



ELSEVIER

Enfermedades Infecciosas y Microbiología Clínica

www.elsevier.es/eimc



Consensus statement

Executive summary of outpatient parenteral antimicrobial therapy: Guidelines of the Spanish Society of Clinical Microbiology and Infectious Diseases and the Spanish Domiciliary Hospitalisation Society[☆]



Luis Eduardo López Cortés (Coordinator)^{a,*}, Abel Mujal Martínez (Coordinator)^b, Magdalena Fernández Martínez de Mandojana^c, Natalia Martín^d, Mercè Gil Bermejo^e, Joan Solà Aznar^f, Eulalia Villegas Bruguera^g, Maria José Peláez Cantero^h, Pilar Retamar Gentil^a, Miriam Delgado Vicenteⁱ, Víctor José González-Ramallo^j, Miguel Ángel Ponce González^k, Manuel Mirón Rubio^l, M. Montserrat Gómez Rodríguez de Mendarozquetaⁱ, Miguel Ángel Goenaga Sánchez^m, Pedro Sanroma Mendizábalⁿ, Elena Delgado Mejía^o, Marcos Pajarón Guerreroⁿ, on behalf of the Sociedad Española de Enfermedades Infecciosas y Microbiología Clínica (SEIMC), the Sociedad Española de Hospitalización a Domicilio (SEHAD) Group¹

^a Unidad Clínica de Enfermedades Infecciosas y Microbiología, Hospital Universitario Virgen Macarena/Instituto de Biomedicina de Sevilla (IBIS)/Universidad de Sevilla/Centro Superior de Investigaciones Científicas, Seville, Spain

^b Home Hospital Unit, Department of Internal Medicine, Sabadell Hospital, Corporació Sanitària Parc Taulí, Universitat Autònoma de Barcelona, Spain

^c OSI Debarrena, Spain

^d Hospital San Pedro, Logroño, Spain

^e Hospital Universitario de Bellvitge, Barcelona, Spain

^f Parc Taulí Hospital Universitari, Barcelona, Spain

^g Hospital Dos de Maig, Barcelona, Spain

^h Hospital Materno-Infantil Carlos Haya, Málaga, Spain

ⁱ Hospital Universitario de Álava, Spain

^j Hospital General Universitario Gregorio Marañón, Madrid, Spain

^k Hospital Universitario de Gran Canaria Dr. Negrín, Spain

^l Hospital de Torrejón, Madrid, Spain

^m OSI Donostialdea, Spain

ⁿ Hospital Marqués de Valdecilla, Santander, Spain

^o Hospital Son Espases, Palma de Mallorca, Spain

A B S T R A C T

Keywords:

Outpatient parenteral antimicrobial therapy
Intravenous therapy
Home

Outpatient parenteral antimicrobial therapy (OPAT) programmes make it possible to start or complete intravenous antimicrobial therapy for practically any type of infection at home, provided that patient selection is appropriate for the type of OPAT programme available. Although the clinical management of infections in the home setting is comparable in many respects to that offered in conventional hospitalization (selection of antibiotics, duration of treatment, etc.), there are many aspects that are specific to this care modality. It is essential to be aware of them so that OPAT continues to be as safe and effective as inpatient care. The objective of this clinical guideline is therefore to provide evidence- and expert-based recommendations with a view to standardizing clinical practice in this care modality and contribute to a progressive increase in the number of patients who can be cared for and receive intravenous therapy in their own homes.

© 2018 Elsevier España, S.L.U. and Sociedad Española de Enfermedades Infecciosas y Microbiología Clínica. All rights reserved.

[☆] The complete consensus statement is available as Appendix in supplementary material.

* Corresponding author.

E-mail address: luislopezcortes@gmail.com (L.E. López Cortés).

¹ See Appendix A.

