# Neuroendocrine Neoplasms Policy Recommendations

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It is undeniable that the EU has taken bold decisions in the field of cancer and rare diseases, even more so in recent years and during the Covid-19 pandemic. Member States are adapting, more or less constantly, their national strategies and plans. By 2019, almost all Member States had implemented a strategy or plan for rare diseases, with a variable status in terms of renewal. For cancer, Member States were encouraged to align their national cancer plans with ongoing initiatives, in particular the Beating Cancer plan.

The Cancer Subgroup of the Steering Group on Health Promotion, Disease Prevention and Management of Non-communicable Diseases is also conducting a baseline study to address the links between the European Beating Cancer plan and the Member State-level action plans it aims to publish in early 2022. However, the Rare 2030 Foresight Study (a two-year project completed in February 2021) highlighted the many unmet needs of people living with rare diseases and the continuing need to improve the policies, programmes and services that currently address them at European and national level.

The EU has a strong role in facilitating many of these changes, through coordination efforts and by funding infrastructure and educational improvements. However, there are gaps - particularly in rare and less common cancers - that need to be addressed now. Neuroendocrine neoplasms (NENs) are a specific group of rare cancers that have shown an exponential increase in incidence over the last 2 decades, due to their heterogeneity, NENs represent a challenge both clinically and for the healthcare system. This non-site-specific cancer often follows a non-traditional oncological pathway - showing great variety in presentation, disease behaviour, diagnostic requirements, treatment and care options. The problems inherent in this variability are exacerbated by the equivalent variety in Member States' health care infrastructure and ability to provide equitable access and care according to recommended standards of care. There are limitations in the availability of specialised training and education programmes for healthcare professionals, specific diagnostic equipment, and the availability and accessibility of recommended evidence-based treatment and care options - leading to disparities and inequalities for people with NEN.

At the policy level, in 2015, a set of recommendations on NENs were launched and endorsed by a group of MEPs at the European Parliament. With this set of updated recommendations, we review the progress and achievements made over the past seven years and call on policymakers at EU and Member State level to help all countries move up the ladder by following the priorities in this recommendations document - which are relevant for all countries, from those where diagnosis remains a pressing challenge, to those facing an increasing need to make referrals and multidisciplinary care in centres of excellence sustainable. Many advancements in this field since 2015 have been driven by work from the European Neuroendocrine Tumor Society (ENETS) and much of the work of ENETS is referenced through this document including the development of guidelines and standards of care as well as educational programmes and more. Patient advocates have also made major contributions in supporting NEN patients and advocating for their needs across Europe, under the umbrella of the International Neuroendocrine Cancer Alliance (INCA).


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This recommendations paper has been edited by RPP Group with the financial support from Advanced Accelerator Applications for meeting costs, development, design and printing of this document. The contents of the recommendations are based on desk research and stakeholder interviews. We would like to express our thanks to the aforementioned authors who have reviewed and provided guidance and input on the drafting of this document. This document is intended to provide guidance to policy makers, healthcare professionals and patients in strengthening the efforts to improve care for patients with neuroendocrine neoplasms.


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# I. Foreword

Rare cancers share many of the same challenges. However, given their biological, age-related, and organisational specificities, and diversities, they must be addressed separately and specifically[1]. Against this background, neuroendocrine neoplasms (NENs) represent a clinical challenge due to heterogeneity in their diagnosis, different natural histories, and care options[2], and Europe finds itself with vast inequalities in the set-up and delivery of care for patients.

NENs require strong legislative support from both cancer and rare diseases policy frameworks to overcome the persistent challenges for patients. In this sense, the European Union has taken strong steps to tackle cancer in recent years. Likewise, the policies to improve the diagnosis and treatment of people with rare diseases have steadily grown in their impact. NENs must be well represented in the policies covering rare diseases, rare cancers and broader cancers as the issues affecting the care for NEN patients are wide and multifaceted. The policy actions of the EU and its Member States have a major impact on the care of people with NENs and we must strive for a coherent policy across all levels that tackles these multifaceted issues. The data for good policymaking in this space is available. Thanks to the work of the European Neuroendocrine Tumor Society (ENETS), standards of care[3,4,5,6,7,8,9,10,11,12] and consensus guidelines[13,14,15,16,17,18,19,20] have been developed and continue to be reviewed to ensure decision making in the management of NEN patients.

With a prevalence of 5.1 million rare cancer patients in Europe, representing almost 25% of all cancer cases, rare cancers are a major public health issue[21]. For this reason, rare cancers, under the umbrella of rare diseases, are considered a priority of the European Commission. In the Communication on Rare Diseases: Europe Challenges from 2008, the European Commission stressed how the lack of specific health policies for rare diseases and the scarcity of expertise translates into delayed diagnosis and difficult access to care[22]. Initiatives and policies to support research, diagnosis and treatment of rare diseases and rare cancers have been periodically featured in the EU policy agenda over the last two decades. On the legislative level, the Orphan Medicinal Products Regulation[23] delivered a set of incentives to encourage research, development, and marketing of medicines to treat, prevent or diagnose rare diseases. Ten years later, the Council of the European Union adopted its recommendations on action in the field of rare diseases[24], encouraging EU Member States to adopt national strategies or plans for rare diseases. The Commission also sought to encourage collaboration across Member States through the Directive on the application of patients' rights in cross-border healthcare[25]. The Directive contains specific directions on how to foster collaboration in the field of rare diseases (art. 13) and especially calls for the creation of European Reference Networks (ERNs), a cornerstone in the EU cooperation on rare diseases. ERNs were created to incentivise cooperation for highly specialised healthcare and improve research, and the delivery of high-quality, accessible and cost-effective healthcare, with a special focus also on rare diseases. The formal activation of ERNs represented a cornerstone in the EU cooperation on rare cancers. While bringing together 10 different groups of rare neoplastic diseases, the ERN dedicated to rare adult solid cancers, EURACAN, identified NEN as one of the specific domains of this ERN, with specificities in presentations and management, already investigated and constructed in the past decades with the ENETS. The degree of development of each domain is substantially different in this ERN. The role of EURACAN in this context is to provide transversal support for all domains, and specific help for less mature domains, acting as the bricks and mortar with considerable differences in nature. In the case of NENs, it built upon the accreditation of Centres of Excellence, already established since 2009 by ENETS.

Groups such as Rare Cancers Europe (RCE) have been urging policy prioritisation for Rare Cancers for more than a decade, having identified several common challenges for rare cancer patients which are highly relevant to the NEN community. RCE focuses on improving the methodology of clinical studies and regulatory practices, improving the organisation of healthcare, improving access to treatments and standard of care, and improving the education of Health Care Professionals (HCPs). Addressing these 4 issues are fundamental for the improvement of access to quality care for NEN patients[26].

