Commissioning Statement:

Parenteral nutrition for the treatment of adults and children with Type 2 and Type 3 intestinal failure requiring home parenteral support

Summary

This commissioning statement sets out the pathway for the treatment of adults and children with type 2 and type 3 Intestinal Failure (IF) with home parenteral support (HPS).

This commissioning statement aims to maximise the best use of the available limited compounding capacity by identifying patients suitable for Multi Chamber Bags (MCBs), or a hybrid approach, thereby prioritising compounded parenteral nutrition (PN) for patients requiring individualised nutrition.

Links and updates to other policies and documents

This commissioning statement relates to the following guidance, practices and specification:

- National Institute for Health and Care Excellence (NICE)
    - NICE guidance on nutrition support for adults: oral nutrition support, enteral tube feeding and parenteral nutrition: https://www.nice.org.uk/guidance/cg32/evidence/full-guideline-194889853
- European Society for Clinical Nutrition and Metabolism (ESPEN) guideline on home parenteral nutrition
    - https://www.espen.org/files/ESPEN-Guidelines/ESPEN_guideline_on_home_parenteral_nutrition.pdf
- The European Society for Paediatric Gastroenterology Hepatology and Nutrition (ESPGHAN) guidelines on paediatric parenteral nutrition
    - ESPGHAN/ESPEN/ESPR/CSPEN guidelines on paediatric parenteral nutrition: Standard versus individualized parenteral nutrition - PubMed (nih.gov)

Plain language summary

About type 2 and 3 intestinal failure

Intestinal Failure (IF) is defined as “the reduction of gut function below the minimum necessary for the absorption of macronutrients and/or water and electrolytes, such that intravenous supplementation is required to maintain health and/or growth”. It is an umbrella term as there are various conditions which can cause IF (Pironi et al., 2020). Examples include Crohn's disease, mesenteric ischemia, surgical complications, and radiation enteritis.

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Type 2

Type 2 IF describes patients under a multi-professional specialist team and frequently with changing metabolic or nutritional needs. Type 2 IF requires prolonged (meaning > 28 days) parenteral nutrition usually over an extended period of weeks or months. Type 2 IF is associated with complications of abdominal surgery, especially intestinal fistulation and abdominal sepsis and therefore patients often need intensive care unit (ICU) or high dependency unit (HDU) admission during their stay in hospital. They may also be discharged with home parenteral nutrition or tube feeding pending corrective surgery. Type 2 IF patients awaiting definitive surgery will be defined as “type 2”, even when discharged home.

Type 3

Type 3 IF describes patients with a chronic condition requiring long term parenteral feeding. The patient characteristically has stable nutrition needs or metabolic needs but cannot maintain his or her nutrition and/or fluid balance adequately by absorbing nutrients or fluid and electrolytes via the intestinal tract. Type 3 IF patients include but are not limited to:

- Candidates for autologous gastrointestinal reconstruction or intestinal transplantation to restore nutritional autonomy.
- Patients with IF related to advanced malignancy and needing HPS. Normally these would be patients with significant intra-abdominal/pelvic disease preventing normal intestinal function. In this situation, to be accepted for HPS, life expectancy is usually at least 3 months.

About home parenteral support

Throughout this commissioning statement, the word home refers to the patient’s usual environment. Home Parenteral Support (HPS) involves feeding directly into the bloodstream to meet the patient’s requirements. HPS can include fluids alone, fluids and electrolytes (salts) or macronutrients and micronutrients. Macronutrients are carbohydrates, proteins and fat, and micronutrients are vitamins and minerals needed by the body in very small amounts. The phrase parenteral nutrition (PN) refers to the intravenous administration of macronutrients and micronutrients (Pironi et al., 2015).

The current patient treatment pathway is that suitable patients will be discharged home on HPS as either compounded PN tailor-made to the patient's individual requirements or commercially available PN in the form of Multi Chamber Bags (MCBs), or a combination of the two, known as the hybrid approach. There are two types of MCBs: triple-chamber 3-in-1 bags (containing lipid, glucose, and amino acid solutions), or dual-chamber 2-in-1 MCBs (containing glucose and amino acid solutions) (Harrison et al., 2022). A range of MCBs are licensed for use in the UK for IF and details of these are available on NHS Futures. Compounded PN is an unlicensed product by definition, has an additional requirement of cold chain storage and has a shorter shelf life.

Epidemiology and needs assessment

The prevalence of patients on HPN in England is about 50 per million population (all ages). Therefore, the number of patients currently accessing home PN services is 2500, with approximately 30% being on HPN long term (5 years). There has been an increase in Type 2 IF, and an increase in patients now being able to be managed long

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term at home (NHS England, 2019). The prevalence of HPN has therefore been increasing at a rate of approximately 20% per annum. If this trend continues within the next 5 years, there are projected to be 4000 cases/year. This is reflected by the 2016 statement from the British Association of Parenteral and Enteral Nutrition (BAPEN) which highlighted a greater than 200% increase in new HPN patients over the last 5 years (BAPEN, 2017).

Evidence summary

Please see appendix 1 for the three paper summary of relevant evidence produced by Solutions for Public Health which supports this commissioning statement.