Resumen ejecutivo del tratamiento antimicrobiano domiciliario endovenoso: guía de la Sociedad Española de Enfermedades Infecciosas y Microbiología Clínica y la Sociedad Española de Hospitalización a Domicilio

R E S U M E N

Palabras clave:

Tratamiento antibiótico domiciliario endovenoso
Tratamiento endovenoso
Casa

Los programas de tratamiento antibiótico domiciliario endovenoso (TADE) permiten iniciar o completar el tratamiento antimicrobiano por vía endovenosa de prácticamente cualquier tipo de infección en el domicilio, siempre y cuando se realice una selección del paciente acorde al tipo de programa de TADE que se dispone. Aunque hay aspectos del manejo clínico de las infecciones en el domicilio que son superponibles en la mayoría de los casos a la realizada en la hospitalización convencional (selección de la antibioterapia, duración del tratamiento, etc.), existen numerosos aspectos que son específicos de esta modalidad asistencial. Resulta imprescindible conocerlos para que el TADE siga siendo igual de eficaz y seguro que la hospitalización convencional. El objetivo de esta guía clínica es por tanto, proporcionar recomendaciones basadas en la evidencia realizadas por expertos para homogeneizar la práctica clínica de esta modalidad asistencial y contribuir a que se incremente progresivamente el número de pacientes que pueden ser atendidos y recibir tratamiento endovenoso en su propio domicilio.

© 2018 Elsevier España, S.L.U. y Sociedad Española de Enfermedades Infecciosas y Microbiología Clínica. Todos los derechos reservados.

Introduction

OPAT (outpatient parenteral antimicrobial therapy) is a care modality that allows patients to receive intravenous antibiotics in their own homes or in an outpatient setting. The term was coined by Rucker et al. in 1974, in a publication about children with cystic fibrosis who received outpatient parenteral antibiotic therapy which allowed them sleep at home. The first experience involving adults was described by Antoniskis et al. in 1978, in which thirteen patients, mainly with osteomyelitis, self-administered intravenous antibiotics. OPAT programmes have gradually been developed in different countries such as Canada, Australia, New Zealand, Singapore, Italy, Ireland, the United Kingdom, Belgium and Spain, with demonstrable benefits for both patients and the healthcare system. OPAT has been shown to be a safe, effective and more efficient care modality than conventional hospitalization for the treatment of very different types of infectious diseases. Experience with OPAT programmes has gradually increased and evolved, as a review of the literature shows, leading to a reduced length of stay in hospital and a corresponding increase in the duration of OPAT, initiation of antibiotic treatment without previous hospitalization, increased use of peripherally inserted central catheters (PICC line) for prolonged treatment, as well as provision of care for paediatric patients and the elderly. In Spain, the development of OPAT has been uneven for multiple reasons, depending on the needs of the individual hospital services, the resources of each centre and, above all, the knowledge and decision of the Health Departments themselves as to whether to include this care modality in the hospitals of their autonomous community. The key elements required for an OPAT programme are: (1) to define the service structure of the programme and OPAT team members; (2) appropriate patient selection; (3) antimicrobial management and drug delivery; (4) monitoring the patients during the process; (5) monitoring outcomes and appropriate clinical management.

The present statement was written following SEIMC guidelines for consensus statements (www.seimc.org), as well as Agree Collaboration (www.agreecollaboration.org) recommendations for evaluating the methodological quality of clinical practice guidelines. Over various meetings, the authors selected a set of questions designed to form the basis of the document. Their recommendations are based on a systematic critical review of the literature including, when necessary, the opinion of experts, who are SEIMC and SEHAD members. Their recommendations have been adjusted according to the scientific evidence available ([Appendix B](#)). All authors and coordinators of the statement have agreed on the

contents and conclusions of the document. Before final publication, the manuscript was made available online for all SEIMC members to read and to make comments and suggestions.

Definition of OPAT. Composition of an OPAT team. Care assignment in the OPAT programme

Recommendations:

- Administration of parenteral antibiotic therapy in the outpatient environment (OPAT) is an increasingly common, safe and effective practice with reduced costs (**A-II**).
- OPAT can be used to treat a wide variety of infections (**A-III**).
- Patients eligible for this therapy can be referred from any level of care (**B-II**).
- The programme should be multidisciplinary, involving medical, nursing and administrative staff assigned to the programme, working closely with pharmacists and microbiologists (**A-II**).
- Guideline recommendations and appropriate supervision are required to guarantee the suitability and safety of the treatment (**A-II**).