Among the most recent initiatives, the European Commission launched in November 2020 the "Pharmaceutical Strategy for Europe", which aims to create a future proof regulatory framework and support the industry in promoting research and technologies, addressing unmet medical needs in rare areas diseases. Europe's Beating Cancer Plan was also launched in 2021 but, unfortunately, the Plan modestly covers rare forms of cancer. To support these initiatives, in 2021 the European Commission also launched the EU4Health Programme, which will provide funding to eligible entities, health organisations and NGOs to invest in urgent health priorities, including Europe's Beating Cancer Plan, the Pharmaceutical Strategy for Europe and the expansion of successful initiatives like the European Reference Networks (ERNs) for rare diseases. The financial support to ERNs has also been significantly increased



## KEY POLICY INITIATIVES

| 2008 | 2009 | 2011 | 2015 |
|---|---|---|---|
| Communication on Rare Diseases: Europe's Challenges | Council Recommendation on an action in the field of rare diseases | Entry into force of Directive 2011/24 on patients' rights in cross-border healthcare | **Policy Recommendations on Neuroendocrine Tumours** |
| **2017** | **2020** | | **2021** |
| Establishment of the European Reference Networks (ERNs) | Launch of the Pharmaceutical Strategy for Europe<br>• Proposal for Revision of Regulation 141/2000 on Orphan Medicinal Products → foreseen Q4 2022<br>• Proposal for Revision of the EU general pharmaceuticals legislation → foreseen Q4 2022 | Launch of Horizon2020 Mission on Cancer | Launch of Europe's Beating Cancer Plan |
| **2021** | | | **2022** |
| Launch of EU4Health Programme | Publication of Rare 2030 Foresight Study | Evaluation of Cross-border healthcare Directive – evaluation of patients' rights | Launch of European Health Data Space |

by the European Commission.

The EU has taken bold decisions, even more in the past years and during the Covid-19 pandemic, and Member States are adapting, more or less steadily, their national strategies and plans in the field of cancer and rare diseases. By 2019, almost all Member States had implemented a Rare Disease strategy or plan, with varying statuses regarding renewal[27]. Also on cancer, Member States have been encouraged to align their national cancer plans with current initiatives, notably the Beating Cancer Plan, as well as the priorities defined b y Mission Cancer Europe. The Subgroup on Cancer of the Steering Group on Health Promotion, Disease Prevention and Management of Non-Communicable Diseases[28] is carrying out a background study to address the linkages between Europe's Beating Cancer Plan and Member States' level action plans.

Nonetheless, the Rare 2030 Foresight Study[29] (a two-year project that ended in February 2021) highlighted the many unmet needs of people living with rare diseases and the continuing need to improve policies, programmes and services that currently address them at EU and national levels. This is noted very clearly in the NEN field where many unmet challenges still exist, and the inequalities across Europe are wide[30].

The EU has a strong role in facilitating many of these changes, through coordination efforts as well as through funding for infrastructure and education improvements. We are calling on European policymakers, at EU and Member State level, to help level up all countries, by following the priorities in this recommendations paper which are relevant for all countries – from those where an increased and faster diagnosis of quality remains a pressing challenge, to those who face a growing need to make referrals and multi-disciplinary care sustainable in centres of excellence.

# II. Executive summary: Neuroendocrine Neoplasms: a patient pathway needing all of Europe´s policy tools

Neuroendocrine Neoplasms (NENs) is a term used to describe cancers that start in neuroendocrine cells and non-neuroendocrine organs[31]. The neuroendocrine cells produce hormones that may be released into the bloodstream. Neuroendocrine cells are distributed throughout the body, and as such, neuroendocrine neoplasms (NENs)[32] can originate in most organs. The classification and nomenclature of NENs have always been complex because classifications have always focused on tumours arising in a specific

organ system[33]. The system of classification and terminology of neuroendocrine neoplasms was updated in 2017 by the American Joint Committee on Cancer (AJCC), in 2022 by the World Health Organisation (WHO), and it is now recommended for general use[34]. However, unlike with sarcomas, there is no unique nomenclature and classification system that is suitable for all NENs, regardless of origin.[35]. Therefore, the development of a common NEN classification for all organs would be desirable[36,37].

At the policy level, in 2015, a set of recommendations on NENs were launched and endorsed by a group of MEPs at the European Parliament[38]. For NEN[39] patients, the management of the disease varies considerably, even though the incidence of NETs has been rising worldwide, potentially leaving many with suboptimal care[40]. Diagnosis is a major hurdle for NETs as symptoms may resemble those of other more common diseases. This results in late diagnosis, with a median time from symptom to diagnosis being around 4.5 years[41], and with 60-80% of patients diagnosed at an advanced stage[42]. Once diagnosed, effective care requires a multi-disciplinary team to review the case and create a treatment plan. Treatment availability may not be equal across the EU and as such may further delay the care for people once diagnosed.

### Since 2015, there are many changes in the NET area worth noting:

1. There is a demonstrable increase of GEP-NET incidence over the past two decades; however, this may be a consequence of the improved classifications and increased awareness of the disease, and in general better diagnostic methods[44].
2. The expansion of centres of excellence accredited by the European Neuroendocrine Tumor Society (ENETS) has meant that more countries have an excellence centre to manage patient care
3. The establishment of the European Reference Networks has developed a Network “EURACAN” which brings together expertise on rare adult solid cancers and holds a Domain on Rare Cancers of the Neuroendocrine System
4. Improving care and treatment options are extending survival rates, now indicating that NENs have a significantly higher prevalence than gastric, pancreatic, oesophageal or hepatobiliary adenocarcinomas[45]
5. Treatment options have also improved for NET patients and include Somatostatin Analogs (SSAs) and Molecular targeted agents[46]. Furthermore, a major advance in the last decade has been the use of Peptide Receptor Radionuclide Therapy (PRRT) with lutetium(177Lu) oxodotreotide (hereinafter 177Lu-DOTATATE), licensed for use in gastroenteropancreatic NETs. However, not all options are available for all types of NEN. Chemotherapy also remains a treatment option for some advanced or less differentiated NENs[47].
6. Significant growth of NEN advocacy globally focusing on the unmet needs of the global community across issues such as access, influence, mental and physical health[48].

Despite these advances and the progress on many recommendations issued in 2015, diagnosis and treatment issues persist in the NET community. As such, we must reflect on the recommendations of 2015, and identify those where progress has been made, those where more needs to be done, and what new recommendations must be at the heart of new policy decisions.