Commissioning position

Patients should receive licensed treatments, in this case MCBs, where possible, over non-licensed compounded HPN. Furthermore, capacity for compounded PN continues to exceed the capacity of the service and therefore compounding must be prioritised for those patients with the greatest clinical need. With manufacture of compounded PN there is also an associated risk of contamination and a requirement for resource intensive aseptic conditions, and manufacture is therefore limited for safety reasons to a small number of specialised providers who are part of the commercial framework. During a recent three-year period in the UK where capacity for providing compounded PN has been reduced, patients' needs have been appropriately met with licensed non-compounded MCBs as either a short, medium, or long-term alternative to a compounded product.

The commissioning statement is in line with the European Society for Clinical Nutrition and Metabolism (ESPEN) guideline on HPN, which states that either MCBs or customised compounded bags can be used. European paediatric guidelines also support the use of MCBs as a first line in the majority of paediatric and new-born patients.

This commissioning statement refers to two groups of patients. The first group are patients newly starting HPN who have been identified as needing this intervention by designated severe IF centres and who are able to be safely managed outside the acute hospital setting. The second group are patients who are currently established on fully compounded HPN or a hybrid regimen involving compounded HPN bags and MCBs.

For adults and children with Type 2/3 IF starting on HPN the treatment options are as follows:

- First-line: MCBs/supplemented MCBs +/- additional IV fluids
- Second-line: hybrid approach. A hybrid approach may involve a combination of MCBs, fluids and compounded bags across a week. It describes a situation where not all the PN and fluids need to be compounded in order to meet a patient's need.
- Third-line: fully compounded regime

During periods of shortages of compounding a national prior approval MDT, known as the Clinical Advice and Management Group (CAMG), will be formed. Clinicians/teams are required to be aware of changes to the status of the CAMG, which will be

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communicated through existing national communications processes including Futures NHS. The rest of this guidance assumes a period of shortage, therefore all patients being discharged with supplemented MCBs, hybrid approaches or fully compounding regimens must receive approval of the proposed regime by the CAMG prior to discharge.

Starting arrangements for all patients:

The decision to start PN for IF will be made by a severe IF Multi-Disciplinary Team (MDT) on an individual patient basis.

When making a decision on the treatment regimen the MDT should consider:

- Clinical and nutritional history and assessment
- Compatibility
- Burden of treatment regimen
- Risk assessment of treatment regimen, including home environmental and social factors

The starting arrangements differ based on the type of PN as follows:

- MCBs can be started by designated severe IF centres (see the Severe Intestinal Failure (Adults) Service Specification for guidance)
- Patients being discharged with supplemented MCBs, hybrid approaches or fully compounded regimens must be referred to, and discussed by, the National HPN CAMG meeting who must approve the proposed regime.[1]

For adults, more information on starting arrangements is available in the Severe Intestinal Failure Service Specification.

There is a requirement for completion of the relevant prior approval forms for each patient where PN is being prescribed.

Adults starting on Home Parenteral Nutrition

Patients should be started on HPN in line with the treatment pathway outlined above. The third line treatment of a fully compounded regimen should only be used if the two first lines of treatment are not possible or have been tried and did not meet the needs of the patient.

First line: Multi Chamber Bags

Inclusion criteria

MCBs are intended to be used as the first-line treatment option for adult patients newly starting on HPN if they fulfil the following criteria:

[1] Clinicians are required to be aware of changes to the status of the CAMG and whether prior approval through CAMG is required. Please see Commissioning Position for more information.

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- Individual weekly requirements for macronutrients, micronutrients, fluid and electrolytes can be met using an MCB/supplemented MCB +/- additional intravenous fluids[2].**AND**

- Nutrition nursing team feel that patient ability and dexterity can appropriately support administration and practical requirements of MCBs. Dexterity may be impacted by clinical condition, comorbidities and social factors.

Exclusion criteria

Patients meeting the following exclusion criteria should not be started on MCBs as first-line treatment and should be assessed for second-line treatment:

- Patient electrolyte requirements per week are significantly outside of the range of MCBs/supplemented MCBs available. For example, patients requiring a calcium-free regimen.

Monitoring requirements

Monitoring requirements are patient specific and to be determined by the MDT. Patients should ideally have blood tests taken for urea and electrolytes (U+Es), liver function tests (LFTs), corrected calcium, phosphate and magnesium with follow up consultation within two weeks of a change in HPN prescription. Patients are suggested to have trace elements and vitamins checked within 1 – 3 months of a change in prescription and results reviewed in clinic/virtual clinic.

Stopping criteria

If there is clinical or biochemical evidence of nutrient deficiency or excess/toxicity with MCBs, patients should be reviewed by MDT and considered for the next line of treatment.

Second line: hybrid approach

A hybrid approach may involve a combination of MCBs, fluids and compounded bags across a week. It describes a situation where not all of the PN and fluids need to be compounded in order to meet a patient's need.

