Glutaric aciduria type 1 (GA1) Dietetic Management Pathway

Presumptive positive screen for GA1
See Clinical Management Guidelines and Clinical Referral Guidelines and Standards (www.bimdg.org)

Unwell baby: admit to local hospital for assessment
Transfer to specialist centre as soon as appropriate

Metabolic Dietitian - liaise with local dietitian/team and see 'face to face' within 24 hrs of screening result, if possible

Well baby: day case (metabolic centre or local hospital)
Metabolic or local dietitian see same day. If not possible, dietetic advice by local consultant/registrar
Metabolic dietitian - liaise with local dietitian and see 'face to face' within 24 hours of screening result, if possible

Temporarily stop breast feeds/infant formula
IV 10% dextrose infusion and carnitine

Support for mum to express milk

Ensure adequate feeding: breast and/or bottle feed at least 3 to 4 hourly day & night. Check weight

NG/oral feeds and $ IV fluids as tolerated
Reintroduce natural protein (usual feeds) within 24 - 48 hrs
Aim normal energy requirements from IV and enteral feeds
Breast fed baby: start to re-establish breast feeds
If diagnosis confirmed commence GA1 feeding regimen*

Discharge home with BIMDG Emergency guidelines (www.bimdg.org) and glucose polymer
Instruct to take to hospital if unwell

Specialist team review within 5 working days of diagnostic sampling

Biochemically abnormal GA1 confirmed
Carnitine 100mg/Kg/day
Commence GA1 feeding regimen
Limit lysine intake

Biochemically normal or equivocal
DNA results by 15days
Normal feeds
Emergency regimen

Not confirmed
GA1 unlikely

GA1 confirmed
Commence GA1 feeding regimen
Limit lysine intake

***Breast feeding regimen**
Give: 1g/Kg/day of protein equivalent from lysine free, low tryptophan infant formula (this will reduce lysine intake from breast feed to provide around 90 - 135mg/Kg/day, depending on breast feed intake).

Divide total volume of infant formula and give equally before 4 to 6 breast feeds over 24h, evenly distributed.

Additional breast feeds can be given if required

(see Dietetic Management and Appendices 1 to 5, for full details)

***Infant formula/bottle feeding regimen**
Give: 1.3g/Kg/day natural protein from whey based infant formula (equates to approx 114 mg/Kg/day lysine).
Give: lysine free, low tryptophan infant formula - 1.3 - 1.4g/Kg/day protein equivalent but can exceed this if infant is hungry.

The infant milks can be given separately or mixed together providing both natural protein and lysine free protein equivalent requirements are met.
Feed 6 to 8 times, evenly over 24 hours.

(see Dietetic Management and Appendices 1 to 5, for full details)

Emergency Regimen
10% glucose polymer and lysine free/low tryptophan infant formula or amino acids
See **appendix 3** for full details
For hospital ER guidelines see www.bimdg.org.uk
During first hospital admission for illness, consider training caregiver nasogastric

Liaise with local dietitian, if appropriate

Glutaric aciduria type 1 - Dietetic Management

- Carnitine supplementation (100mg/kg/day, adjust according to response) to prevent deficiency
- Low lysine (low protein) diet with lysine free low tryptophan and micronutrient supplements
- Regular monitoring of plasma amino acids, specifically lysine (aim lower end of normal reference range) and arginine (aim normal reference range)
- Dietary emergency regimen (oral/tube)
- Emergency hospital treatment as per BIMDG emergency guidelines (www.bimdg.org)

Dietary treatment

Figures adapted from: Kölker S, Christensen E, Leonard JV, Greenberg CR, Boneh A, Burlina AB, Burlina AP, Dixon M, Duran M, García Cazorla A, Goodman SI, Koeller DM, Kyllerman M, Mühlhausen C, Müller E, Okun JG, Wilcken B, Hoffmann GF, Burgard P. Diagnosis and management of glutaric aciduria type I-revised recommendations. J Inherit Metab Dis. 34: 677-94. Epub 2011 Mar 23.