Recently, a new term has been proposed and is now used recurrently: Neuroendocrine Neoplasm. Neuroendocrine Neoplasm, or NEN, was introduced as a new umbrella term to help clarify the differences between all abnormal growths of the neuroendocrine system (benign or malignant). This term, therefore, serves to help distinguish between the two specific types of neuroendocrine (malignant) cancer: the well differentiated NET, and poorly differentiated NEC, as indicated in the WHO 2022 classification[49]. In a broader sense, sometimes paragangliomas are also included in the term NEN. NEN may also include non-cancerous abnormalities of neuroendocrine cells[50]. In recognition of these recent developments in the terminology, the recommendations developed in this document will consider the broader concept of **Neuroendocrine Neoplasm (NEN).**



## COMPARATIVE TABLE:
## What has been achieved after the 2015 Policy Recommendations on NENs

| 2015 Recommendation | Status |
|---|---|
| Member States should support the NET community in its effort to educate healthcare professionals and foster knowledge-sharing on NETs regarding symptoms and diagnosis methods. | Ongoing. Needs actions policies at Member State level |
| Member States that do not have a focused policy on NETs should consult specialists and utilise recommendations for best practices drafted by those specialists, based on their experience. | Not advanced in many countries |
| The NET community should work collaboratively on knowledge & diagnosis to identify recommendations for the European Union such as on hurdles to access to appropriate diagnosis and awareness-raising on NETs. | ENETS, INCA, and other organisations have continued to offer evidence-based recommendations – but these need further integration into ongoing cancer policy prioritization (example Study on Unmet Needs in Functional and Non-functional Neuroendocrine Neoplasms”[51] |
| European Reference Network covering NETs, as a more formal step for currently existing national networks, would be beneficial and it is important that any future European Reference Network take into consideration the views of experts in this field and rely on already existing networks. | Achieved – ERN EURACAN includes a workstream on Rare Cancers of the Neuroendocrine system. |
| Considerable variation exists across Europe in the care pathway for NETs and best practices from different Member States must be identified and disseminated, for example through EU initiatives such as CANCON. | Major area of increased need. Inequalities across Member States in the care pathway is drastic[52]. |
| Member States should improve access to specialist care effectively including surgeons, physicians and nurses. Standards of care developed by ENETS and national networks or centres of expertise should be utilised to fight inequalities in the treatment of NETs in Europe. | ENETS have expanded the accreditation of centres of excel-lence, but more is needed to level-up centres in central and Eastern Europe. |
| Member States should support a multidisciplinary treatment approach for NET patients by including all relevant experts across disciplines to identify appropriate treatment | Huge variation in the effective referral to MDTs across Europe. |
| Governments and healthcare providers must proactively consult NET patients and medical experts on NETs when elaborating policies affecting NET patients. | So far, the EU policies on cancer have not well addressed rare cancers, nor the specifics of NENs. |
| The NET community should work collaboratively on the topic of patient journey to identify recommendations for the European Union | Patient journey largely depends on the availability of diagnostic and therapeutic options of each center |
| Member States should ensure appropriate incentives to support the development of additional treatment options. | New licensed treatments have come to the market, thanks to the existence of the Orphan Medicinal Products Regulation and incentives. Newer radiopharmaceuticals that have been licensed do not have clear regulatory pathways which may hamper future innovations uptake across countries. |
| The NET community should work collaboratively on research & innovation to identify recommendations for the European Union such as on an assessment of opportunities for support to research for NETs under Horizon 2020 and research funding programs | Project MESI-NET was funded under the Horizon 2020 pro-gramme. The assessment of new funding opportunities must continue to take place under Horizon Europe[53]. |

Unfortunately, despite advances in several of the areas above, many issues remain – and new challenges have emerged for the patient community. As such, this paper will highlight the need to focus on several policy areas required to improve the level of NEN care in Europe. These include:

### Diagnosis and care referral

a. The implementation of good diagnostic practices across the EU and care referral remains unequal across the Union. This should be tackled primarily at national level, with EU best practices to encourage local NEN prioritisation

b. The certification within Member States of NEN excellence centres, either as standalone or integrated into comprehensive cancer centres

c. The development of a sustainable model to support and reimburse multi-disciplinary care. With the increasing specialisation of centres around NENs, Multidisciplinary teams have been called on to volunteer time to tumour boards, which is an unsustainable practice

d. Increasing local human infrastructure and resources to manage MDTs from national healthcare systems

### Improving treatment and care

a. Reducing the current barriers to treatment in many countries including through promoting cross-speciality education, support for infrastructure, needs for diagnostics and new therapies, reduction of regulatory barriers for new therapies

b. Creating a framework of supportive care for NENs, including oncology nurses and clinical pharmacists in decision making.

Based on these focus areas, this paper identifies several key recommendations for European and national decision-makers to help improve the care of NEN patients. The recommendations are contained within the text, contextualised by the challenges they look to resolve, but a summary of all the recommendations can be found here below.

# III. Recommendations

## POLICY ADAPTATION AND ADOPTION

### RECOMMENDATION 01

The European Union should revise the policy framework on rare diseases to align it with the current unmet needs of patients suffering from these diseases. Taking into account the results of the evaluation of the cross-border healthcare directive, the evaluation of the third health programme and the results of the RARE 2030 pilot project, the Commission should consider revising the policy framework on rare diseases in 2023[54]. The European Union should promote access to different care pathways in less advanced regions, improve infrastructure and preparedness of healthcare systems in general, and at the same time Promote alternative, less costly solutions to provide more flexibility across borders for patients, e.g. through the Cross-Border Healthcare Directive. In the light of the current evaluation of the Directive on patients' rights in cross-border healthcare (2011/24/EU), the European Union should take into consideration the different status of rare diseases and discuss with Member States the possibility of creating alternative pathways for obtaining and reimbursing treatments related to rare diseases.



### RECOMMENDATION 10

Within the foreseen EU flagship programme establishing dedicated Comprehensive Cancer Centres in every Member States, specific needs of rare cancers and NENs must be well recognised. These centres should also be a flagship for a new, more sustainable, care referral with appropriate remuneration for referral. For dissemination, these centres should also be included in the EURACAN location map and similar lists of expert centres.

### RECOMMENDATION 11

National bodies should look to support in a greater way expert centres, aligned with the policy to refer all patients to sufficiently high-volume centres. Financial resources must be dedicated to high-performance centres where quality of patient care is truly valued (on the basis of equal performance indicators, for which guidelines would be welcomed).

### RECOMMENDATION 16

Streamline regulatory procedures for rare cancer therapies and involve patients in all decision making to ensure patient-relevant outcomes drive decision making around treatment availability.