Inclusion criteria

Patients are eligible to be considered by CAMG[3] for discharge on a hybrid approach if either:

- First-line treatment with a regimen involving MCBs/supplemented MCBs +/- intravenous fluids is not possible

OR

- First-line treatment been trialled and was not tolerated by patient or did not meet their requirements

AND both of the following criteria are met:

[2] The extent to which requirements are exactly met or approximately met should be carefully considered by an MDT and should be determined by patient specific factors and the MCBs/supplemented MCBs available. Patient specific factors include social and environmental factors as well as clinical and nutritional needs.

[3] Clinicians are required to be aware of changes to the status of the CAMG and whether prior approval through CAMG is required. Please see Commissioning Position for more information.

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- Individual weekly requirements for macronutrients, micronutrients, fluid and electrolytes can be met using a hybrid approach[4].
- Nutrition nursing team feel that patient ability and dexterity can appropriately support administration and practical requirements of a regimen that includes MCBs. Dexterity may be impacted by clinical condition, comorbidities and social factors.

Monitoring requirements

Monitoring requirements are patient specific and to be determined by the MDT. Patients should ideally have blood tests taken for U+Es, LFTs, corrected calcium, phosphate and magnesium with follow up consultation within two weeks of a change in HPN prescription. Patients are suggested to have trace elements and vitamins checked within a 1 – 3 months of a change in prescription and results reviewed in clinic/virtual clinic.

Stopping criteria

If there is clinical or biochemical evidence of nutrient deficiency or excess/toxicity with this approach, patients should be reviewed by MDT and considered for the next line of treatment.

Third line: compounded parenteral nutrition

Inclusion criteria

Patients are eligible to be considered by CAMG[5] for discharge on a fully compounded approach if the following criteria are met:

- Treatment with MCBs/supplemented MCBs +/- fluids is not possible

  OR

- Treatment with MCBs/supplemented MCBs +/- fluids has been trialled and was not tolerated by patient or did not meet their requirements

AND

- Treatment with a hybrid approach is not possible

  OR

- Treatment with a hybrid approach has been trialled and was not tolerated by patient or did not meet their requirements.

Monitoring requirements

Monitoring requirements are patient specific and to be determined by the MDT. Patients should ideally have blood tests taken for U+Es, LFTs, corrected calcium, phosphate and magnesium with follow up consultation within two weeks of a change in HPN prescription. Patients are suggested to have trace elements and vitamins checked within a 1 – 3 months of a change in prescription and results reviewed in clinic/virtual clinic.

[4] The extent to which requirements are exactly met or approximately met should be carefully considered by an MDT and should be determined by patient specific factors and the MCBs/supplemented MCBs available. Patient specific factors include social and environmental factors as well as clinical and nutritional needs.

[5] Clinicians are required to be aware of changes to the status of the CAMG and whether prior approval through CAMG is required. Please see Commissioning Position for more information.

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Children starting on Home Parental Nutrition

MCBs should be considered first line before starting individualised HPN in the majority of paediatric patients. A fully compounded PN approach should only be used if a patient's clinical and nutritional needs cannot be met by the two first lines of treatment. The decision should always take into account patient and family specific factors, and social and environmental aspects as well as clinical and nutritional needs.

First line: multi chamber bags

Inclusion criteria

MCBs are intended to be used as the first-line treatment option for paediatric patients with type 2/3 IF who are newly starting HPN, if they fulfil the following criteria:

- Individual weekly requirements for macronutrients and electrolytes can be met using an MCB/supplemented MCB +/- additional intravenous fluids[6] **AND**
- Individual requirements for fluids/volume can be met using an MCB/supplemented MCB +/- additional fluids **AND**
- Individual requirements for micronutrients (vitamins and minerals) can be met either by enteral supplementation[7] or by the use of supplemented MCBs **AND**
- Patient likely to be compliant with monitoring at month 1 and 3 monthly **AND**
- Nutrition nursing team feel that family and patient dexterity and environment can appropriately support administration and practical requirements of MCBs +/- enteral supplementation.

Exclusion criteria

MCB-only treatment should not be initiated in patients who meet any of the following criteria:

- Patients with organ failure e.g. patients requiring haemodialysis, or with a diagnosis of advanced cardiac disease
- Patient electrolyte requirements per week are significantly outside of the range of MCBs available. For example, patients requiring a calcium-free regimen.

There are some situations where MCBs would not routinely be considered but may be suitable according to MDT and patient/carer decision. For example, if the patient weight is under 10kg.

Monitoring requirements

Monitoring requirements are patient specific and to be determined by the MDT. Patients should ideally have blood tests taken for U+Es, LFTs, corrected calcium, phosphate and magnesium with follow up consultation within two weeks of a change in

[6] The extent to which requirements are exactly met or approximately met should be carefully considered by an MDT and should be determined by patient specific factors and the MCBs/supplemented MCBs available. Patient specific factors include social and environmental factors as well as clinical and nutritional needs.

[7] Enteral supplementation in this context refers to the provision of vitamins and micronutrients through the oral route.

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HPN prescription. Patients are suggested to have trace elements and vitamins checked within a 1 – 3 months of a change in prescription and results reviewed in clinic/virtual clinic.

Stopping criteria

If there is clinical or biochemical evidence of nutrient deficiency or excess/toxicity with MCBs +/- intravenous fluids, patients should be reviewed by MDT and considered for the next line of treatment.

