CPAG Summary Report for Clinical Panel – Susoctocog alfa for treating bleeding episodes in people with acquired haemophilia A NHS England Unique Reference Number 1703 / CSP ID006

The Benefits of the Proposition – Susoctocog alfa for treating bleeding episodes in people with acquired haemophilia A			
No	*Outcome measures*	*Grade of evidence*	*Summary from evidence review*
1.	Survival	Not measured	
2.	Progression free survival	Not measured	
3.	Mobility	Not measured	
4.	Self-care	Not measured	
5.	Usual activities	Not measured	
6.	Pain	Not measured	
7.	Anxiety / Depression	Not measured	
8.	Replacement of more toxic treatment	Not measured	
9.	Dependency on care giver / supporting independence	Not measured	
10.	Safety	Adverse events identified [C]	This outcome shows the number of serious side effects that were thought to be caused by susoctocog in the study No serious side effects were reported. Side effects were generally mild or moderate, and most were not considered to be related to treatment with susoctocog alfa The study included only 29 participants, was open-label and uncontrolled, and is subject to bias and confounding. Therefore, it is of low-quality and the results should be

			interpreted with caution. Nevertheless, the European public assessment report for susoctocog alfa states that the design and conduct of the study are acceptable because of the rarity of AHA and the emergency nature of the bleeding, and the marketing authorisation was granted under exceptional circumstances, subject to collection and analysis of further data
11.	Delivery of intervention	Not measured	

Other health outcome measures determined by the evidence review			
No	Outcome measure	Grade of evidence	Summary from evidence review
1.	Proportion of serious bleeding episodes that responded to treatment	Grade C	This outcome shows the proportion of serious bleeds that stopped or reduced so that the person's condition became stable within 24 hours of the first susoctocog alfa infusion (injection). Bleeding responded to treatment within 24 hours in all 28 people with AHA who received susoctocog alfa The study included only 29 participants (1 was later found not to have AHA), was open-label and uncontrolled, and is subject to bias and confounding. Therefore, it is of low-quality and the results should be interpreted with caution. Nevertheless, The European public assessment report for susoctocog alfa states that the design and conduct of the study are acceptable because of the rarity of AHA and the emergency nature of the bleeding, and the marketing authorisation was granted under exceptional circumstances, subject to collection and analysis of further data.
2.	Proportion of serious bleeding episodes	Grade C	This outcome shows the proportion of serious bleeds that, in the opinion of the investigator, were

	successfully controlled at the final dose		successfully controlled when the person stopped having treatment with susoctocog alfa at the end of the study. Bleeding was successfully controlled after a course of treatment in more than 8 out of 10 people with AHA who received susoctocog alfa in the study. In the other people, bleeds were controlled at first, but they later had complications or more bleeds, which did not stop with susoctocog alfa. The study included only 29 participants, was open-label and uncontrolled, and is subject to bias and confounding. Therefore, it is of low-quality and the results should be interpreted with caution. Nevertheless, The European public assessment report for susoctocog alfa states that the design and conduct of the study are acceptable because of the rarity of AHA and the emergency nature of the bleeding, and the marketing authorisation was granted under exceptional circumstances, subject to collection and analysis of further data.
3.	Median dose of susoctocog alfa in participants whose primary bleed was successfully controlled	Grade C	This outcome shows the average dose of susoctocog alfa that was given in 1 infusion at a single time point, across the 24 people in the study whose bleed was successfully controlled with treatment. The average dose in people whose bleed was controlled, was 200 units/kg in the first 24 hours and 100 units/kg after 24 hours The study included only 29 participants, was open-label and uncontrolled, and is subject to bias and confounding. Therefore, it is of low-quality and the results should

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4.	Median dose of susoctocog alfa in all participants exposed to treatment	Grade C	This outcome shows the average dose of susoctocog alfa that was given in 1 infusion at a single time point, across all 29 people who took part in the study. The average dose in everyone who was treated with susoctocog alfa was about 130 units/kg, but varied between different people from below 50 units/kg to 400 units/kg. The study included only 29 participants, was open-label and uncontrolled, and is subject to bias and confounding. Therefore, it is of low-quality and the results should be interpreted with caution. Nevertheless, The European public assessment report for susoctocog alfa states that the design and conduct of the study are acceptable because of the rarity of AHA and the emergency nature of the bleeding, and the marketing authorisation was granted under exceptional circumstances, subject to collection and analysis of further data.
5.	Median cumulative dose of susoctocog alfa in all participants exposed to treatment	Grade C	This outcome shows the average total dose of susoctocog alfa that was given in a course of infusions throughout the study, across all 29 people who took part in the study. The average total dose of susoctocog alfa that people received during the study was