## INFRASTRUCTURES AND EQUIPMENT

### RECOMMENDATION 02

Deployment and better promotion of funding opportunities for Member States to invest in PET/CT/MRI machines and hospital infrastructure, including European funding opportunities from the EU4Health Programme, European Regional Development Funds, as well as the Cohesion Fund.

### RECOMMENDATION 07

Based on the recognized standards established in the ENETS accreditation, national health systems should set up mandatory care referrals for patients to centres with either 1) accreditation by ENETS, or 2) which see a sufficient volume of patients in one year to be considered as holding relevant expertise.

### RECOMMENDATION 08

If it is not possible to offer patients treatments at an ENETS accredited centre within a Member State, patients should be referred to specialist care - this could be an ENETS accredited CoE, Comprehensive Cancer Centre or High-volume institution. The institution needs to have the infrastructure and collaborative links to provide gold standard care. It should also be facilitated/reimbursed a pathway for patients to receive diagnosis in an expert centre abroad – using European mechanisms available (e.g.: CBHC with a reimbursement system put in place).

### RECOMMENDATION 15

Deploy EU funding mechanisms to support upscaling of infrastructure for the treatment of NETs patients through investments in radioprotection rooms, waste disposal and storage facilities.

## ACCESS, REFERRAL, DIAGNOSTICS & TREATMENTS

### RECOMMENDATION 3

Clear national or international pathway for NEN patients should be established so that all patients have reliable access to a consistent standard of care in each EU region. The Beating Cancer Plan proposes tools for the expert exchange of knowledge, such as the new EU Networks of expertise on cancer. The development of referral pathways could be prioritised and tackled at EU level in rare disease action plans as well as supported through data and knowledge exchange initiatives. With many national and global advocacy organisations taking on this work, collaboration between these groups to leverage relationships and data pools is crucial. At the same time, these priorities should be reflected at national level, where NENs should be promoted in national cancer plans and national rare disease plans. In order to do so, these recommendations aim to provide a reference point for Member States and governments in order to 1) analyse the current state of the art and 2) enable them to determine where to start to improve the state of care.

### RECOMMENDATION 04

Provide (and, if not available, develop) a set of written materials to NEN patients at the time of consultation and refer patients to local organisations and patient associations that can provide further information and support. Consider the role of ERNs to increment dissemination of informative material.

### RECOMMENDATION 05

Sustainable care referral system in Europe should take into consideration the key role of multidisciplinary teams to improve patients' outcome and more efficient diagnosis and treatment.

### RECOMMENDATION 06

Based on the specific needs of each Member State (population, incidence, distance among centres, number of patients, etc.), each Member State should identify, with the support of specialised organisations or institutions, how many centres of excellence each country should have.

### RECOMMENDATION 09

The EU should look to develop a model for the incorporation of expert care into national healthcare system tariffs. Member States must open a dialogue on reimbursing expert care and, where relevant to the local healthcare system, begin a discussion with insurers and hospital managers on how to appropriately value this expert care, given the demonstrable impact on patient outcomes that this referral has. Dialogue within European and national institutional fora on reimbursement policies should cover how to integrate the remuneration of MDTs, which is globally recognised as an integral part of optimal care for these (and other) diseases.



## WORKFORCE, EDUCATION & TRAINING

### RECOMMENDATION 12

Initiate the creation of established protocols for the follow-up through research and data collection activities, promoted through initiatives such as the Knowledge Centre on Cancer, the European Health Data Space or the European Cancer Information System. At the same time, strengthen telemedicine and remote monitoring and consultation systems. Towards this objective, funding opportunities under the EU4Health and Digital Europe Programmes should be considered. Call will be opened between 2021 and 2023 as foreseen in the Beating Cancer Plan to reduce health inequalities.

### RECOMMENDATION 13

Encourage the adoption, dissemination and regular adaptation of relevant guidelines according to needs (as other rare cancer guidelines) through sharing in professional networks, including in relevant educational platforms and profiling in national congresses. Benchmark the adherence to these guidelines when considering new tools, such as the proposed European Cancer Dashboard[55].

### RECOMMENDATION 14

Ensure a clear focus on the research needs of rare cancers such as NENs, and that all policies are driven towards stimulating new treatments for patients.

### RECOMMENDATION 17

Deploy training programmes foreseen in Europe´s Beating Cancer Plan and the SAMIRA initiative to improve education around NENs in Europe and reach homogenous high-quality management of NEN for all European countries – with priority on those countries with basic need for improved HCP training.

### RECOMMENDATION 18

Support the educational and professional needs of specialist nurses given the fundamental role they play in improving supportive care for patients. This should include, but not be limited to, providing legal recognition to more cancer specialists to elevate the role of cancer nurses and aligning the remuneration foreseen with the high standards of training.

### RECOMMENDATION 19

Ensure that within the framework of National Comprehensive Cancer Centres there is a clear focus on supportive care, empowered by specialist nurses and a patient-involved MDT.

# IV. Introduction – the NEN landscape and rare diseases in the EU

NENs are rare cancers that, by definition, affect fewer than 6 out of 100,000 members of the general population. Data shows an increasing tendency over the past years[56], however, due to their low incidence and limited opportunities for experience in large volumes of patients. However, as explained above, NENs can originate in most organs. This should be kept in mind because it can make its classification complex and also affects incidence data[57]

The 'Surveillance of Rare Cancers in Europe' (RARECARE) project has been one of the few major projects to provide a population-based database (including patients diagnosed from 1978 to 2002 and registered in 76 population-based cancer registries), delivering a unique overview of the burden of NETs in Europe by incidence, and survival[58]. Like many other rare cancers, NENs are characterised by major challenges in diagnosis, challenges related to access to treatment, as well as care and treatment referral. In the early 2000s, important progress was made with the development of a new World Health Organisation (WHO) morphological classification for predicting the biological behaviour of the tumour. Subsequently, a TNM (Tumour-Node and Metastases) classification and the ENETS classification system became available[59]. Now, as mentioned above, the system of classification and terminology of neuroendocrine neoplasms recommended for general use is the 2022 WHO classification[60]. In general, the rarity of these neoplasms, the way they present throughout the body and the variability, are all factors responsible for the delays in diagnosis, which occur frequently. In the case of NETs, an average delay of 52 months (roughly 4.5 years) has been reported in patients between first symptoms and diagnosis, and it is quite common for patients to be examined by several physicians before receiving the correct diagnosis[61]. Although correct and rapid diagnosis has been challenging due to their heterogeneous pathology, recent advances in their histopathological characterisation are allowing diagnosis to become timely and more accurate– which may also be the reason behind their increasing incidence[62].