Second line: hybrid approach

Inclusion criteria

A hybrid approach may involve a combination of MCBs, fluids and compounded bags across a week. It describes a situation where not all the PN and fluids need to be compounded in order to meet a patient's need.

Patients are eligible to be considered by CAMG[8] for discharge on a hybrid approach if either:

- Criteria for first line treatment with MCBs/supplemented MCBs +/- fluids were not met

  OR

- Treatment with MCBs/supplemented MCBs +/- fluids has been trialled and was not tolerated by patient, family and/or nursing team, or caused nutritional deficiencies/excesses

AND both of the following criteria are met:

- Individual weekly requirements can be meet using a hybrid approach[9].
- Nutrition nursing team feel that family and patient dexterity and environment can appropriately support administration and practical requirements of regimens that may involve MCBs +/- enteral supplementation

Exclusion criteria

Treatment should not be initiated in patients who meet any of the following criteria:

- Patients with organ failure e.g. haemodialysis, advanced cardiac disease
- Patient electrolyte requirements per week are significantly outside of the range of MCBs available. For example, patients requiring a calcium-free regimen.

There are some situations where MCBs would not routinely be considered but may be suitable according to MDT and patient/carer decision. For example, if the patient weight is under 10kg.

Monitoring requirements

Monitoring requirements are patient specific and to be determined by the MDT. Patients should ideally have blood tests taken for U+Es, LFTs, corrected calcium,

[8] Clinicians are required to be aware of changes to the status of the CAMG and whether prior approval through CAMG is required. Please see Commissioning Position for more information.

[9] The extent to which requirements are exactly met or approximately met should be carefully considered by an MDT and should be determined by patient specific factors and the MCBs/supplemented MCBs available. Patient specific factors include social and environmental factors as well as clinical and nutritional needs.

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phosphate and magnesium with follow up consultation within two weeks of a change in HPN prescription. Patients are suggested to have trace elements and vitamins checked within a 1 – 3 months of a change in prescription and results reviewed in clinic/virtual clinic.

Stopping criteria

If there is clinical or biochemical evidence of nutrient deficiency or excess/toxicity with this approach, patients should be reviewed by MDT and considered for the next line of treatment.

Third line: compounded PN only

Inclusion criteria

Paediatric patients are eligible to be considered by CAMG[10] for discharge on a fully compounded approach if the following criteria are met:

- Treatment with MCBs/supplemented MCBs +/- fluids is not possible

  OR

- Treatment with MCBs/supplemented MCBs +/- fluids has been trialled and was not tolerated by patient or did not meet their requirements

AND

- Treatment with a hybrid approach is not possible

  OR

- Treatment with a hybrid approach has been trialled and was not tolerated by patient or did not meet their requirements.

Monitoring requirements

Monitoring requirements are patient specific and to be determined by the MDT. Patients should ideally have blood tests taken for U+Es, LFTs, corrected calcium, phosphate and magnesium with follow up consultation within two weeks of a change in HPN prescription. Patients are suggested to have trace elements and vitamins checked within a 1 – 3 months of a change in prescription and results reviewed in clinic/virtual clinic.

Patients established on Home Parenteral Nutrition

The evidence summary demonstrates equivalent safety and clinical efficacy of MCBs, which are the licensed product, to compounded HPN. Therefore, patients with type 2/3 IF already established on regimens involving compounded HPN should be considered for a trial of non-compounded regimens.

For adult and paediatric patients established on a fully compounded HPN regime, these patients should be reviewed at least annually by MDT for consideration of switching to:

- First line: multi chamber bags/supplemented MCBs +/- fluids

[10] Clinicians are required to be aware of changes to the status of the CAMG and whether prior approval through CAMG is required. Please see Commissioning Position for more information.

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- Second line: hybrid approach. This may involve a combination of MCBs, fluids and compounded bags across a week.

For adult and paediatric patients established on a hybrid regimen including compounded bags, these patients should be reviewed at least annually by MDT for consideration of switching to:

- Multi chamber bags/supplemented MCBs +/- intravenous fluids

MDT review for a switch should be patient and family specific and should take into account social and environmental in addition to clinical and nutritional factors. Please see NHS Futures for guidance on assessment for switching, in particular HPS (HPN /HPE) prescriptions for IF patients - assessing for non compounded /hybrid regimens and completing the formulation template June 2022

When making a decision, MDT should consider:

- Compatibility
- Burden of treatment regimen
- Risk assessment of treatment regimen, including home environmental and social factors
- Whether the patient is being treated post-operatively following reconstructive surgery for IF and is already being weaned off PN
- Clinical and nutritional history and assessment.

Any change in prescription will require completion of the appropriate prior approval forms.

Adult established Home Parenteral Nutrition patients

If the following criteria are met during MDT review of the adult HPN user, a trial switch should be considered:

- Nutritional need has been stable over at least 3 months.
- Individual weekly requirements for macronutrients, micronutrients, fluid and electrolytes can be met using an approach of MCBs/supplemented MCBs +/- intravenous fluids, or a hybrid approach[11].
- MDT +/- community team feel that patient can be appropriately monitored during MCB or hybrid trial period.
- Patient or carer has given informed consent to trying a switch.