Role of members of the OPAT team. Inclusion criteria for patients in OPAT programmes

Recommendations:

- Because of its special characteristics, the care team for OPAT programmes providing “hospital at home” treatment should be multidisciplinary, and be made up of medical and nursing staff, pharmacists, auxiliary staff, as well as the patient and his/her caregivers (**A-III**).
- The essential factor for ensuring the success of an OPAT programme is appropriate patient selection (**A-III**).
- For OPAT to be safe and effective, the patient must be clinically and hemodynamically stable and comply with the general and specific criteria for inclusion in an OPAT programme (**A-III**).
- High et al. summarize the questions involved in assessing patients suitable for outpatient parenteral antimicrobial therapy (**A-III**).

Modes of antimicrobial delivery in OPAT and venous access. Complications of venous access

Recommendations:

- One of the key elements in the success of OPAT lies in the correct selection of the mode of administration, as well as type of venous access, depending on the antibiotic to be administered,

length of treatment and the characteristics and skills of the patient/caregiver (A-III).

- Self-administration of OPAT has been shown to be safe and effective, and makes it easier to combine two or more antibiotics at the same time (A-II).
- If the antibiotic remains stable for several days at temperatures between 2 and 8°C, several doses can be prepared in advance and stored in the refrigerator. In such cases, it is advisable to prepare infusion devices in a laminar airflow cabinet to ensure microbiological stability after dilution (A-III).
- Proper selection of intravenous access is key to the success of OPAT and will depend on the characteristics of the drug infusion, number of doses daily, duration of treatment and the characteristics of the patient (A-III).
- Peripheral venous catheters (PVC), both short and midline, are not recommended for administration of vesicant drugs or those with osmolarity of >500–600 mOsm and/or pH <5 or >9 (A-III).
- Short PVCs are recommended when OPAT is expected to last less than 7 days (B-III).
- Midline PVCs are recommended in OPAT for treatments of between 7 and 14 days (B-III).
- Central venous catheters (both the peripherally inserted central catheter (PICC) and the centrally inserted CVC) are recommended for administration of vesicant treatment or those with osmolarity of >500–600 mOsm and/or pH <5 or >9 (A-III).
- PICCs are recommended when OPAT is expected to last more than 15 days (B-III).
- It is recommended not to use PICCs for patients with stage 3b chronic kidney disease (glomerular filtration rate <45 ml/min) and who may be possible candidates for haemodialysis (A-II).
- Likewise, it is recommended not to use the subclavian approach for patients with stage 3b chronic kidney disease (glomerular filtration rate <45 ml/min) and who may be possible candidates for haemodialysis (A-I).
- It is recommended that clinical criteria be used to determine replacement of short peripheral venous catheters or for it to be scheduled every 72–96 h to reduce the rate of infection and phlebitis (B-I).
- For other catheters, including the midline, replacements are only advised in accordance with clinical criteria (A-III).
- Catheter-related complications in OPAT are similar to those reported in hospital cases and occasionally require patient readmission (A-III).

Pharmacokinetic and pharmacodynamic properties and stability of drugs administered in OPAT. Criteria for antimicrobial selection. Simultaneous delivery of antimicrobial combinations in OPAT

Recommendations:

- The pharmacokinetic and pharmacodynamic properties of the infusion drug in an OPAT program will determine the mode of infusion (manual or mechanical) and choice of vascular access (B-II).
- If the antimicrobial is not going to be administered immediately, preparation of the dilution in a laminar flow hood is recommended (B-II).
- Self-administration of parenteral antibiotics by the patient or with the assistance of a caregiver is a safe and efficient method of administering more complex forms of OPAT (multiple doses and multiple antibiotics) (B-II).
- Electronic infusion pumps are useful devices for administering antimicrobials in multiple doses (B-II).