A range of therapies with different profiles is available for NEN patients[63] and an expert multidisciplinary meeting to guide management decisions remains paramount[64]. The treatment of neuroendocrine neoplasms, in general, and especially those of lung origin, continues to evolve. Surgical resection is the mainstay of treatment, but several options have been investigated in the treatment of NETs of various origins that may potentially play a role in the treatment of these tumours, namely: Somatostatin analogues (SSA), Chemotherapy, Targeted therapy, Immunotherapy and Peptide receptor radionuclide therapy (PRRT – also known as radioligand therapy or RLT), and palliative care[65].

Studies have highlighted a number of unmet needs and ongoing challenges[66]. Compared to other cancers, the experience of NEN patients is markedly different. Limited understanding of the pathogenesis of NENs hinders further development. Finding the right treatment sequence may also be complex due to the variability of individual patient disease progression and the lack of studies demonstrating an optimal procedure[67]. In this context of limited evidence, the contribution of MDTs of reference centres is crucial. NEN care faces another fundamental challenge in Europe, that it has advanced much more rapidly in some countries than in others. While there are pressing challenges to manage, for example, the sustainable care referral system in major hospitals in Western Europe, in Central and Eastern Europe there remain considerable issues with the set-up of diagnosis, the application of medical guidelines, the education of healthcare professionals, and a process of referral to expert centres[68]. As such, we see a "two-paced" system in Europe where challenges are being tackled on very different levels, which may make it difficult to address the issues in a holistic manner.

As such, the authors of this paper have developed a table (Figure 1.0) to highlight priorities at Member State and European level for countries based on the current development of NEN care. Without addressing priority 1 topics, it does not make sense to try to implement priority 3 topics. This table also facilitates a clear demarcation for national and European policy-makers of where prioritisation and resources are most needed. There is no designation of countries by phase, but rather the authors of this paper encourage the NEN community to identify the current development in their countries, and in an iterative way advocate for the below changes at local level, in order to build toward a gold standard of policy set up for NEN care.

| | Level 1 Priorities | Level 2 Priorities | Level 3 Priorities |
|---|---|---|---|
| Member State level | Policy prioritisation of NENs, in the form of rare disease or rare cancer plans | ENETS accreditated centre of excellence | Effective financing of MDTs and tumour boards |
| | Initiating the implementation of standard diagnostic procedures to ensure more efficient disease management protocols | Effective multi-disciplinary care team set up | Mandatory referral to designated expert centres |
| | Implementation/application of international guidelines to national level | Infrastructure development to accommodate new treatment modalities | Funding for procedures in Expert settings based on quality of healthcare not quantity of procedures |
| | Referral guidelines set up to ensure treatment in expert centres (hub-and-spoke models to ensure patients are referred to experts | Nationally resourced expert centres | |
| | Cross-speciality education programmes to have specialised physicians in each country - not too far away to reach for patients | Creation of established protocols as well as strengthening telemedicine and remote consultations for follow up care | |
| | Assessment of needs for expert centres | | |
| European level | Improved functioning of the Cross Border Healthcare Directive to allow patient mobility | Administrative support for ERNs | Facilitate exchange of expertise between centres in Europe via education grants and programmes |
| | | Funding for infrastructure needs | Improved recognition of specialty cancer nurses |

Figure 1.0

# V. Improving diagnosis and care referral

As stated in the introduction, NENs are characterised by great challenges in diagnosis due to their rarity and the way they present in the body. In the past two decades, there has been an increasing incidence of GEP-NENs[69], which may be a consequence of better diagnostic methods, improved classifications and increased awareness of the disease. The Global.NET Survey in 2017 found that nearly 60% of NETs are advanced at the time of diagnosis. At the moment of diagnosis, with either locoregional or distant metastases, about 50% of all NEN are localised and 40% have metastases[70,71]. Survival rates can vary widely, from 6 months to over 30 years.

Comprehensive imaging is necessary during the diagnosis phase to identify all tumour sites and optimise therapeutic management. Multi-contrast computed tomography (CT), magnetic resonance imaging (MRI), colonoscopy, gastroscopy can be used, as well as positron emission tomography (PET/CT). The latter technique allows scanning of the whole body, and has proved to be the most sensitive method for diagnosing and staging of NETs[72]. Access to diagnostic imaging equipment is crucial for correct diagnosis and timely access for patients. The majority of patients surveyed on unmet needs in NENs highlighted that availability of

PET/CT scans was limited and also that there is a major challenge of travelling to a specialist for diagnosis and treatment[73]. In several countries, there are simply not enough PET scan-ners to offer a robust diagnosis to patients[74]. Europe´s Beating Cancer Plan called for greater access to diagnosis and the idea that European Cohesion funds could be used to up-scale the early detection infrastructure[75].

### RECOMMENDATION 02

Deployment and better promotion of funding opportunities for Member States to invest in PET/CT/MRI machines and hospital infrastructure, including European funding opportunities from the EU4Health Programme, European Regional Development Funds, as well as the Cohesion Fund.

There is still limited availability of data on NEN patients' unmet needs. Especially when it comes to information at the time of diagnosis, patients would need to receive better guidance, as they may encounter difficulties in finding relevant information[76] – e.g.: many patients report referring to the internet or patient associations for information. Several studies published in recent years on neuroendocrine tumours[77] showed a lack of a clear pathway of care for the patient throughout their journey with NETs, in particular patients may find it difficult:

- obtaining a diagnosis
- finding and obtaining appropriate information about NETs
- finding treatment centres that could treat NETs
- finding specific support for NETs.

The implementation of standard diagnostic procedures should be prioritised, and the presence of comorbidity and multimorbidity should be considered to develop more efficient disease management protocols[78]. Designing shared care plans with community oncologists could provide a model to reduce this burden.

A clear pathway for NEN patients should be established so that all patients have reliable access to a consistent standard of care. All national health systems should also aim to create pathways leading all patients to specialised centres to improve outcomes for NEN patients. Especially in Western Europe, ENETS certifies NET centres of excellence and for patients within these centres of excellence, the chance of survival appears to be more than three times higher than in other institutions. However, as there are few of these centres, NEN patients may face long journeys, also creating problems for the care system around the patient, their family and follow-up.

### RECOMMENDATION 03

Clear national or international pathway for NEN patients should be established so that all patients have reliable access to a consistent standard of care in each EU region. The Beating Cancer Plan proposes tools for the expert exchange of knowledge, such as the new EU Networks of expertise on cancer. The development of referral pathways could be prioritised and tackled at EU level in rare disease action plans as well as supported through data and knowledge exchange initiatives. At the same time, these priorities should be reflected at national level, where NENs should be promoted in national cancer plans and national rare disease plans. In order to do so, these recommendations aim to provide a reference point for Member States and governments in order to 1) analyse the current state of the art and 2) enable them to determine where to start to improve the state of care.



