HEPATITIS B VACCINE (rDNA)

DESCRIPTION
Hepatitis B vaccine (rDNA) is a non infectious recombinant DNA Hepatitis B vaccine. It contains purified surface antigen of the virus obtained by culturing genetically-engineered *Hansenula polymorpha* yeast cells having the surface antigen gene of the Hepatitis B virus. The Hepatitis B surface antigen (HBsAg) expressed in the cells of *Hansenula polymorpha* is purified through several chemical steps and formulated as a suspension of the antigen adsorbed on aluminium hydroxide and thiomersal is added as preservative. The vaccine does not contain any material of human or animal origin. The vaccine meets the requirements of W.H.O. when tested by the methods outlined in W.H.O., TRS 978 (2013).

COMPOSITION

Paediatric

Each dose of 0.5 ml contains :-
10 mcg of purified Hepatitis B surface antigen
Adsorbed on Aluminium hydroxide (Al^{+++}) 0.25 mg to 0.40 mg
Preservative : Thiomersal 0.005%
Produced in *Hansenula polymorpha* (yeast)
Dose : 0.5 ml by intramuscular injection

Adult

Each dose of 1 ml contains :-
20 mcg of purified Hepatitis B surface antigen
Adsorbed on Aluminium hydroxide (Al^{+++}) 0.50 mg to 0.80 mg
Preservative : Thiomersal 0.005 %
Produced in *Hansenula polymorpha* (yeast)
Dose : 1 ml by intramuscular injection

INDICATIONS
Hepatitis B vaccine is indicated for active immunisation against Hepatitis B infection in subjects considered at risk of exposure to HBV-positive material.
Immunisation against hepatitis B is expected in the long term to reduce not only the incidence of this disease, but also its chronic complications such as chronic active hepatitis B and hepatitis B associated cirrhosis and primary hepatocellular carcinoma.
In areas of low prevalence of hepatitis B, immunisation with Hepatitis B vaccine is recommended for neonates/infants and adolescents as well as for subjects who are, or will be, at increased risk of infection such as:
- Health Care Personnel.
- Patients receiving frequent blood products.
- Personnel and residents of institution.
- Persons at increased risk due to their sexual behaviour.
- Illicit users of addictive injectable drugs.
- Travellers to areas with a high endemicity of HBV.
- Infants born of mothers who are HBV carries.
- Persons originating from areas with a high endemicity of HBV.
- Others: Police personnel, fire brigade personnel, armed forces personnel and anybody who through their work or personal lifestyle may be exposed to HBV.
- Household contacts of any of the above groups and of patients with acute or chronic HBV infection.

In areas of intermediate or high prevalence of hepatitis B, with most of the population at risk of acquiring the disease, immunisation should be offered to all neonates and young children. Immunisation should also be considered for adolescents and young adults.
The vaccine can be safely and effectively given simultaneously but at different injection site with DTP, DT, TT, BCG, Measles, Polio vaccine (OPV and IPV), yellow fever vaccine and vitamin A supplementation. It should not be mixed in the vial or syringe with any other vaccine unless it is manufactured as a combined product (e.g. DTP-HepB).

CONTRA-INDICATIONS.
Hepatitis B vaccine should not be administered to subjects with known hypersensitivity to any component of the vaccine, or to subjects having shown signs of hypersensitivity after previous Hepatitis B vaccine administration.

WARNINGS AND PRECAUTIONS.
Because of the period of latency of hepatitis B infection it is possible for unrecognised infection to be present at the time of immunisation. The vaccine may not prevent hepatitis B infection in such cases.
The vaccine will not prevent infection caused by other agents such as hepatitis A, hepatitis C and hepatitis E and other pathogens known to infect the liver.
The immune response to Hepatitis B vaccines is related to age. In general, people over 40 years of age respond less well.
In haemodialysis patients and persons with an impaired immune system, adequate anti-HBs antibody titres may not be obtained after the primary immunisation course and such patients may therefore require administration of additional doses of vaccine (see Dosage recommendation for immunocompromised persons).
As with all injectable vaccines, appropriate medication (e.g. adrenaline) should always be readily available for treatment in case of rare anaphylactic reactions following the administration of the vaccine.
Hepatitis B vaccine should not be administered in the gluteal muscle or intradermally since this may result in a lower immune response.
Hepatitis B vaccine may be used to complete a primary immunisation course started either with plasma-derived or with other genetically-engineered hepatitis B vaccines, or as a booster dose in subjects who have previously received a primary immunisation course with plasma-derived or with other genetically-engineered hepatitis B vaccines.