Monitoring of patients in OPAT. Pharmacological interventions. Adverse effects. Managing complications in OPAT

Recommendations:

- Side effects are relatively frequent in OPAT and may require the patient to be readmitted to hospital, so that the pathways for detection of complications and ensuring a rapid response by professionals should be clear and prompt, with protocols in place (B-II).
- Monitoring should be individualized according to the clinical profile of the patient, the care environment, the characteristics of the drug and route of drug delivery (A-III).
- All outpatient parenteral antibiotic therapy should follow the guidelines and recommendations of the relevant medical societies, include appropriate clinical and analytical surveillance, and should be accurately recorded in the documentation for the episode (A-II).
- The professionals involved must be familiar with the potential drug interactions of OPAT, since they can lead to an increase or decrease in drug concentrations, influence the effectiveness of the drugs in interaction (by raising them or lowering them) and/or the severity of side effects (A-II).
- Monitoring for foreseeable adverse drug reactions is recommended: for example, close monitoring of trough gentamicin levels to prevent nephrotoxicity, or of creatinine-phosphokinase (CPK) levels when daptomycin is used to reduce the risk of severe rhabdomyolysis (A-II).
- Professionals in OPAT teams must be provided with the treatment necessary to deal with potentially serious adverse drug reactions in the home setting in accordance with the known risk (corticosteroids in beta-lactams, anticonvulsants with carbapenems, among others) (A-III).
- It is advisable to carry out analytical controls once a week, including a blood count (haemogram) and tests of liver and kidney function (B-II).

Considerations for paediatric patients in OPAT

Recommendations:

- OPAT in paediatrics provides a better quality of life and greater satisfaction for the patients and their families (A-I).
- OPAT in paediatrics is safe and effective in previously selected patients (B-II).
- For paediatric patients, the choice of antimicrobials in OPAT should follow the same criteria (pharmacokinetics, efficacy and safety) as for adult patients (B-II).
- Short peripheral venous catheters are recommended when the expected duration of the OPAT is less than 7 days (B-III).
- Midline peripheral venous catheters are recommended for OPAT of between 7 and 14 days (B-III).
- Peripheral venous catheters are recommended when the expected duration of the OPAT is more than 15 days (B-III).
- Although nursing personnel normally administer the antimicrobial, with appropriate training, this can also be safely and efficiently carried out by the patient's caregivers (C-III).

OPAT programmes and programmes for optimizing the use of antibiotics (PROA): a necessary relationship

Recommendations:

- It is recommended that one of the members of the OPAT team should be a member of the hospital's programme for the optimization of antibiotic use (PROA) (C-III).
- It is recommended that the selection and use of antibiotics for OPAT programmes should fit in with the reference PROA guidelines (C-III).
- An OPAT facilitates optimization of antimicrobial use in empiric situations when it is neither possible nor desirable to use the

oral route, or in targeted therapies when alternative effective therapies are not available (**B-II**).

- For sequential therapy, OPAT should follow the criteria used in the PROA (**B-II**).
- The total duration of treatment should be planned on the basis of available evidence (**A-I**), with evaluation and control measures in place to ensure that it is carried out (**C-III**).

Evidence of the efficacy and safety of OPAT in urinary infection:
Recommendations:

- The antimicrobial treatment regimens for urinary infections as well as their duration under OPAT should be the same as for patients receiving conventional hospital treatment (**C-III**).
- Ertapenem has been shown to be a cost effective option for patients under OPAT with UTIs due to extended-spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae (**B-III**).

Evidence of the efficacy and safety of OPAT in skin and soft tissue infections (SSTIs):

Recommendations:

- The antimicrobial treatment regimens for skin and soft tissue infections as well as their duration under OPAT should be the same as for conventional hospital patients (**C-III**).
- It is feasible to managed patients with moderate and severe forms of skin and soft tissue infections under OPAT if the criteria of safety, effectiveness and efficiency are applied (**B-II**).
- Many patients with a diagnosis of cellulitis can be referred directly from the emergency department to OPAT after a period of observation and initiation of empiric antibiotic therapy. In patients of this kind, the presence of fever and a white blood cell count above 15,000 cells is associated with a higher rate of OPAT failure and consequently a higher rate of hospital readmission (**B-III**).
- For skin and soft tissue infections, closer clinical control is recommended for women, diabetic patients and use of teicoplanin in OPAT, since some studies have shown that these factors are independently associated with OPAT failure (**B-III**).