Dietary Treatment	**Age**	
	0-6m	**7-12m**
Lysine mg/kg/day	114 mg	114 mg
Protein (natural) g/Kg/day	1.3g	1.3g
Lysine-free, low tryptophan amino acid mix g/Kg/day	1.3-1.4g	1g
Total protein equivalent	2.6-2.7g	2.3g
Energy kcal/Kg/days	80-115 kcal	80-95 kcal

Dietary management information (as per local centres own resource)

- Emergency regimen information (when to use, preparation, local hospital details)
- GA1 dietary information
- Weaning: low protein diet
- Weaning low protein recipes
- 1g protein exchanges
- Emergency feeds
- Summary of suitable lysine-free, low tryptophan L-amino acid supplements
- Special low protein food lists and advice sheet to GPs
- Home delivery

Appendix 1 - Breast feeding regimen

Kölker S *et al* 2007, 2011 recommendation is 0.8-1.3 g/kg/day protein equivalent from lysine-free, low tryptophan L-amino acid supplement between 0-6m. Propose give 1g/Kg/day protein equivalent from protein substitute. *GA 1* Anamix Infant, Nutricia contains 2g/100 ml protein equivalent.

Kölker S *et al* 2007, 2011 recommendation for lysine requirement is: 100mg/Kg/day between 0-6 m of age.
Volume of breast milk unknown unless expressed. Human milk: protein = 1.3g/100 ml (Food Standards Agency).
Average lysine content is 69 mg/g protein or 90mg lysine/100ml (WHO/FAO/UNU 2007).
Normal lysine intake from breast milk only at: 150 ml/Kg/day = 135 mg/Kg/day; at 175 mg/kg/day = 157 mg/Kg/day: at 200 ml/Kg/day = 179 mg/kg/day

GA1 Infant - breast feeding regimen for 0-6mths

Weight of infant	Total daily volume of lysine-free/low tryptophan infant formula to provide 1g/Kg/d, divided by 4-6 feeds in day	Fluid requirement			Theoretical lysine intake (mg/kg/day) from breast feeds, assuming fluid intake from lysine-free/low tryptophan infant formula decreases breast milk volume by same amount. Total volume is for combined intake of breast milk and lysine-free/low tryptophan formula.			Total protein intake (g/Kg/day) (from lysine free/low tryptophan infant formula and breast milk)		
		Total daily fluid intake from all feeds if given at 150 ml/Kg/day	Total daily fluid intake from all feeds if given at 175 ml/Kg/day	Total daily fluid intake from all feeds if given at 200 ml/Kg/day	Feeding at 150 ml/Kg/day fluids	Feeding at 175 ml/Kg/day fluids	Feeding at 200 ml/Kg/day fluids	Feeding at 150 ml/Kg/day fluids	Feeding at 175 ml/Kg/day fluids	Feeding at 200 ml/Kg/day fluids
3 kg	150 ml	450	525	600	90	112	135	2.3	2.6	2.95
4 kg	200 ml	600	700	800	90	112	135	2.3	2.6	2.95
5 kg	250 ml	750	875	1000	90	112	135	2.3	2.6	2.95
6 kg	300 ml	950	1050	1200	90	112	135	2.3	2.6	2.95
7 kg	350 ml	1125	1225	1400	90	112	135	2.3	2.6	2.95

If baby is drinking a higher volume, it is probably growing rapidly and should cope with higher lysine intake.

Appendix 2 - Infant formula/bottle feeding regimen

Kölker *et al* 2007, 2011 recommendation is 0.8-1.3g/Kg/day protein equivalent from lysine-free, low tryptophan L-amino acid supplement is given between 0-6m of age. Infant protein substitute [e.g. *GA Anamix Infant,* Nutricia] contains 2g/100 ml protein equivalent.