ADVERSE REACTIONS
The undesirable events are temporally related to the administration of Hepatitis B vaccine. They are usually mild and confined to the first few days of the vaccination. The most common reactions are mild soreness, erythema, induration, fatigue, fever, malaise, influenza-like symptoms
Less common systemic reactions include nausea, vomiting, diarrhoea, abdominal pain, abnormal liver function tests, arthralgia, myalgia, rash, pruritus, urticaria.

DOSAGE AND ADMINISTRATION
Paediatric dose vaccine: 10 mcg dose (in 0.5 ml suspension) is recommended for neonates, infants, children and adolescents upto 19 years of age.
Adult dose vaccine: 20 mcg dose (1.0 ml suspension) is recommended for adults aged 20 years and above.

IMMUNISATION SCHEDULE
Primary Immunisation: A series of three intramuscular injections is required to achieve optimal protection.
The following immunisation schedules can be recommended.:
- 6,10,14 weeks for infants.
- 0,1,6 months
- 0,1,2 months (rapid schedule).

The immunisation schedule should be adapted to meet local immunisation recommendations.

BOOSTER DOSE.
The need for the booster dose in healthy individuals who have received the full primary immunization, is not recommended. It would seem advisable to recommend a booster dose when Anti-HBs antibody titres fall below 10 IU/L for all people at risk and especially for patients who are immunocompromised (HIV infected patients) or those on haemodialysis.

SPECIAL DOSAGE RECOMMENDATIONS
DOSAGE RECOMMENDATION FOR NEONATES BORN OF MOTHERS WHO ARE HBV CARRIERS.
The 0, 1, 2 month immunisation schedule is recommended, and should start at birth. Concomitant administration of Hepatitis B immunoglobulin not necessary, but when Hepatitis B immunoglobulin is given simultaneously with Hepatitis B vaccine a separate injection site must be chosen.

DOSAGE RECOMMENDATION FOR KNOWN OR PRESUMED EXPOSURE OF HBV
In circumstances where exposure to HBV has recently occurred (eg needle stick with contaminated needle) the first dose of Hepatitis B vaccine can be administered simultaneously with Hepatitis B immunoglobulin which however must be given at a separate injection site. The rapid immunisation schedule should be advised.

DOSAGE RECOMMENDATION FOR IMMUNOCOMPROMISED PERSONS.
The primary immunisation schedule for chronic haemodialysis patients or persons who have an impaired immune system is four doses of 40 mcg at 0, 1, 2 and 6 months from the date of first dose. The immunisation schedule should be adapted in order to ensure that the anti-HBs antibody titre remains above the accepted protective level of 10 IU/L

METHOD OF ADMINISTRATION.
Hepatitis B vaccine (rDNA) should be injected intramuscularly in the deltoid region in adults and children or in the anterolateral thigh in neonates, infants and young children. The vaccine may be administered subcutaneously in patients with thrombocytopenia or bleeding disorders. The vaccine should be well shaken before use. Only sterile needle and syringes should be used for each injection. Once opened, multi-dose vials should be kept between +2°C and +8°C. Multi-dose vials of Hepatitis B from which one or more doses of vaccine have been removed during an immunisation session may be used in subsequent immunisation sessions for upto a maximum of 4 weeks, provided that all of the following conditions are met
- The expiry date has not passed.
- The vaccines are stored under appropriate cold chain conditions;
- The vaccine vial septum has not been submerged in water;
- Aseptic technique has been used to withdraw all doses;
- The vaccine vial monitor (VVM), if attached, has not reached the discard point (see figure).

The vaccine should be visually inspected for any foreign particulate matter and / or variation of physical aspect prior to administration. In event of either being observed, discard the vaccine.

IMMUNE DEFICIENCY
Individuals infected with human immuno-deficiency virus (HIV), both asymptomatic and symptomatic, should be immunized with heptatitis B vaccine according to standard schedules.

