Publication date: 19 December 2025

Clinical commissioning policy:

Human normal immunoglobulin for preventative treatment of idiopathic systemic capillary leak syndrome following an acute episode (adults) [2270]

Summary

Human normal immunoglobulin is recommended to be available as a routine commissioning preventative treatment option for idiopathic systemic capillary leak syndrome (SCLS) within the criteria set out in this document.

The policy is for adults in line with the findings from the evidence review[1].

Committee discussion

Clinical Panel considered the evidence base and the recommendation was made to progress the policy as for routine commissioning. Please see Clinical Panel reports for full details of Clinical Panel's discussion.

The Clinical Priorities Advisory Group committee papers can be accessed on the NHS England website.

What we have decided

NHS England has carefully reviewed the evidence to treat Idiopathic Systemic Capillary Leak Syndrome with Human normal immunoglobulin. We have concluded that there is enough evidence to make the treatment available at this time.

The evidence review which informs this commissioning position can be accessed NHS England website.

Plain language summary

About idiopathic systemic capillary leak syndrome

Idiopathic Systemic Capillary Leak Syndrome (SCLS; also referred to as Clarkson's Syndrome) is an extremely rare condition characterised by episodes in which capillaries (small blood vessels) become leaky. This causes movement of fluid from inside the vessels to other spaces in the body, which can result in whole body swelling. Episodes are also associated with low blood pressure because of fluid shifts, which is life threatening and can cause complications such as organ failure and blood clots. Patients will often require hospital and intensive care admission during these acute episodes. The condition is diagnosed by ruling out other causes of this presentation. Most patients follow a relapsing

[1] Access for use in children (from neonates upwards) is available in line with the Commissioning Medicines for Children in Specialised Services policy 170001/P (commissioning medicines children).

course after diagnosis with acute episodes occurring up to monthly. The underlying cause for the condition is not fully understood, partly because it is so rare.

About current treatment

Standard care during acute episodes often involves admission, including to intensive care, to stabilise the fluid balance. Sometimes medication is required to increase the blood pressure in order for organs to function, and treatments to remove excess fluid may also be required. After an acute episode has resolved, preventative treatment is often started to try and stop future episodes.

About human normal immunoglobulin

Immunoglobulins are proteins found within plasma, which is the liquid component of blood. Human normal immunoglobulin (Ig) is a blood product prepared from donor plasma. It can be given to patients through an infusion into the veins or underneath the skin as treatment for certain conditions. In this policy, Ig is being proposed as preventative therapy, and the preventative effect lasts for several weeks between the treatment being delivered.

Ig is not licensed for the use in SCLS and therefore use will be off-label.

Epidemiology and needs assessment

SCLS was first described in 1960 and around 250 patients have been described worldwide since then (Baloch et al). The incidence in the UK is estimated at 5 per year (4 for England by extrapolation of ONS data) and the prevalence is approximately 15 (13 for England by extrapolation of ONS data) according to clinical consensus. It is primarily a condition of middle-age with a mean age at diagnosis of 47 years, although there are case reports in paediatric patients, and there is a male to-female ratio of 1.4:1 (Baloch et al).

Implementation

Inclusion criteria

Patients will be eligible for Ig preventative treatment after an acute episode of SCLS if they fulfil **ALL** of the following criteria:

- Diagnosis of idiopathic SCLS made by a relevant specialist or specialists, which may include the following specialities: immunology, haematology, rheumatology, renal
- Patient has been discussed by a multidisciplinary team (MDT) with relevant specialist involvement (likely to include some or all of the following specialties: immunology, haematology, rheumatology, renal) and they agree with the proposed treatment.

Exclusion criteria

Patients with **ANY** of the below features are not eligible for treatment:

- Patients who have never had an acute episode of SCLS during which blood biochemistry shows haemoconcentration with hypoproteinaemia
- Patients where SCLS is secondary to a documented cause as assessed by an MDT including the relevant specialties (for example, medication-induced capillary leak).

Starting criteria

Patients that meet the inclusion criteria and do not meet any of the exclusion criteria should start preventative Ig after an acute episode has resolved.

Provider organisations must register all patients using prior approval processes and ensure internal trust monitoring arrangements are in place to capture patient outcomes. Treatment should not proceed without prior panel approval from Sub Regional Immunoglobulin Assessment Panels (please see governance section below).

Recommended dose

The optimal dose of Ig therapy in idiopathic SCLS remains to be determined and therefore this policy gives a dose range of 1-2g/kg IV based on ideal body weight, or equivalent subcutaneous dose. The most frequently given starting dose according to the evidence is 2g/kg but clinical judgement shall determine the appropriate starting dose and, if appropriate, the tapering dose (see tapering criteria below).