Evidence of the efficacy and safety of OPAT in infective endocarditis (IE):

Recommendations:

- Patients with IE who may be suitable for OPAT should be evaluated and stabilized previously in hospital (**C-I**).
- Patients should be at low risk for complications, the most frequent of which are development of congestive heart failure or systemic embolism (**C-I**).
- They should therefore have successfully completed at least two weeks of appropriate treatment in hospital care (7–10 days in the case of *Streptococcus viridans*) with clinical and haemodynamic stability and negative blood cultures (**B-II**).
- For forms of endocarditis different from the previous one, the decision as to whether the patient can be referred to an OPAT programme should always be taken in consultation with the patient's surgical and medical team (**C-III**).
- Duration of antibiotic treatment in OPAT will be the same as for hospital patients (**B-II**).
- For treatment of endocarditis due to *S. viridans* in OPAT, ceftriaxone is recommended (**A-I**).
- For endocarditis due to methicillin-susceptible *Staphylococcus aureus*, cloxacillin is recommended whenever possible (**C-III**).
- Patients with IE due to MRSA or *Enterococcus* spp. are not likely to satisfy the criteria for OPAT and in such cases, their inclusion in an OPAT programme will depend on the experience of the team

and the decision to do so should always be taken in consensus (**C-III**).

Evidence of the efficacy and safety of OPAT in respiratory infections and pneumonia

Recommendations:

- OPAT is safe and effective for the treatment of respiratory infections (**B-II**).
- The antimicrobial treatment regimens for respiratory infections should be the same as for conventional hospital patients, including antipseudomonal antibiotics (**C-III**).
- There are no differences with respect to safety and effectiveness in the treatment of respiratory infections under OPAT: acute exacerbations of COPD, community-acquired pneumonia, cystic fibrosis and non-CF bronchiectasis (**B-II**).
- There is scant evidence on respiratory infections involving lung abscess and pleural empyema treated in OPAT (**C-III**).
- Duration of OPAT in respiratory infections will be the same as prescribed for conventional hospital patients (**B-II**).
- OPAT for respiratory infections due to *Pseudomonas aeruginosa*, including multidrug-resistant strains, is safe and effective (**B-II**).
- Chronic respiratory patients should continue with essential respiratory therapies at home (oxygen therapy, aerosol therapy, home non-invasive ventilation) as well as other standard treatments for respiratory exacerbations, such as oral or intravenous corticosteroids (**A-I**).

Evidence of the efficacy and safety of OPAT in intra-abdominal infections, intra-abdominal abscesses and biliary tract infections

Recommendations:

- Any intra-abdominal infection can be treated in OPAT if the healthcare-associated requirements provided for this care model are followed (**C-III**).
- Most intra-abdominal infections require a previous period of treatment in hospital before OPAT can be considered. Only uncomplicated diverticulitis can be treated directly in the emergency department (**B-III**).
- The antimicrobial treatment guidelines for intra-abdominal infections as well as their duration under OPAT, should be the same as for conventional hospital patients (**C-III**).

Evidence of the efficacy and safety of OPAT in bone and joint infection:

Recommendations:

- The treatment of bone and joint infections occasionally requires a combination of surgery and antibiotic therapy (**A-II**).
- Parenteral therapy followed by oral antibiotics is as effective as long-term parenteral therapy (**B-III**).
- Close coordination between the orthopaedics and infectious diseases departments is advisable (**B-III**).
- The antimicrobial treatment regimens for bone and joint infections as well as their duration under OPAT should be the same as for patients under conventional hospital care (**C-III**).
- When performed properly, OPAT is more comfortable for the patient, reduces the risk of nosocomial infections and is also cost-effective for the health system (**B-III**).

Evidence of the efficacy and safety of OPAT for infections of the central nervous system:

Recommendations:

- Infections of the central nervous system can be safely treated in the patient's home, so that treatment of some cases of bacterial

meningitis, herpes meningoencephalitis or brain abscesses can be completed in OPAT without further risk of complications than in conventional hospital care, with good clinical results (**C-III**).