### RECOMMENDATION 04

Provide (and, if not available, develop) a set of written materials to NEN patients at the time of consultation and refer patients to local organisations and patient associations that can provide further information and support. Consider the role of ERNs to increment dissemination of informative material.

A practice that has become increasingly common in medicine for the treatment of cancer is tumour boards (even though it is not yet so common in Europe)[79]. Tumour boards are multidisciplinary team meetings (MDTs), created as a response to the complex, rapidly evolving science[80]. The boards require a team of specialists to provide expertise in different medical fields for the assessment and treatment of patients with cancer. The review of patient cases aims to lead to action plans that can better orientate the care pathway and limit unnecessary tests and procedures[81]. It may be necessary to have separate tumour boards for specific specialties[82] - however, this may depend and vary based on the size of hospital and the specialised healthcare professionals.
As the number of treatment options for patients with NENs is increasing, the number of different health professionals is also expanding (this also applies to cancer patients more generally). Due to the complexity of neuroendocrine neoplasms care, a multidisciplinary approach has been strongly encouraged by the European and North American Neuroendocrine Tumour Society for effective patient care[83]. In fact, it has been reported that MDT meetings improve the quality of care by focusing on communication between different health professionals and that survival probability improves in centres that adopt a multidisciplinary approach[84]. it must be acknowledged that the effective impact of MDT meetings on patients' survival may depend on structural and functional components and the expertise of the participants[85]. In the past two years, during the COVID-19 pandemic, multidisciplinary care (often at a distance when necessary) proved essential[86], as different treatments could be considered as well as risks and benefits weighed at the level of the individual patient.

### RECOMMENDATION 05

Sustainable care referral system in Europe should take into consideration the key role of multidisciplinary teams to improve patients' outcome and more efficient diagnosis and treatment.

In many countries, there may not be a centre of excellence near to where the patient lives, which means they will be referred to a larger, hopefully more experienced, centre either in another part of the country or outside of their country. The problem of care referral in Europe is two-fold:

1. There must be appropriate referral mechanisms within a country´s network that can ensure patients move to highly specialised centres where their treatment outcomes are improved (be that within their country, or abroad)
2. The increasing referral to specialised centres is putting an unprecedented burden on excellence centres. The formation of MDT tumour board to assess new cases (either in person or virtually) is extremely time intensive and is neither recognised nor compensated appropriately by national health systems (and subsequently by hospital management) and thus relies largely on unpaid hours by overworked but dedicated specialists

To deal with the first challenge of care referral, we must first recognise that care (diagnosis, treatment and follow-up) in referred multidisciplinary expert centres (MRC) is associated with improved outcomes for patients. This has been demonstrated in several studies and relies on two core principles. Firstly, the MRC is typically appropriately staffed with the different specialties that make up a correct MDT for NENs (including but not limited to: surgical oncology and medical oncology disciplines; nurses well experienced in the treatment of NENs; gastroenterologists, pneumologists, endocrinologists, diagnostic radiologists, interventional radiology specialists and nuclear medicine physicians)[87]. They are also associated with the necessary infrastructure to offer an effective range of diagnostic and therapeutic options.

The ENETS accreditation of Centres of Excellence[88] (CoE) is the gold standard for recognising centres that offer a high-value MDT service in Europe (although must be noted that ENETS accreditation is not a prerequisite for MDT). They have successfully accredited 62

CoEs since 2009, providing patients with identifiable high-value services.

Secondly, on a more basic level that is common across rare cancers, centres that see a higher volume of patients offer improved outcomes to patients and should be the focal point of highly specialized care[89]. There are instances where patients are not referred to expert centres due to logistical or bureaucratic challenges or misjudgement of the internal resources available, and this may be a major hindrance to good patient care. Various countries have adopted guidelines in several cancer types to ensure that patients are not treated in hospitals without an appropriate "minimum caseload" per year. This is developed to ensure a minimum standard of treatment offered to patients.

### RECOMMENDATION 06

Based on the specific needs of each Member State (population, incidence, distance among centres, number of patients, etc.), each Member State should identify, with the support of specialised organisations or institutions, how many centres of excellence each country should have.

### RECOMMENDATION 07

Based on the recognised standards established in the ENETS accreditation, national health systems should set up mandatory care referrals for patients to centres with either 1) accreditation by ENETS, or 2) which see a sufficient volume of patients in one year to be considered has holding relevant expertise.

### RECOMMENDATION 08

If it is not possible to offer patients treatments at an ENETS accredited centre within a Member State, patients should be referred to specialist care - this could be an ENETS accredited CoE, Comprehensive Cancer Centre or High volume institution. The institution needs to have the infrastructure and collaborative links to provide gold standard care. It should also be facilitated/reimbursed a pathway for patients to receive diagnosis in an expert centre abroad – using European mechanisms available (e.g.: CBHC with a reimbursement system put in place)[90].

Once patients are referred to expert centres, we must consider the second major challenge for care referral in Europe – the sustainability of the referral pathway for the receiving expert centre. Setting up a tumour board to deal with new patients (either physically or virtually) is a time-consuming exercise. It does not only involve finding time for the 6-7 relevant healthcare professionals to meet together, but it also includes a large administrative burden, logistic aspects (e.g.: establishment of the team and maintenance of meetings, equipment, updated clinical information on the patient, IT support, and so on)[91] and the full review of paperwork and imaging prior to these tumour boards[92]. The benefits of tumour boards have been taken for granted for a long time, and have recently been questioned. In fact, the positive outcomes of tumour boards depend on the presence of qualified faculty, good preparation and selection of cases, the format and structure of the meeting, effective leadership, and interactions among the attending physicians. Team dynamics are not always harmonious and conducive to effective communication and productive educational opportunities[93]. Measuring the production of individual MDT (in terms of time to referral, recommendations and their application, outcome of patients) remains therefore essential.

Rather than being built into regular schedules of these expert physicians, it is mostly considered the extra time that should be put in. This is primarily because the value-added to patient outcomes by multidisciplinary expert centres is not valued monetarily in the relevant national health system tariffs (e.g. in the Diagnosis Related Group). Where no money is associated for the expert diagnosis of patients, hospital managers will not foresee additional time or personnel resources for this exercise as it is simply not economically viable. Continuing to expect highly dedicated, but overworked, specialists to deliver a full MDT in their centres outside of their normal hours will eventually lead to a drop in the quality of care, either in terms of the quality of the tumour board, or in the management of patients in that centre. While there is no known country that has employed a tariff approach that includes expert fees in the DRGs, this is an urgently needed approach to sustain the model of hub-and-spoke expert care in Europe. Health systems must recognise that quality care, is more important than quantity care in NENs and health systems must look to reward this as a matter of urgency, to preserve the sustainability of the referral model in Europe.