Exclusion criteria

Patients meeting any of the following exclusion criteria should not be switched and should remain on compounded PN:

- Patient electrolyte requirements per week are well outside of the range of MCBs available. For example, patients requiring a calcium-free regimen.

[11] The extent to which requirements are exactly met or approximately met should be carefully considered by an MDT and should be determined by patient specific factors and the MCBs/supplemented MCBs available. Patient specific factors include social and environmental factors as well as clinical and nutritional needs.

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- Prognosis is expected to be <1-3 months.

Monitoring criteria:

Monitoring requirements are patient specific and to be determined by the MDT. Patients should ideally have blood tests taken for U+Es, LFTs, corrected calcium, phosphate and magnesium with follow up consultation within two weeks of a change in HPN prescription. Patients are suggested to have trace elements and vitamins checked within a 1 – 3 months of a change in prescription and results reviewed in clinic/virtual clinic.

Stopping criteria

MDT should review the patient to decide whether a trial regimen should be stopped if:

- There is clinical or biochemical evidence of nutrient deficiency or excess or toxicity

Paediatric established Home Parenteral Nutrition patients

If the following criteria are met during MDT review of the paediatric HPN user, a trial switch should be considered:

- Nutritional need has been stable over at least 3 months.
- Individual weekly requirements for macronutrients, micronutrients, fluid and electrolytes can be met using an approach of MCBs/supplemented MCBs +/- intravenous fluids, or a hybrid approach[12].
- MDT including community team feel that patient can be appropriately monitored during MCB or hybrid trial period.
- Patient or carer has given informed consent to trying a switch.

Exclusion criteria

Patients meeting ANY of the following exclusion criteria should not routinely be switched and should remain on compounded PN:

- Patients with organ failure. For example, patients requiring renal replacement therapy, patients with a diagnosis of advanced cardiac disease.
- Patient and family factors, including dexterity/manual ability, social factors and home environment, would not support administration of MCBs.
- Patient electrolyte requirements per week are well outside of the range of MCBs available. For example, patients requiring a calcium-free regimen.

Patients with body weight < 10kg would not be routinely switched, but this is not an absolute contraindication.

Monitoring criteria:

Monitoring requirements are patient specific and to be determined by the MDT. Patients should ideally have blood tests taken for U+Es, LFTs, corrected calcium, phosphate and magnesium with follow up consultation within two weeks of a change in

[12] The extent to which requirements are exactly met or approximately met should be carefully considered by an MDT and should be determined by patient specific factors and the MCBs/supplemented MCBs available. Patient specific factors include social and environmental factors as well as clinical and nutritional needs.

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HPN prescription. Patients are suggested to have trace elements and vitamins checked within a 1 – 3 months of a change in prescription and results reviewed in clinic/virtual clinic.

Stopping criteria

MDT should review the patient to decide whether the trial regimen should be stopped if:

- There is clinical or biochemical evidence of nutrient deficiency or excess or toxicity

Governance arrangements

As some MCBs are unlicensed for patients under 1 or under 2 years of age and all compounded PN is unlicensed, any provider organisation treating patients with this intervention will be required to provide assurance that the internal governance arrangements have been completed before the medicine is prescribed. These arrangements may be through the Trust's Drugs and Therapeutics committee (or similar) and NHS England may ask for assurance of this process. Approved providers will be expected to follow local and regional policies for the safe prescribing and monitoring of off-label licensed medications including compliance with the Medicines and Healthcare products Regulatory Agency (MHRA) safety alerts. Prescribers need to also be aware of their responsibilities as specified in MHRA Drug Safety Update.

Audit requirements

All centres will return data on all patients with type 2 and 3 IF to the national IF Registry in line with the NHS Standard Contract

All information on patients being assessed as appropriate for HPN will also be required to be entered on the national prior approval system.

This will ensure that only patients assessed as eligible and meeting the criteria will proceed to the appropriate line of treatment.

Outcomes will be measured annually by all centres, to include the following:

- Proportions of patients on compounded vs. hybrid vs. MCB PN
- Rates of catheter related blood stream infections in patients receiving compounded vs. hybrid vs. MCB PN
- Rates of hospital admissions for reasons related to HPN in patients receiving compounded vs. hybrid vs. MCB PN
- Switches between HPN types, with reason

Any suspected adverse reactions from treatment with MCBs should be reported directly to the MHRA via the Yellow Card reporting site at: https://yellowcard.mhra.gov.uk/

Commissioning statement review date

This document will be reviewed when there are significant changes in clinical evidence and/or HPS capacity which indicate that the commissioning statement 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.