STORAGE
Hepatitis B vaccine (rDNA) should be stored at 2 - 8°C. Do not Freeze. Discard if vaccine has been frozen.

SHELF LIFE
Thirty six months from the date of manufacture.

PRESENTATIONS
0.5 ml - Single dose ampoule (Paediatric).
0.5 ml - Single dose vial (Paediatric).
5 ml - 10 doses vial (Paediatric).
1 ml - Single dose ampoule (Adult).
1 ml - Single dose vial (Adult).
10 ml - 10 doses vial (Adult).

THE VACCINE VIAL MONITOR (Optional)

Inner square lighter than outer circle. **If the expiry date has not passed, USE the vaccine.**


At a later time, inner square still lighter than outer circle. **If the expiry date has not passed, USE the vaccine.**


Discard point:
Inner square matches colour of outer circle.
DO NOT use the vaccine.


Beyond the discard point:
Inner square darker than outer ring.
DO NOT use the vaccine.

Vaccine Vial Monitors (VVMs) are part of the label on Hepatitis B Vaccine (rDNA) supplied through Serum Institute of India Ltd. The colour dot which appears on the label of the vial is a VVM. This is a time-temperature sensitive dot that provides an indication of the cumulative heat to which the vial has been exposed. It warns the end user when exposure to heat is likely to have degraded the vaccine beyond an acceptable level.
The interpretation of the VVM is simple. Focus on the central square. Its colour will change progressively. As long as the colour of this square is lighter than the colour of the ring, then the vaccine can be used. As soon as the colour of the central square is the same colour as the ring or of a darker colour than the ring, then the vial should be discarded.

Manufactured by:
SERUM INSTITUTE OF INDIA LTD.
212/2, Hadapsar, Pune 411028, INDIA

Protection from birth onwards

[illegible]

VACUNA DE LA HEPATITIS B (rADN)

DESCRIPCIÓN
La vacuna de la Hepatitis B (rADN) es una vacuna recombinante de ADN no infecciosa. Contiene el antígeno superficial purificado del virus obtenido por el cultivo de células genéticamente manipuladas de la levadura *Hansenula polymorpha*, que contienen el gene del antígeno superficial del virus de la Hepatitis B. El antígeno superficial de la Hepatitis B (HbsAg) manifiesto en las células de *Hansenula polymorpha* se purifica por varios pasos químicos y se to formula en forma de suspensión del antígeno adsorbido en hidróxido de aluminio, con la adición de tiomersal como preservativo. La vacuna no contiene ningun material de origen humano o animal. La vacuna cumple con los requisitos de la O.M.S. cuando se la comprueba según los métodos descritos en la O.M.S., TRS 978 (2013).

COMPOSICIÓN

Pediatrica

Cada dosis de 0.5 ml contiene:-
10 mcg de antígeno superficial purificado de la Hepatitis B
adsorbido en Hidróxido de Aluminio (Al^{+++}) 0,25 mg a 0,40 mg
Preservativo : Tiomersal 0,005%
Producido en *Hansenula Polymorpha* (levadura)
Dosis : 0.5 ml por inyección intramuscular

Adultos

Cada dosis de 1 ml contiene:-
20 mcg de antígeno superficial purificado de la Hepatitis B
adsorbidos en Hidróxido de Aluminio (Al^{+++}) 0,50 mg a 0.80 mg
Preservativo : Tiomersal 0,005%
Producido en *Hansenula Polymorpha* (levadura)
Dosis : 1 ml por inyección intramuscular

INDICACIONES
La vacuna de la Hepatitis B está indicada en la inmunización activa contra la infección de la Hepatitis B en personas que corren riesgo de exposición a material VHB- positivo.
Se considera que la inmunización contra la Hepatitis B, a largo plazo, no sólo reduce la incidencia de la enfermedad, sino también las complicaciones crónicas de ella, tales como la hepatitis B activa tipo crónica, la cirrosis asociada a la Hepatitis B y la carcinoma primaria hepatocelular.