### RECOMMENDATION 09

The EU should look to develop a model for the incorporation of expert care into national healthcare system tariffs. Member States must open a dialogue on reimbursing expert care and, where relevant to the local healthcare system, begin a discussion with insurers and hospital managers on how to appropriately value this expert care, given the demonstrable impact on patient outcomes that this referral has. Dialogue within European and national institutional fora on reimbursement policies should cover how to integrate the remuneration of MDTs, which is globally recognised as an integral part of optimal care for these (and other) diseases.

### RECOMMENDATION 10

Within the foreseen EU flagship programme establishing dedicated Comprehensive Cancer Centres in every Member States, specific needs of rare cancers and NENs must be well recognised. These centres should also be a flagship for a new, more sustainable, care referral with appropriate remuneration for referral. For dissemination, these centres should also be included in the EURACAN location map and similar lists of expert centres.

### RECOMMENDATION 11

National bodies should look to support in a greater way expert centres, aligned with the policy to refer all patients to sufficiently high-volume centres. Financial resources must be dedicated to high-performance centres where quality of patient care is truly valued (on the basis of equal performance indicators, for which guidelines would be welcomed).

The final piece of the care "puzzle" is ensuring appropriate follow-up care locally after patients are seen at a highly specialised centre. This challenge may be exacerbated in cases where patients are treated abroad and must return back to their home country. For patients with NEN, treatment does not end when the active phase of treatment is over. The healthcare team must check that the tumour has not returned and manage any side effects. NENs tend to grow slowly and may be similar to a chronic disease. It is therefore essential for patients to learn and be aware of how to live with chronic cancer and the importance of follow-up care[94].

Usually, patients undergo a lifelong follow-up that varies according to the initial diagnosis, aggressiveness, function, surgical outcome and other factors, such as the presence of inherited disease. The timing of follow-up will also vary according to these factors. Patients may continue to see their oncologist, while others may return to the care of their general practitioner or another health professional. This decision depends on several factors, including the stage and grade of the tumour, side effects, health insurance rules and personal preferences. However, if a doctor has not been directly involved in the treatment for NEN, the patient should be provided with explanations of the treatment and survivorship scenario. This requires established procedures and schematic arrangements to help patients keep track of the pathway and care they have received in order for the doctor that will take care of the follow up to develop a coherent plan. However, there is currently no established protocol for the follow-up of patients with NEN, as evidence-based studies are lacking[95]. The ENETS recommendations suggest that follow-up should be performed in specialised centres with regular cancer committees with expert panels.

### RECOMMENDATION 12

Initiate the creation of established protocols for the follow-up through research and data collection activities, promoted through initiatives such as the Knowledge Centre on Cancer, the European Health Data Space or the European Cancer Information System. At the same time, strengthen telemedicine and remote monitoring and consultation systems. Towards this objective, funding opportunities under the EU4Health and Digital Europe Programmes should be considered. Call will be opened between 2021 and 2023 as foreseen in the Beating Cancer Plan to reduce health inequalities.

## VI.Improving treatment and care

The treatment of patients with NENs has advanced rapidly over recent years and there is increasing hope for NEN patients when confronted with a diagnosis, especially if it is done in an early and coordinated way, as detailed in Chapter 1. Treatments for patients with NENs are considered by several European guidelines which can support specialists and MDTs to make informed decisions (e.g.: ESMO/EURACAN Guidelines[96], ENETS guidelines[97]). Core to the improvement of care across the European Union, as indicated in Figure 1.0 is adoption, dissemination and regular adaptation of clinical guidelines to pursue a gold standard of NEN care across Europe.

### RECOMMENDATION 13

Encourage the adoption, dissemination and regular adaptation of relevant guidelines according to needs (as other rare cancer guidelines) through sharing in professional networks, including in relevant educational platforms and profiling in national congresses. Benchmark the adherence to these guidelines when considering new tools, such as the proposed European Cancer Dashboard[98].

The treatment chosen is based on symptoms, tumour type, disease burden, but patient performance is also a determining factor. The primary treatment approach remains surgery, but in many cases, this is not possible due to the tumour spread or progression. Depending on the type of NET, medications that may be used may include Somatostatin analogues (SSA), Chemotherapy, Targeted therapy, Immunotherapy and Peptide receptor radionuclide therapy (PRRT – also known as radioligand therapy or RLT)[99]. Despite these advances for NETs, the heterogeneity of NENs means that a broad portfolio of treatments is required, and further innovation and research is necessary. As such, the lack of specific policies to encourage R&D in the rare cancer field in either the Europe Beating Cancer Plan or the Pharmaceutical Strategy for Europe, is a concern for future treatments for patients.

### RECOMMENDATION 14

Ensure a clear focus on the research needs of rare cancers such as NENs, and that all policies are driven towards stimulating new treatments for patients.

Viewed in the context of Europe´s emerging policies to increase innovation in the pharmaceutical sphere[100], the variety of treatment options may indicate a success story of increasing innovation for patients. Nonetheless, there remain several gaps in the access to these treatments, several of which may be tackled at European level. In a survey of patients, healthcare professionals and patient advocates, a consensus emerged that access to some novel therapies for NETs, such as RLTs, remain challenging[101]. In that study, patients indicated the access challenges to be based primarily on their healthcare system, the lack of referral, financial issues (treatment not being included by their social insurance) or the inability to afford treatment[102]. Distance to treatment centres is another paramount issue for novel therapies where the need for speciality care meant that patient advocates estimated 48% of patients had to travel more than 300km for treatment[103].

Another major challenge for access to treatment and care is the infrastructure available in European countries. Chapter 1 addresses the personnel infrastructure that is required in the form of MDTs, as well as the “bricks and mortar” infrastructure elements around diagnosis. Likewise, for treatment, there may be necessary radio pharmacies, shielded rooms and waste disposal and storage facilities that must be in place in order to offer the best treatment.

### RECOMMENDATION 15

Deploy European funding mechanisms to support upscaling of infrastructure for the treatment of NETs patients through investments in radioprotection rooms, waste disposal and storage facilities.

Looking at the core issues of patients reported in the aforementioned studies, more must also be done across the EU to ensure new treatments are available to patients. This means a streamlined regulatory process for rare cancer therapies and clinical trials, with data expectations for regulatory review aligned with data expected by national bodies reviewing reimbursement of therapies. Furthermore, it means recognising at national level the value of improved quality of life for patients and involving patients across the decision-making process to ensure that treatments which truly improve patient relevant outcomes are made available. The role of patients in decision making is also enshrined in the Rare Cancer Agenda 2030, which was an output from the EU Joint Action on Rare Cancers[104].