Kolker *et al* 2007, 2011 recommendation for lysine requirement is 100mg/Kg/day between 0-6 m of age.
Whey based Infant formulas contain protein: 1.3g -1.4g/100 ml. Average lysine content is 88 mg/g protein or 114mg lysine/100ml

Normal lysine intake at: 150 ml/Kg/day = 171 mg/Kg/day; at 175 mg/kg/day = 200 mg/Kg/day: at 200 ml/kg/day = 228 mg/Kg/day

GA 1 Infant formula/bottle feeding regimen 0-6mths

Weight of infant	Total volume of whey based infant formula to provide 114mg lysine/kg/day (if formula contains 114mg lysine/100ml)	Total natural protein intake g/kg/day - from whey based infant formula providing 114mg lysine/kg/day	Daily feed volume to be provided by lysine-free, low tryptophan infant formula to provide protein equivalent requirements g/Kg/day Aim is 0.8-1.3g/kg/day			Total protein intake (if infant formula provides 114 mg/kg/day lysine and fluid intake deficit is made up from lysine-free/low tryptophan infant formula, (2g protein equivalent/100ml)		
			Feeding at 150ml/Kg/day	Feeding at 175ml/Kg/day	Feeding at 200ml/Kg/day	Feeding at 150ml/Kg/day	Feeding at 175ml/Kg/day	Feeding at 200ml/Kg/day
3 kg	300 ml	1.3	150 (1.0)	225 (1.5)	300 (2.0)	2.3	2.8	3.3
4 kg	400 ml	1.3	200 (1.0)	300 (1.5)	400 (2.0)	2.3	2.8	3.3
5 kg	500 ml	1.3	250 (1.0)	375 (1.5)	500 (2.0)	2.3	2.8	3.3
6 kg	600 ml	1.3	300 (1.0)	450 (1.5)	600 (2.0)	2.3	2.8	3.3
7 kg	700 ml	1.3	350 (1.0)	525 (1.5)	700 (2.0)	2.3	2.8	3.3

Appendix 3

Emergency regimen

With every episode of vomiting, diarrhoea or high temperature it is important to:

1. start glucose polymer and continue lysine-free, low tryptophan amino acid supplement
2. stop natural protein immediately

In any other illness, such as cough or cold without high temperature but impaired appetite it is important to ensure that at least the normal energy intake (using fat and carbohydrate sources) is achieved and the usual daily amount of lysine free/low tryptophan L- amino acid supplement is given. Nasogastric tube feeding may be needed to achieve this. It may be unnecessary to stop or reduce natural protein at this stage, unless symptoms become more severe.

3. for hospital ER guidelines (enteral and IV), refer to www.bimdg.org.uk emergency guidelines

Reference: Kölker S, Christensen E, Leonard JV, Greenberg CR, Boneh A, Burlina AB, Burlina AP, Dixon M, Duran M, García Cazorla A, Goodman SI, Koeller DM, Kyllerman M, Mühlhausen C, Müller E, Okun JG, Wilcken B, Hoffmann GF, Burgard P. (2011) Diagnosis and management of glutaric aciduria type I-revised recommendations. J Inherit Metab Dis. 34: 677-94. Epub 2011 Mar 23

Appendix 4

Protein substitutes for Glutaric Aciduria Type 1 - (all ACBS prescribable)

Nutrient	Unit	GA Anamix Infant	GA Gel *	GA Gel*	XLys, Low Try Maxamaid*	XLys, Try Glutaridon *	GA Amino 5
		Nutricia	Vitaflo	Vitaflo	Nutricia	Nutricia	Vitaflo
		per 100 ml	per 100g	per 24g sachet	per 100g	per 100g	per 100g
Suggested suitable age		0-1y	6m -10y	6m -10y	6m -10y	All ages	All ages
Energy	kJ	287	1413	339	1311	1386	1411
	kcal	69	338	81	309	326	332
Protein equivalents	g	2	41.7	10	25	77	83
Total amino acids	g				30	93	
Carbohydrate	g	7.4	42.9	10.3	51	4.5	0
Fat	g	3.5	0.05	0.02	<0.5	0	0
Fibre	g	0.8	0	0	0	0	0
Vitamins A	µg	59	600	144	525		
Vitamins D	µg	1.3	14.6	3.5	12		
Vitamins E	µg	0.7	9	2.2	4.35		
Vitamins C	mg	7.4	63	15	135		
Vitamins K	µg	5.6	41	9.8	30		
Thiamin	mg	0.08	1	0.24	1.1		
Riboflavin	mg	0.08	1.2	0.29	1.2		
Niacin	mg	0.33	14	3.4	12		
Niacin equivalents	mg	0.56	18.5	4.4	14.7		
Vitamin B6	mg	0.08	1.1	0.26	1.4		
Folic acid	µg	8.3	208	50	240		
Vitamin B_{12}	µg	0.18	2	0.48	3.9		
Biotin	µg	2.7	25	6	120		
Pantothenic acid	mg	0.4	5	1.2	3.7		

