Autoimmune congenital heart block

Condition for which Ig use is in exceptional circumstances only

Specific Conditions	• Risk of autoimmune congenital heart block – previously affected sibling • Confirmed autoimmune congenital heart block in a fetus • Confirmed autoimmune congenital heart block in a neonate
Indication for Ig Use	• Prevention of recurrent autoimmune congenital heart block where maternal SSB (La) and/or SSA (Ro) antibodies are present • Maternal therapy for treatment of congenital heart block where maternal SSB (La) and/or SSA (Ro) antibodies are identified • Postnatal treatment of congenital heart block where SSB (La) and/or SSA (Ro) are present
Level of Evidence	Insufficient data (Category 4a)
Description and Diagnostic Criteria	Congenital heart block (CHB), the most serious manifestation of neonatal lupus erythematosus, is an autoantibody mediated disorder potentially caused by placental transmission of maternal autoantibodies to 52-kd and 60-kd SSA/Ro +/-48-kd SSB/La ribonucleo- proteins. These antibodies can cause permanent and often life-threatening damage to the fetal heart. The incidence of CHB in the offspring of mothers with pathologic autoantibodies is one to two percent, but the recurrence rate in subsequent pregnancies following the birth of a child with neonatal lupus is 18 percent.
Justification for Evidence Category	Multiple positive case reports and case series preceded and followed the report of a multicenter open-label study (Friedman et al 2010). Enrollment criteria included: maternal anti-SSA/Ro antibody, a previous child with CHB/rash, </= 20 mg prednisone, less than 12 weeks pregnant. IVIG (400mg/kg) was given every three weeks from 12 to 24 weeks of gestation. Study prematurely ceased after 20 patients because the predetermined stopping rule of three affected cases was reached. However, majority of successful reports used higher doses +/- frequency of IVIG (1-2g/kg 2 to 4 weekly) which are more likely to be immunomodulatory, often throughout the pregnancy and sometimes, when evidence of early disease, extending to the newborn until disappearance of maternal antibodies. A combination treatment of steroids, plasmapheresis and IVIg until delivery followed by IVIg in the infant until disappearance of maternal antibodies resulted in reversal of the severity of heart block detected in the infants of two women without previous affected infants. The general conclusion is that it is well tolerated and although replacement dose IVIg does not prevent CHB, high dose IVIg is effective in some patients.
Diagnosis Requirements	A diagnosis must be made by an Immunologist, Maternal-Fetal Medicine Specialist or an Obstetrician.
Qualifying Criteria for Ig Therapy	Prevention of recurrent autoimmune congenital heart block where maternal SSB (La) and/or SSA (Ro) antibodies are present • Current pregnancy with a history of autoimmune congenital heart block in at least one previous pregnancy AND • Maternal SSB (La)-and/or SSA (Ro)-antibodies are present

Maternal therapy for treatment of congenital heart block where maternal SSB (La) and/or SSA (Ro) antibodies are identified

- Current pregnancy and evidence of congenital heart block

  AND

- Maternal SSA (Ro) and/or SSB (La) antibodies are identified

AND

- Ig therapy will be given concurrently with steroid therapy with or without plasmapheresis

  OR

- Steroid treatment is contraindicated or has resulted in unacceptable side effects or significant toxicity

Postnatal treatment of congenital heart block where SSB (La) and/or SSA (Ro) are present

This indication relates only to treatment of congenital heart block where SSB (La) and/or SSA (Ro) are present in patients up to 6 months of age. Pregnant women are eligible under the indications **prevention of recurrent autoimmune congenital heart block where maternal SSB (La) and/or SSA (Ro) antibodies are present** or **maternal therapy for treatment of congenital heart block where maternal SSB (La) and/or SSA (Ro) antibodies are identified.**

- Neonate with congenital heart block

  AND

- SSB (La) and/or SSA (Ro) antibodies are present in the neonate

Review Criteria for Assessing the Effectiveness of Ig Use

Prevention of recurrent autoimmune congenital heart block where maternal SSB (La) and/or SSA (Ro) antibodies are present

Review is not mandated for this indication, however the following criteria may be useful in assessing the effectiveness of Ig therapy.

- Absence of symptoms of CHB in fetus and/or live birth of healthy neonate

  AND
- Reduction in the level or absence of maternal SSA (Ro) and/or SSB (La) antibodies

Maternal therapy for treatment of congenital heart block where maternal SSB (La) and/or SSA (Ro) antibodies are identified

Review is not mandated for this indication, however the following criteria may be useful in assessing the effectiveness of Ig therapy.

- Congenital heart block has improved in response to Ig therapy

  AND
- Reduction in the level or absence of maternal SSB (La) and/or SSA (Ro) antibodies

Postnatal treatment of congenital heart block where SSB (La) and/or SSA (Ro) are present

This indication relates only to treatment of congenital heart block where SSB (La) and/or SSA (Ro) are present in patients up to 6 months of age. Pregnant women are eligible under the indications **prevention of recurrent autoimmune congenital heart block where maternal SSB (La) and/or SSA (Ro) antibodies are present** or **maternal therapy for treatment of congenital heart block where maternal SSB (La) and/or SSA (Ro) antibodies are identified.**

Review is not mandated for this indication however the following criteria may be useful in assessing the effectiveness of Ig therapy.

- Congenital heart block has improved in response to Ig therapy

  AND
- Reduction in the level or absence of SSA and/or SSB antibodies

Dose	Prevention of recurrent autoimmune congenital heart block where maternal SSB (La) and/or SSA (Ro) antibodies are present • **Induction Dose (IVIg)** - Up to 2g/kg in a single or divided dose. This may be given as two doses of 1g/kg at fortnightly intervals. • **Maintenance Dose (IVIg)** - 1-2g/kg monthly in single or divided doses. A maximum dose of 2g/kg may be given in any four week period. This might be by divided doses more frequently than monthly. Refer to the current product information sheet for further information on dose, administration and contraindications. Maternal therapy for treatment of congenital heart block where maternal SSB (La) and/or SSA (Ro) antibodies are identified • **Induction Dose (IVIg)** - Up to 2g/kg in a single or divided dose. This may be given as two doses of 1g/kg at fortnightly intervals. • **Maintenance Dose (IVIg)** - 1-2g/kg monthly in single or divided doses. A maximum dose of 2g/kg may be given in any four week period. This might be by divided doses more frequently than monthly. Refer to the current product information sheet for further information on dose, administration and contraindications. Postnatal treatment of congenital heart block where SSB (La) and/or SSA (Ro) are present • **Induction Dose (IVIg)** - Up to 2g/kg in a single or divided dose. This may be given as two doses of 1g/kg at fortnightly intervals. • **Maintenance Dose (IVIg)** - 1-2g/kg monthly in single or divided doses. A maximum dose of 2g/kg may be given in any four week period. This might be by divided doses more frequently than monthly. Refer to the current product information sheet for further information on dose, administration and contraindications.

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