- The antimicrobial treatment regimens for infections of the central nervous system as well as their duration under OPAT should be as for conventional hospital patients (**C-III**).

Evidence of the efficacy and safety of OPAT for infections in patients with febrile neutropenia

Recommendations:

- OPAT for patients with neutropenia is safe, effective and efficient, even for paediatric patients (**B-III**).
- OPAT for patients with febrile neutropenia improves the quality-of-life parameters with respect to those receiving conventional hospital care (**B-II**).
- The antimicrobial treatment regimens for febrile neutropenia as well as their duration under OPAT should be the same as for patients receiving conventional hospital treatment (**C-III**).

Evidence of the efficacy and safety of OPAT in infections due to multidrug-resistant bacteria

Recommendations:

- There is evidence that OPAT is safe and effective for infections due to multidrug-resistant bacteria (**A-II**).
- The antimicrobial treatment regimens for infections due to multidrug-resistant bacteria as well as their duration under OPAT should be the same as for conventional hospital care (**C-III**).
- During the period of treatment, the standard hygiene measures associated with control and prevention of microorganisms should be respected, with hand hygiene being the basis of measures to be adopted in the home (**A-II**).
- In light of the lack of stability of meropenem at room temperature, intravenous meropenem therapy in the home setting requires the willing participation of the patient or caregiver, as well as manual dexterity in handling ambulatory infusion devices (**A-II**).
- Daptomycin is an ideal option for OPAT as an alternative to vancomycin, because it can be administered once daily, plasma levels do not need to be monitored, and it carries a lower rate of adverse effects than vancomycin, principally with respect to nephrotoxicity (**B-II**).

Evidence of the efficacy and safety of OPAT in infections associated with biological therapy

Recommendations:

- Patients with infectious processes related to biological agents should satisfy the criteria for clinical and haemodynamic stability before OPAT can be performed (**B-II**).

- The antimicrobial treatment guidelines for infections associated with biological therapy as well as their duration under OPAT should be the same as for conventional hospital patients (**C-III**).
- In the case of OPAT in viral and fungal infections and those caused by opportunistic pathogens, the therapeutic recommendations found in existing guidelines should be applied (**C-III**).

Conflicts of interest

LELC has served as speaker for Merck, Sharp and Dohme, and Angellini, has received research support from Novartis, and has served as trainer for Merck, Sharp and Dohme. PRG has been a member of advisory boards and trainer for Merck, Sharp and Dohme y Roche. The rest of the authors declare no conflicts of interest.

Acknowledgements

We gratefully acknowledge the help of the following people in the preparation, revision and writing of this document: Carlos Cervera, Rafael Luque, Laura Álvarez, José Miguel Cisneros and Miguel Ángel Goenaga.

Supported by the Plan Nacional de I+D+i and Instituto de Salud Carlos III, Subdirección General de Redes y Centros de Investigación Cooperativa, Ministerio de Economía y Competitividad, Spanish Network for Research in Infectious Diseases (REIPI RD12/0015) – cofinanced by European Development Regional Fund “A way to achieve Europe” ERDF.

Appendix A.

Other REIPI/SEHAD group authors: Carmen Garde Orbaiz (Hospital Universitario Donostia), Mario García Lezcano (Hospital de Can Mises, Ibiza), Andima Basterretxea Ozamiz (Hospital Universitario Cruces, Vizcaya), María Victoria Gil Navarro (Hospital Universitario Virgen del Rocío, Sevilla), Sara Ortonobés Roig (Parc Taulí Hospital Universitari, Barcelona), Eva Llobet Barberí (Hospital Dos de Maig, Barcelona), Francisca Sánchez Martínez (Hospital del Mar, Barcelona), Manuel Mirón Rubio (Hospital Universitario de Torrejón, Madrid), and Manuel del Río Vizoso (Hospital Son Espases, Palma de Mallorca).

Appendix B. Supplementary data

Supplementary data associated with this article can be found, in the online version, at [doi:10.1016/j.eimc.2018.03.012](https://doi.org/10.1016/j.eimc.2018.03.012)