Choline	mg	13.7	279	67	110		
Myo-inositol	mg	14.7	0	0	55.5		
Sodium	mmol	1.2	16.3	3.9	25.2		
Potassium	mmol	1.9	23.5	5.6	21.5		
Chloride	mmol	1.5	16.3	3.9	12.7		
Calcium	mg	62	1083	260	810		
Phosphorus	mg	45	825	198	810		
Magnesium	mg	9	167	40	200		
Iron	mg	1.2	14	3.4	12		
Copper	mg	0.065	0.8	0.19	1.8		
Zinc	mg	0.9	11	2.6	13		
Manganese	mg	0.06	1.7	0.41	1.6		
Iodine	µg	12.5	138	33.1	100		
Molybdenum	µg	1.8	50	12	100		
Selenium	µg	2.3	35	8.4	40		
Chromium	µg	2.1	71	17	40		
Package size		400g Scoop 5g		24g sachet	500g	500g	6g sachet
Flavours					unflavoured		
Other		Contains prebiotics					

*Analysis unflavoured

Appendix 5

Follow-up in first year- 'suggested' dietetic management for GA1

Age of infant	Dietetic intervention	Assessment
Diagnostic sample review (within 5 days)	Introduce lysine free, low tryptophan infant formula, limit natural protein as dietetic management (see appendices 1 or 2). Advise on emergency regimen appendix 3	Review dietary intake and adjust natural and lysine free, low tryptophan infant formula intake according to weight gain.
Confirmed diagnosis to 6mths	Increase intake of lysine free/low tryptophan formula according to increasing body weight (see appendices 1 or 2)	Weekly weight and feeding review
2 months	Dietetic review and discuss expected feeding plan over first year.	Review dietary intake and adjust natural and lysine free, low tryptophan infant formula intake according to weight gain. Review emergency feeds
4 months	Dietetic review and discuss expected feeding plan over first year. 1. Discuss when to start low protein fruits and vegetables or low protein commercial baby foods (less than 0.5g/100g). 2. When intake of low protein foods exceeds 30g per portion, consider gradually replacing breast/infant formula feeds with 1g protein food exchanges. 3. Introduce 50% of natural protein intake as cereal/vegetable sources and the rest as animal/milk protein e.g. yoghurt	Review dietary intake and adjust natural and lysine free, low tryptophan infant formula intake according to weight gain. Review emergency feeds.
6 months	1. Introduce low protein finger foods and more texture into diet (as per usual weaning practices). 2. Expand range suitable low protein weaning foods. 3. Gradually introduce second stage lysine-free, low tryptophan L- amino acid powder (as paste or added to lysine-free, low tryptophan infant formula).	Review dietary intake and adjust natural and lysine free, low tryptophan infant formula intake according to weight gain. Review emergency feeds
8 months	1. Introduce more texture/finger foods into diet (as per usual weaning practices). 2. Introduce more family low protein meal choices.	Review dietary intake and adjust natural and lysine free, low tryptophan infant formula intake according to weight gain. Review emergency feeds
12 months	Gradually encourage more variety into the diet. Give advice re: toddler feeding. Adjust emergency feeds to 15% glucose polymer (in addition to lysine-free, low tryptophan L-amino acids).	Review dietary intake and adjust natural and lysine free, low tryptophan infant formula intake according to weight gain. Review emergency feeds.