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Equality statement

Promoting equality and addressing health inequalities are at the heart of the three nation'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

Intestinal failure (IF)	The reduction of gut function below the minimum necessary for the absorption of macronutrients and/or water and electrolytes, such that intravenous supple-mentation is required to maintain health and/or growth
Type 2 Intestinal Failure	A prolonged acute condition, often in metabolically unstable patients, requiring complex multi-disciplinary care and PN over periods of weeks or months
Type 3 Intestinal Failure	A chronic condition, in metabolically stable patients, who require PN over months or years. It may be reversible or irreversible
Enteral	Refers to methods of feeding where the gut is used for delivery and absorption of nutrition. This can include normal oral intake, liquid supplements, or use of a tube.
Parenteral	Refers to methods of feeding that bypass the gut. Nutrition is delivered intravenously.
Compounded parenteral nutrition	Bags of PN which are individually tailored to the patient's requirements and which are manufactured under strictly controlled aseptic conditions in an approved pharmacy manufacturing unit
Macronutrients	The three macronutrients are carbohydrates, proteins and fats

References

Harrison S, Kopczynska M, Leahy G, Taylor M, Farrer K, Barrett M, Mallawaarachchi P, Abraham A, Teubner A, Lal S (2022). Hybrid model of compounded and multichamber bag parenteral nutrition for adults with chronic intestinal failure. JPEN Journal of Parenteral and Enteral Nutrition, 46(7):1632-1638.

Pironi, L., Boeykens, K., Bozzetti, F., Joly, F., Klek, S., Lal, S., Lichota, M., Mühlebach, S., van Gossum, A., Wanten, G., Wheatley, C., & Bischoff, S. C. (2020). ESPEN

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guideline on home parenteral nutrition. *Clinical Nutrition*, *39*(6). https://doi.org/10.1016/j.clnu.2020.03.005

NHS England (2019) Service specification: Severe Intestinal Failure Service (Adults). Available at https://www.england.nhs.uk/publication/intestinal-failure-service-adult/

Appendix 1: Three paper summary of evidence

As produced by Solutions for Public Health.

Multi-chamber (generic, licensed) parenteral nutrition[13] as a first line therapy for adults and children with type 2 and 3 intestinal failure requiring parenteral nutrition (in home or as an inpatient)

Narrative summary of papers presented for review

Three papers were presented for summarisation by NHS England. Paper 1 is a retrospective cohort study from two Dutch centres comparing 16 children who received standardised, commercially available home parenteral nutrition[14] (PN) to 34 children who received individualised home PN. Paper 2 is a retrospective cohort study using data from a prospectively maintained database from a UK national referral centre. Patients were commenced on either ready-made home PN multi-chamber bags (n=60) or customised home PN (n=45). Paper 2 also included 18 patients who switched from customised to ready-made home PN multi-chamber bags. Paper 3 is a prospective time and motion study from three US centres comparing preparation time and costs for prescriptions for PN in hospitalised adults using three-chamber bags (i.e. standardised/ ready-made) (n=66) or hospital pharmacy-compounded bags (i.e. individualised/ customised) (n=70).

Paper 1: Nagelkerke et al 2020. Standardized and individualized parenteral nutrition mixtures in a pediatric home parenteral nutrition population

This paper reports a retrospective cohort study of 50 children with chronic intestinal failure (median age 6.5 years (interquartile range (IQR) 3.5 to 10.5)). Children had visited two Dutch centres between June 2017 and July 2018 and had received home PN for at least six months (median PN duration 62 months (IQR 18 to 99)). Children received either standardised, commercially available PN (n=16) or individualised PN (n=34). Children were prescribed standardised PN when nutritional need was stable over at least three months and the composition of an available mixture met their nutritional needs. Individualised PN was compounded by the hospital pharmacy. The authors stated that both groups received the same amount of vitamin and trace elements per bag. The authors stated that age (11 (IQR 8.5 to 14) vs 5 (IQR 2.5 to 7.5) years), gestational age (39.2 (35.3 vs 41) vs 36.2 (34.3 to

[13] The intervention is multi-chamber parenteral nutrition bags. These are pre-mixed (i.e. standardised) bags which contain carbohydrate, protein and fat sources in three chambers or carbohydrate and fat in two chambers, in pre-defined ratios. Current UK treatment is bespoke (i.e. individualised) 'compounded' parenteral nutrition for individual patients tailored to their exact nutritional requirements

[14] The terminology used to describe the parenteral nutrition received by patients in the included papers is replicated in this summary. In Paper 1, the term 'multi-chamber' was not specified in the description of commercially available home parenteral nutrition

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37.8 weeks) and PN duration (97 (IQR 40 to 134) vs 39 (13 to 80) months) were statistically significantly higher in the group receiving standardised PN. The amount of PN infusions per week was statistically significantly lower in the group receiving standardised PN (7 (IQR 4 to 7) vs 7 (IQR 7 to 7) days/week). All outcome measures were assessed for the period that patients received PN. The authors stated that six children received PN without any concurrent enteral or oral intake (one child (6%) receiving standardised, commercially available PN and five children (15%) receiving individualised PN). For children who received concurrent enteral nutrition, the amount of macronutrients was recorded and it was also noted if children were partially fed orally. Detailed information regarding oral intake was not available. If children switched the type of PN during the study period they were only assessed after the switch. The number of children who switched type of PN was not stated. All children received an antimicrobial solution (Taurolidine locks) for the prevention of central-line associated bloodstream infections. Twenty children were matched for age (median age 9 years (IQR 6 to 11)) in an additional analysis. The groups in this additional analysis were described as having comparable baseline characteristics.