### RECOMMENDATION 16

Streamline regulatory procedures for rare cancer therapies and involve patients in all decision making to ensure patient-relevant outcomes drive decision making around treatment availability.

Another fundamental part of delivering excellent care to patients with NENs is ensuring sufficient education opportunities for the broad range of medical specialists involved in the MDT. Patients have reported that their information needs were mostly met in only 30% of cases by HCPs, requiring greater reliance on individual research and patient support groups[105]. With a complex treatment pathway for patients, involving many different medical specialists such as - but not limited to - gastroenterologists, oncologists, surgical oncologists, endocrinologists, radiologists, nuclear medicine specialists, hospital pharmacists (or hospital radio pharmacists), specialist oncology nurses, general practitioners (to whom patients might turn for everyday problems or if they feel lost in their pathway), palliative care teams, it is no surprise that ensuring sufficient training opportunities for all these specialities is a challenge. An additional point for reflection arises. If patients feel lost in their journey, they will sooner or later also contact their general practitioner, thus highlighting the crucial importance of education for all practitioners.

Cross-speciality training is a fundamental part of improving the access to good quality care. Europe´s new flagship programmes contain several provisions around education that can be deployed to meet the needs of the NEN community. The focus should primarily on countries where there is a basic need for improved HCP training, in order to reach homogenous high-quality management of NEN for all EU patients at all stages of the patient pathway.

### RECOMMENDATION 17

Deploy training programmes foreseen in Europe´s Beating Cancer Plan and the SAMIRA initiative to improve education around NENs in Europe and reach homogenous high-quality management of NEN for all European countries – with priority on those countries with basic need for improved HCP training.

## Supportive Care

To complete the view on improving access to good treatment and care we must also consider the fundamental role of supportive care. Supportive care is defined as the "Care given to improve the quality of life of patients who have a serious or life-threatening disease. The goal of supportive care is to prevent or treat as early as possible the symptoms of a disease, side effects caused by treatment of a disease, and psychological, social, and spiritual problems related to a disease or its treatment [106]." This means we should consider the role of supportive care during, and after a patient´s admission for treatment.

Given the advanced stage at which many NEN patients are diagnosed, psychological support may be even more necessary than in other disease areas. In the previously referenced survey of patients, HCPs and patient advocates, there was a consensus that supportive care, for example, for mental and emotional health as well as nutritional needs, is lacking and that contact needs with an MDT are unmet for about 15 in 100 patients[107]. Patient inclusion in the MDT seems to be a core factor in improving these factors – patients with access to their MDT reported improved satisfaction and knowledge of their condition[108].

One of the key roles in improving supportive care is the presence of NEN specialist nurse who can dedicate more time to patient education and provide holistic support, and may assist, particularly to provide psychological care . Unfortunately, evidence suggests that despite the existence of psychological dedicated staff, nurses do not have the confidence to help and support NEN patients, which speaks to a broader challenge of empowering and valuing specialist nurses. Specialist cancer nursing provision has been associated with improved management of chronic problems in cancer patients; improving patient knowledge and self-management; as well as in symptoms and a reduction in the rate of emergency admissions, length of hospital stays and fewer follow-up appointments[110]. The European Society for Oncology Nurses highlights many of the needed policy reforms for specialised nurses in the EU, many of which are of high relevance to NENs.

### RECOMMENDATION 18

Support the educational and professional needs of specialist nurses given the fundamental role they play in improving supportive care for patients. This should include, but not be limited to, providing legal recognition to more cancer specialists to elevate the role of cancer nurses and aligning the remuneration foreseen with the high standards of training.

### RECOMMENDATION 19

Ensure that within the framework of National Comprehensive Cancer Centres there is a clear focus on supportive care, empowered by specialist nurses and a patient-involved MDT.

The 2020 ESMO Clinical Guidelines on GEP-NENs highlight that follow-up care should be life-long[111]. As such we must also recognise the life-long supportive care that patients may need to deal with potential cancer recurrence. When recalling the ideas from Chapter 1, we must ensure that patients can also be referred to appropriate psychological support in their follow-up care, and that supportive care is not forgotten through the life course of a patient.

# VII. Conclusions

Despite marked progress in the diagnosis, treatment, and care of NENs in Europe, there are many challenges facing patients and healthcare systems. What is more, the challenges are not well-known amongst countries, hospitals, or patients. As such, this document looks to provide a holistic review of recommendations for policy-makers at European and Member State level to integrate stepwise policy improvements that can enhance the care of patients with NENs regardless of the current state of care.



The European policy context offers great hope to prioritise funding where it is most needed such as in infrastructure, to level up education in professions crucial to NEN care, to improve the incentives for innovation for new NEN therapies, to review the access pathways to make sure treatments reach patients in a correct manner, and to improve referrals to expert centres.

Beyond these priorities however, there are a number of recommendations listed here, such as the ideation of new concepts for reimbursing high-quality tumour boards in national insurance systems and of reinforcing the role of specialist cancer nurses, which require new approaches. Fundamental to the success of these recommendations is the connection between European and local solutions. We must spread a prioritisation to care for patients with NENs in the best way, building on recent successes that mean that patients can live dignified lives beyond their diagnosis if detected early, referred to centres of excellence, treated with the most relevant and innovative therapies, and supported in their journey by an appropriate MDT.

We have the mechanisms in Europe to improve care for NEN patients across the Union but we must connect resources and priorities and follow community consensus such as these to drive towards a gold standard of care.

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# Appendix 1

A useful and reliable source of NEN information for patients is the Global NET Patient Information Pack from International Neuroendocrine Cancer Alliance (INCA). It provides access to free to download factsheets on neuroendocrine tumours in 10 languages. These are factsheets that share comprehensive information on NETs and are developed in collaboration with expert patients and physicians. They are aimed at patients, health professionals and anyone wanting to get a better understanding of NETs. The factsheets can be accessed here: https://incalliance.org/net-info-packs/

INCA as well identifies that family doctors play a leading role in NET diagnostics together with gastrointestinal specialists. The role of family doctors in the diagnosis of NETs has considerable room for improvement as does awareness of diagnostic tools. The NET survey SCAN represents the biggest global compendium of NET data and can be accessed here: https://incalliance.org/wp-content/uploads/2022/01/13_04_2020_WONCA_AbuDhabi_2020_SCAN_INCA_Abstract_application.pdf

Recently INCA published a concerted communication effort around late diagnosis and misdiagnosis among patients, carers, healthcare professionals and the general public: Neuroendocrine Cancer Day campaign 'Know the symptoms. The campaign pushes for diagnosis' with global scope in 10 languages and is available here: https://incalliance.org/wp-content/uploads/2022/03/2022-03-INCA-ENETS-Poster.pdf