			about 1,600 units/kg, but varied widely between different people from 100 units/kg to over 20,000 units/kg. The study included only 29 participants, was open-label and uncontrolled, and is subject to bias and confounding. Therefore, it is of low-quality and the results should be interpreted with caution. Nevertheless, The European public assessment report for susoctocog alfa states that the design and conduct of the study are acceptable because of the rarity of AHA and the emergency nature of the bleeding, and the marketing authorisation was granted under exceptional circumstances, subject to collection and analysis of further data.
6.	Median number of infusions of susoctocog alfa in all participants exposed to treatment	Grade C	This outcome shows the average number of infusions of susoctocog alfa that were given in each course of treatment throughout the study, across all 29 people who took part in the study. The average number of infusions was 13 in everyone who was treated with susoctocog alfa, but varied widely between different people from 1 to 140. The study included only 29 participants, was open-label and uncontrolled, and is subject to bias and confounding. Therefore, it is of low-quality and the results should be interpreted with caution. Nevertheless, The European public assessment report for susoctocog alfa states that the design and conduct of the study are acceptable because of the rarity of AHA and the emergency nature of the bleeding, and the marketing authorisation was granted under exceptional circumstances, subject

			to collection and analysis of further data.
7.	Median number of days of exposure to susoctocog alfa in all participants exposed to treatment	Grade C	This outcome shows the average duration of a course of treatment with susoctocog alfa in the study, across all 29 people who took part in the study. Duration of treatment with susoctocog alfa was 7 days, on average, but varied widely between different people from 1 to 25 days. The study included only 29 participants, was open-label and uncontrolled, and is subject to bias and confounding. Therefore, it is of low-quality and the results should be interpreted with caution. Nevertheless, The European public assessment report for susoctocog alfa states that the design and conduct of the study are acceptable because of the rarity of AHA and the emergency nature of the bleeding, and the marketing authorisation was granted under exceptional circumstances, subject to collection and analysis of further data.
8.	Median increase in factor VIII activity levels after the loading dose	Grade C	This outcome shows how much factor VIII levels increased when susoctocog alfa was given to people in the study. In all people in the study, factor VIII levels, on average, increased by about 200% after the first dose of susoctocog was given. In people with a small amount of antibodies to susoctocog alfa, the average increase in factor VIII seen with treatment was lower, at about 100%. In people with a lot of antibodies to susoctocog alfa, the increase was only about 30%. However, eventually, all participants achieved a rise above 100% after 24 hours, and all had a

			positive response to treatment after 24 hours. The study included only 29 participants, was open-label and uncontrolled, and is subject to bias and confounding. Therefore, it is of low-quality and the results should be interpreted with caution. Nevertheless, The European public assessment report for susoctocog alfa states that the design and conduct of the study are acceptable because of the rarity of AHA and the emergency nature of the bleeding, and the marketing authorisation was granted under exceptional circumstances, subject to collection and analysis of further data.
9.	Deaths	Grade C	This outcome shows the number of people who died during the study. 7 people died during the study. These included 3 deaths due to bleeding, but none of the bleeds were considered related to study treatment or to be due to failure of treatment. The study included only 29 participants, was open-label and uncontrolled, and is subject to bias and confounding. Therefore, it is of low-quality and the results should be interpreted with caution. Nevertheless, The European public assessment report for susoctocog alfa states that the design and conduct of the study are acceptable because of the rarity of AHA and the emergency nature of the bleeding, and the marketing authorisation was granted under exceptional circumstances, subject to collection and analysis of further data.
10.	Anti-pFVIII antibody titres	Grade C	This outcome shows the number of people who developed antibodies to susoctocog alfa. Antibodies may

			reduce the treatment's ability to reduce or stop bleeding 5 people developed antibodies to susoctocog alfa. Bleeding was not controlled in 2 of these people The study included only 29 participants, was open-label and uncontrolled, and is subject to bias and confounding. Therefore, it is of low-quality and the results should be interpreted with caution. Nevertheless, The European public assessment report for susoctocog alfa states that the design and conduct of the study are acceptable because of the rarity of AHA and the emergency nature of the bleeding, and the marketing authorisation was granted under exceptional circumstances, subject to collection and analysis of further data.