Treatment should be given every 4-6 weeks.

Total treatment course should be calculated and then rounded down to the nearest dose which can be administered using whole vials. Note in an adult patient, part vials should never be used. Where the dose is split over multiple days, daily dose may differ. The minimum effective clinical dose for each patient should be established.

Tapering criteria

Decisions around dose adjustment and tapering should be made by a MDT with relevant specialist involvement as described above. After commencing treatment, patients should remain on the same dose continuously until the below tapering criteria are met, at which point the MDT can consider tapering the treatment unless the patient is intolerant of therapy in which case it should be discontinued with patient consent:

- The patient has had a complete clinical response as defined by a year without any acute episodes and without any associated hospital admissions **AND**
- The patient has been appropriately counselled and understands that the risk of tapering is that the condition will recur. Tapering dose reduces the duration of infusions and therefore treatment acceptability may be improved for patients. If doses can be reduced it minimises the use of plasma products which are in limited supply.

The use of Ig therapy as outlined in this NHS England Clinical Policy is off-label. Trust Policy regarding off-label use of medicines should apply.

Stopping criteria

Once commenced, patients should remain on treatment continuously unless the below stopping criteria are met:

- No response to treatment as defined in the monitoring requirements outlined below
- Intolerant of the side effects of Immunoglobulin treatment or an adverse event that makes ongoing therapy clinically unsafe
- Patient has undergone dose reduction, remains stable and is willing to trial a period off therapy accepting the risk of relapse

Monitoring

Local guidelines should be followed for monitoring during and immediately after infusions or treatments.

Ongoing care, including assessment of clinical response as below, should be undertaken by a team with relevant experienced specialists, for example, the team that agreed on treatment initiation. Where this is not feasible, local teams should liaise with an appropriate specialist team for advice and guidance.

Clinical response:

Patients must be assessed for clinical response at 3, 6 and 12 months after starting treatment and annually thereafter.

Assessment for clinical response should involve consideration of the following factors:

- Number of acute episodes
- Severity of acute episodes
- Hospital or intensive care admissions for SCLS

Definition of a severe episode includes, but is not limited to, the presence of any of the following criteria: systolic blood pressure <80 mm Hg, mean blood pressure <65 mm Hg, loss of consciousness, admission to the intensive care unit (Pineton de Chambrun et al., 2017).

Dose adjustment:

Patients must be reviewed for dose adjustments at the 12-month mark and then annually. Dose reduction can be considered depending on clinical response as outlined above.