En zonas de baja incidencia de la Hepatitis B, se recomienda la inmunización de recién-nacidos / bebes y adolescentes con la Vacuna de la Hepatitis B así como de personas que corren riesgo o que sean susceptibles al riesgo aumentado de infección tales como:
- Personal de Asistencia Sanitaria
- Pacientes que reciben productos sanguíneos frecuentemente.
- Personal y residentes de instituciones.
- Personas a riesgo de contraer la enfermedad debido a su comportamiento sexual.
- Usuarios de drogas adictivas inyectables ilícitas.
- Personas que viajan a zonas con alta endemicidad de VHB
- Bebés nacidos a madres que son portadoras de VHB.
- Personas que provienen de zonas con alta endemicidad de VHB
- Otros : Personal de la policía, bomberos, militares y cualquier otra persona que este a riesgo de exposición a VHB en el curso de su trabajo o por su estilo de vida.
- Contacto con cualquier de los grupos susodichos y con pacientes con infección crónica o aguda de la infección VHB.

En zonas de alta o intermedia prevalencia de la Hepatitis B, en que la mayor parte de la población está con riesgo de contraer la enfermedad, la inmunización debe hacerse en todos los recién-nacidos y niños. Debe considerarse tambien la inmunización en adolescentes y adultos jóvenes.
La vacuna puede ser administrada con seguridad y eficacia, simultáneamente, pero en distintos sitios de inyección, con DPT, DT, TT, BCG, Sarampión, la vacuna antipoliomelitis (VPO e VPI), la vacuna contra la fiebre amarilla y suplementos de Vitamina A. No debe ser mezclada con cualquier otra vacuna en el frasco o jeringa a no ser que haya sido fabricada en la forma de un producto combinado (p.e. DTP-HepB).

CONTRAINDICACIONES
La vacuna de la Hepatitis B no debe administrarse en personas con hipersensibilidad establecida a cualquier componente de la vacuna, o en personas que manifestaron la hipersensibilidad después de una aplicación previa de la Vacuna de la Hepatitis B.

ADVERTENCIAS Y PRECAUCIONES
Debido al periodo en que la infección de la Hepatitis B esta en un estado latente, es posible que esté presente una infección no detectada en el momento de la inmunización. En tales casos es posible que la vacuna no prevenga la infección de Hepatitis B.
La vacuna no protege contra la infección causada por otros agentes como la Hepatitis A, Hepatitis C, la Hepatitis E y otros patógenos que afectan el hígado.
La respuesta inmunitaria a la vacuna Hepatitis B está ligada a la edad. En general, personas de edad mayor a los cuarenta años no responden tan bien a la vacuna.
En pacientes de hemodialisis y personas con un sistema inmune comprometido, puede ser que no se obtengan títulos adecuados de anticuerpos anti HB despues del curso primario de inmunizacion y tales pacientes pueden por lo tanto necesitar la administración de dosis adicionales de la vacuna (ver Recomendaciones para la Dosificación en personas inmunocomprometidas).
Como para todas las vacunas inyectables, siempre debe tenerse disponible medicamentos apropiados (por ej. adrenalina) para el tratamiento en el evento de raras reacciones anafilácticas despues de la administración de la vacuna.
La vacuna de la Hepatitis B no debe administrarse en el músculo glúteo o intradermicamente ya que esto puede resultar en una baja respuesta inmunitaria.
La vacuna de la Hepatitis B puede ser usada para acabar un curso de inmunizacion primaria que se empieza con vacunas de Hepatitis B derivadas del plasma o geneticamente construidas o como dosis de refuerzo en individuos que han recibido un curso de inmunización primaria con vacunas de la Hepatitis B derivadas del plasma o con otras vacunas geneticamente generadas.

REACCIONES ADVERSAS
Los eventos indeseables que ocurren están temporalmente relacionados con la administración de la vacuna Hepatitis B. Estos son normalmente leves y restrictos a los primeros días de la vacunación. Las reacciones más comunes son el enrojecimiento de la zona en el sitio de la inyección, eritema, induración, fatiga, fiebre, malestar y síntomas parecidos a la influenza.
Otras reacciones sistémicas menos comunes incluyen la nausea, vómitos, diarrea, dolor abdominal, pruebas anormales de la función del hígado, mialgia, erupciones, prurito, urticaria.