Paper 2: Crooks et al 2022. Catheter-related infection rates in patients receiving customized home parenteral nutrition compared with multi-chamber bags

This paper reports a retrospective cohort study of 105 patients with chronic intestinal failure using 14 months of data (from July 2019) from a prospectively maintained database from a UK national referral centre. Sixty patients were newly commenced on ready-made home PN multi-chamber bags. The mean (± standard deviation (SD)) age for this group was 59 ± 13.3 years and the study period included a total of 5,914 catheter days (mean 99, SD not reported). Forty-five patients were newly commenced on customised home PN with a mean (±SD) age of 53 ± 17.1 years and a total of 7,641 catheter days (mean 170, SD not reported). In the group receiving ready-made home PN multi-chamber bags there were statistically significantly more patients with cancer (80% vs 24%) and patients who received nursing care for their PN (77% vs 47%). Patients receiving ready-made home PN multi-chamber bags also manipulated the central venous catheter circuit statistically significantly more times each week (18 episodes vs 13). No statement was made regarding the selection of patients to receive different types of PN or about any concurrent treatments. This paper also reported data relating to 18 patients who switched from customised PN to ready-made multi-chamber bags in July 2019 due to reduced availability of customised PN following manufacturing concerns raised by the regulatory agency. The mean (± SD) age of these 18 patients was 55.6 ± 14.1 years.

Paper 3: Cogle et al 2021. Multi-center prospective evaluation of parenteral nutrition preparation time and resource utilization: 3-chamber bags compared with hospital pharmacy–compounded bags

This paper reports a prospective time and motion study comparing preparation time and resource utilisation for 136 PN prescriptions in hospitalised adults using commercially available three-chamber bags (n=66) or hospital pharmacy-compounded bags (n=70). Data were collected from three US hospitals between June and August 2018. The observation period was from the time of the PN order to completion of the PN preparation process. Parenteral multivitamins and trace elements were added to both types of PN bags as standard practice at all study sites.

Effectiveness

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Growth[15]

Nagelkerke et al 2020 reported median (IQR) change in standard deviation (SD) score after 24 months in weight-for-age, height-for-age and weight-for-height for 12 children who received standardised home PN and 20 children who received individualised home PN. They reported a statistically significant increase in weight-for-age for standardised home PN (0.38 SD (-0.34 to 0.80)) compared to a decrease for individualised home PN (-0.55 SD (-1.11 to -0.07)), p=0.003. There was no statistically significant difference between standardised home PN and individualised home PN for height-for-age (-0.15 SD (-0.65 to 0.39) vs -0.30 SD (-0.86 to 0.35), p=0.580) or weight-for-height (0.54 SD (-0.50 to 1.52) vs -0.18 SD (-0.99 to 0.50), p=0.071).

Nagelkerke et al 2020 also reported an analysis with matching for age. There was no statistically significant difference in median (IQR) change in standard deviation score after 24 months between standardised home PN (n=10) and individualised home PN (n=10) for weight-for-age (0.80 SD (-0.12 to 1.40) vs -0.42 SD (-1.17 to -0.26[16]), p=0.051), height-for-age (-0.24 SD (-0.79 to -0.05) vs -0.78 SD (-0.89 to -0.12), p=0.445) or weight-for-height (1.38 SD (-0.89 to 2.20) vs -0.11 SD (-1.04 to 1.96), p=0.101).

One of the included papers reported a statistically significant increase in weight-for-age after 24 months for standardised home PN (n=12) compared to individualised home PN (n=20). There was no statistically significant difference between groups for height-for-age or weight-for height, or in an analysis with matching for age for any of the growth measures.

Calorie intake

Nagelkerke et al 2020 reported a statistically significant difference in median (IQR) calorie deficit for standardised home PN (n=16) (17 calories/kg/day (-20 to -11)) and individualised home PN (n=34) (4 calories/kg/day (-15 to 6)), (p=0.029.) They reported that there was no statistically significant correlation between this calculated difference and change in weight-for-age standard deviation score for either group (standardised home PN r_T = -0.121, p=0.583; individualised home PN r_T = 0.148, p=0.363).

Nagelkerke et al 2020 also reported an analysis with matching for age. In this analysis there was also a statistically significant difference[17] between groups with a median (IQR) calorie deficit for standardised home PN (n=10) (17 calories/kg/day (-27 to 3)) compared to a surplus for individualised home PN (n=10) (1 calorie/kg/day (-18 to 12)). They reported that there was no statistically significant correlation between this calculated difference and change in weight-for-age standard deviation score for either group (standardised home PN r_T = -0.067, p=0.851; individualised home PN r_T = 0.048, p=0.881).

[15] Dutch national reference standard sex- and age-adjusted standard deviation scores were obtained for weight-for-age, height-for-age and weight-for-height. Growth was assessed by calculating the difference in age-adjusted standard deviation scores between date of inclusion and previous measurements at minus six, 12 and 24 months. This difference indicated a change in growth chart position

[16] The IQR reported differed in the text and results table. The IQR from the results table was extracted

[17] The authors stated that there was a statistically significant difference between the groups. However, the p value reported (p=0.247) is not associated with a statistically significant result. The p value cited was assumed to be an error

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One of the included papers (n=50) reported a statistically significantly higher calorie deficit for standardised home PN compared to individualised home PN. There was no statistically significant correlation between this difference and growth for either group.