Patient pathway

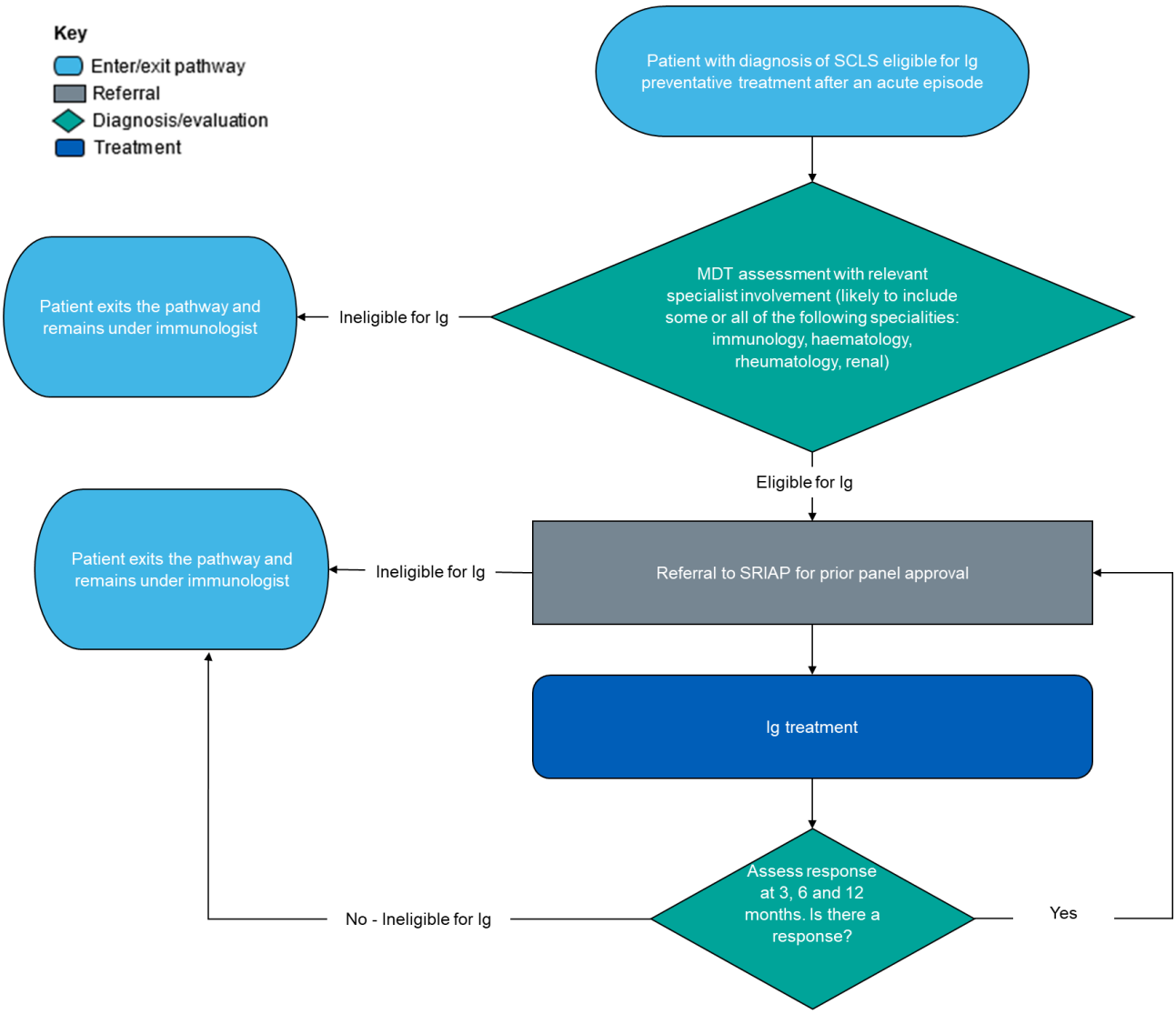

Figure 1: patient pathway

Governance arrangements

Provider organisations must register all patients using the MDSAS prior approval process and a completed referral form is also required for use of Ig in all indications. Treatment should not proceed without prior panel approval from Sub Regional Immunoglobulin Assessment Panels (SRIAPs). For urgent approvals in hours a process will need to be in place on the agreed pathway for approval. For those cases that require out of hours approval, panels will have local processes in place to ensure robust governance for retrospective panel approval. Where local expertise is not available, panels will also be able to advise on dose optimisation and trials of treatment withdrawal.

Please note that this is an off-label use of Ig therapy, therefore Trust policy regarding unlicensed medicines should apply.

Mechanism for funding

Reimbursement for the use of Ig for SCLS meeting the criteria within this policy will be managed, through local contract agreements and terms, by the local NHS England Specialised Commissioning Teams.

Audit requirements

Patients should be registered and data on dose, route and frequency should be submitted to the MDSAS database annually. The following outcome measures should be recorded:

- Number of acute episodes per year
- ITU/hospital admissions per year relating to idiopathic SCLS

Policy review date

This document will be reviewed when information is received which indicates that the policy requires revision. If a review is needed due to a new evidence base then a new Preliminary Policy Proposal needs to be submitted by contacting england.CET@nhs.net.

Our policies provide access on the basis that the prices of therapies will be at or below the prices and commercial terms submitted for consideration at the time evaluated. NHS England reserves the right to review policies where the supplier of an intervention is no longer willing to supply the treatment to the NHS at or below this price and to review policies where the supplier is unable or unwilling to match price reductions in alternative therapies.

Equality statement

Promoting equality and addressing health inequalities are at the heart of NHS England's values. Throughout the development of the policies and processes cited in this document, we have:

- Given due regard to the need to eliminate discrimination, harassment and victimisation, to advance equality of opportunity, and to foster good relations between people who share a relevant protected characteristic (as cited under the Equality Act 2010) and those who do not share it; and
- Given regard to the need to reduce inequalities between patients in access to, and outcomes from healthcare services and to ensure services are provided in an integrated way where this might reduce health inequalities.

Definitions

Capillary	Fine branching blood vessels that form a network between arterioles (small arteries) and venules (small veins)
Immunoglobulin	A protein that is made by B cells and plasma cells (types of white blood cells) and helps the body fight infection
haemoconcentration	An increase in the proportion of red blood cells in blood, usually due to a reduction in the volume of plasma within the vessels
hypoproteinaemia	An abnormally low level of proteins, for example albumin and globulins, in the blood.

References

Noor Ul-Ain Baloch, Marvi Bikak, Abdul Rehman & Omar Rahman. (2018) Recognition and management of idiopathic systemic capillary leak syndrome: an evidence-based review. Expert Review of Cardiovascular Therapy, 16:5, 331-340, DOI: 10.1080/14779072.2018.1456920

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