, or with gamma rays emanated from cobalt 60, and cool to room temperature. Sterilization by methods other than boiling is recommended as much as possible.
2) Disinfect the exposed surface of the rubber stopper and the outer surface of the bottle with a cotton swab soaked in alcohol, and then insert the injection needle to aspirate a designated amount into the syringe. During this procedure, take care not to allow intrusion of any contaminating bacteria. Do not use vaccine which has been transferred into another bottle.
3) Normally inoculate on the extension side of the upper arm after disinfection with alcohol or iodine tincture.
4) Be sure that the tip of the needle is directed away from blood vessels.
5) Use a new injection needle for each person receiving the inoculation.
6) Advise persons to be inoculated to rest and keep injection sites clean on the day of inoculation and also the following day. And consult a physician promptly when any symptoms such as pyrexia or convulsions are noted. Small children should be taken care of by parents or guardians.
7) The following cautions should be taken to avoid any adverse effect on tissue or nerve when intramuscularly injected:
   (1) Avoid injecting at the site of nerve.
   (2) Immediately draw out the needle when serious pain or back flow of blood into the syringe occurs, then, reinject at a different site.

4.5 Interaction with other medical products and forms of interaction

4.6 Pregnancy and lactation

See Contraindication

4.7 Effects on the ability to drive and use machines

4.8 Undesirable effects

Side effects
1. Hypersensitiveness: In some instances, the vaccine may cause pain, itchness, swelling, induration, redness, fever and efflorescence.
2. Digestive system: In some instances, the vaccine may cause nausea, diarrhea or loss of appetite.
3. Psychoneurologic system: In some instances, headache may occur.
4. Others: In some instances, fatigue or joint-pain may be experienced.

4.9 Overdose

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacodynamics and Pharmacology
Hepatitis B virus infects the blood and then transferred to liver cells where it proliferates. Following administration of the HB vaccine, HB virus in the blood stream is neutralized by the antibody before reaching the liver cells, thus preventing the development of hepatitis B infection.
In HB antibody response and HB prevention tests with use of HB vaccine, all chimpanzees tested were found to produce HBs antibody, thus indicating sufficient protective effect.

5.2 Pharmacokinetic properties

5.3 Preclinical safety data

Preclinical tests
1. Acute toxicity
   1) Tests using small animals
      The following tests were conducted by inoculating the vaccine to mice and rats subcutaneously, orally intraperitoneally or intramuscularly.
      (1) LD\textsubscript{50}: more than 50 ml/kg (subcutaneous, oral or intraperitoneal)
          more than 40 ml/kg (intramuscular, mice)
          more than 10 ml/kg (intramuscular, rats)
      (2) General symptoms
          No change in general symptoms in all the animals was seen during the observation period except that some of mice showed transient abnormality in their walking manner immediately after intramuscular injection.
      (3) Pathological tests
          When subcutaneously, intraperitoneally or intramuscularly injected, white nodules at site of the inoculation were observed due to aluminum hydroxide residues. No pathological change was recognized when orally injected.
   2) Tests using beagle dogs
      The following tests were conducted in subcutaneous injection using beagle dogs.
      (1) LD\textsubscript{50}: more than 5 ml/kg
      (2) General symptoms
No serious reaction was observed except that transient quiver at the time of inoculation and skin thickening at injection site were observed.

(3) Pathological tests
Yellowish brown nodules were observed at site of the inoculation in some subjects due to aluminum hydroxide residues.

2. Local injury tests
The vaccine was studied for its harmfulness to rabbit muscle and hemolysis to rabbit and human blood.
1) Muscle harm test
Slight local irritation was observed due to aluminum hydroxide used as an adjuvant.
2) Hemolysis test
No hemolysis was seen either in rabbit or human blood.

3. General pharmacological test
"Influence on respiratory circulatory systems and blood components"
No abnormality due to administration of the vaccine was noted when tested with beagle dogs.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Aluminium hydroxide, Formalin, Disodium hydrogen phosphate, Sodium dihydrogen phosphate, Sodium chloride, Thimerosal, Distilled water for injection

6.2 Incompatibilities

6.3 Shelf life
Two years

6.4 Special precautions for storage
The vaccine should be stored below 10°C. Exposure to sunlight and freezing should be avoided.

6.5 Nature and contents of container
Package
BIMMUGEN 5 µg preparation (0.25 ml) 1 vial
BIMMUGEN 10 µg preparation (0.5 ml) 1 vial
BIMMUGEN 100 µg preparation (5.0 ml) 1 vial

6.6 Special precautions for disposal and other handling
Cautions:
1. Do not use once the vaccine was frozen since its quality may be altered.
2. The vaccine should be warmed to room temperature after taken from refrigerator. Use after shaking it to a homogeneous solution. Shake it thoroughly whenever introduced into a syringe since it particularly tends to precipitate.
7. MARKETING AUTHORISATION HOLDER

BJC Healthcare Company Limited

8. MARKETING AUTHORISATION NUMBER(S)

1C 242/47

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

9-9-2004

10. DATE OF REVISION OF THE TEXT

Remark: The above information base on current approved package insert.