Preparation time

Cogle et al 2021 reported a statistically significantly shorter mean (±SD) preparation time for 66 commercially available three-chamber bags (5.5 ± 1.3 minutes) compared to 70 hospital pharmacy-compounded bags (14.3 ± 6.2 minutes) (mean difference 8.8 minutes, p<0.001). Preparation time tasks included transcription and ordering, review and validation of the order, preparation of PN and general cleaning and disinfection of equipment. The mean time required was shorter for commercially available three-chamber bags for all of the above tasks in the preparation of PN, except for the 'review and validation of the order' which took longer for commercially available three-chamber bags (30 seconds vs 18 seconds, p=0.001).

One of the included papers reported a statistically significantly shorter preparation time for commercially available three-chamber bags (total 66 bags) compared to hospital pharmacy-compounded bags (total 70 bags).

Costs of PN

Cogle et al 2021 reported a mean estimated total cost per PN bag of $81.60 for commercially available three-chamber bags and $131.17 for hospital pharmacy-compounded bags (mean difference -$49.57, no statistical comparison reported). Estimated cost elements included cost of labour, PN products, medical consumables and equipment. The mean estimated cost was lower for commercially available three-chamber bags for each of the cost elements.

One of the included papers reported a lower estimated mean cost per bag for commercially available three-chamber bags (total 66 bags) than for hospital pharmacy-compounded bags (total 70 bags).

Safety

Catheter-related bloodstream infections (CRBSI)

Crooks et al 2021 (n=105) reported no statistically significant difference in the incidence of CRBSI[18] between ready-made home PN multi-chamber bags (0.51/1,000 catheter days) and customised home PN (0.39/1,000 catheter days) (incidence rate ratio 1.29 (95% confidence intervals (CI) 0.17 to 9.65[19])). Total catheter days was 5,914 for ready-made home PN multi-chamber bags and 7,641 for customised home PN. Crooks et al 2021 also considered a number of potential confounders in multifactorial analysis and concluded that none significantly influenced the risk of CRBSI. The

[18] A diagnosis of CRBSI was based on clinical signs of sepsis in tandem with quantitative and/or qualitative analysis of paired central and peripheral blood cultures

[19] In the study abstract the incidence rate ratio is stated as 1.29 (95%CI 0.26 to 6.37). The 95% CI figures cited extracted in this summary are those from the main study text and results table

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confounders considered were catheter care provider (nursed patients vs non-nursed patients or those under shared care); cause of chronic intestinal failure (cancer vs non-cancer); central venous catheter type (non-tunnelled vs tunnelled) or volume of PN infused (low volume vs high volume).

Crooks et al 2021 also reported episodes of CRBSI for 18 patients who initially received customised home PN and then switched to ready-made home PN multi-chamber bags. There was no statistically significant difference in the incidence of CRBSI between the different types of PN (ready-made home PN multi-chamber bags 0.21/1,000 catheter days vs customised home PN 0.27/1,000 catheter days; incidence rate ratio 1.31 (95%CI 0.12 to 14.3)). Total catheter days was 4,834 for ready-made home PN multi-chamber bags and 7,401 for customised home PN.

One of the included papers (n=105) reported no statistically significant difference in incidence of catheter-related bloodstream infections between ready-made home PN multi-chamber bags and customised home PN. The same paper also reported no statistically significant difference in incidence of catheter-related bloodstream infections between types of PN for 18 patients who switched from customised home PN to ready-made home PN multi-chamber bags.

Biochemical values

Nagelkerke et al 2020 reported no statistically significant difference in number of electrolyte disturbances between standardised home PN (n=16) and individualised home PN (n=34). Number of electrolyte disturbances was reported for sodium (0 vs 0, p n/a), potassium (6.3% vs 9.4%, p=1.0), magnesium (6.7% vs 10.0%, p=1.0), calcium (0 vs 9.1%, p=.542), phosphorus (25% vs 28.1%, p=1.0) and chloride (14.3% vs 16.7%, p=1.0). The authors stated that no child was admitted because of abnormal electrolyte concentrations.

Nagelkerke et al 2020 also reported no statistically significant difference in abnormal liver function tests between standardised home PN (n=16) and individualised home PN (n=34. This was reported as no statistically significant difference between the groups in median (IQR) total bilirubin (6.0 µmol/L (5.0 to 13.0) vs 5.0 µmol/L (4.0 to 9.0), p=0.473) or median (IQR) conjugated bilirubin (4.0 µmol/L (2.3 to 6.0) vs 3.0 µmol/L (2.0 to 4.0), p=0.662).

Nagelkerke et al 2020 also reported that there was no statistically significant difference between groups for any electrolyte disturbance or liver function test in an analysis with matching for age (n=20).

One of the included papers (n=50) reported no statistically significant difference in number of electrolyte disturbances or abnormal liver function tests between standardised home PN and individualised home PN.

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