A Survey of Barriers to Treatment Access in Rheumatoid Arthritis

Country Annex Report: Italy

October 2009

1 Interviews

In Italy four rheumatologists, two patient representatives and one health economist were interviewed. The interviewees came from mainly the northern part of Italy (Lombardy) as well as Rome and Puglia.

2 Environment

Italy has a total population of 59.6 million with an adult population of 49.5 million (83%) [1]. Italy's healthcare system is a regionally based NHS that provides universal coverage free of charge at the point of service [2]. The system is organised at three levels: national, regional and local. The national level is responsible for ensuring the general objectives and fundamental principles of the national healthcare system. Regional governments, through the regional health departments, are responsible for ensuring the delivery of a benefit package through a network of population-based health management organizations (local health units) and public and private accredited hospitals. The parliament approves framework legislation, which lays out the general principles for organizing, financing and monitoring the NHS. In particular, the National Health Plan for 1998–2000 prescribes that the whole NHS should be organised according to the following principles.

- *Human dignity.* Every individual must be treated with equal dignity and have equal rights irrespective of her or his personal or social characteristics.
- *Health need.* Everyone in need has a right to healthcare, and resources should be allocated with priority given to satisfying the basic needs of the population.
- *Equity.* NHS resources should be used to eliminate geographical and/or economic barriers that constitute an obstacle to citizens' demand for appropriate services. Behavioural and information gaps among the population should be reduced to provide the same opportunity for access to healthcare services.
- *Protection.* The NHS should give highest priority to protecting and promoting citizens' health status.
- *Solidarity with the most vulnerable people.* Resources should be allocated primarily to the individuals, groups or groups of diseases with the most relevant social, clinical and epidemiological impact.
- *Effectiveness and appropriateness of health interventions.* Resources must be channelled to services with scientifically demonstrated effectiveness and to individuals who can benefit the most from them.

- *Cost-effectiveness.* Services should be provided by the organizations pursuing financial balance through efficient and effective behaviour.

3 Market Access

The AIFA (Italian Medicines Agency) has a range of responsibilities, including drug registration, liaison with the EMEA and pricing. After drug authorisation, the committee within AIFA that is responsible for the pricing and reimbursement process is 'Comitato Prezzi e Rimborsi'. This board, comprising five Members of the Ministry of Health, five members of the Regions-State Committee, one member of the Ministry of Economics and one member of the Ministry of the Productive Activities, negotiates drug pricing through an e-procedure. These negotiations are not open and it is not specified how final decisions are reached.

Pricing is established according to the criteria of cost-effectiveness (for diseases that do not have an effective therapy), risk-benefit (when the disease has an effective therapy) and price and consumption in other European countries. After this phase the authorised drug can be classified in the National Formulary as Class H, for use only in the hospital setting (normally highly innovative drugs), as Class A (reimbursed for use in the community) or as Class C (not reimbursed). All drugs available for use at the national level are included in the national formulary, and no hospital may prescribe a drug that is not included, except in the case of a compassionate study.

Hospital drugs are subject to a budget cap which is fixed nationally and then regionally, and cannot exceed 2.4% of global healthcare costs.

4 Features specific to RA

Due to the decentralization of the healthcare system there is no national RA strategy, and every region defines it own plan. At present, five regions (Lombardy, Friuli, Sardegna, Puglia and Toscana) have RA strategies, either as a separate document (Puglia) or as a segment of the general healthcare strategy plan.

There are two national registries with a specific focus in RA: the LORHEN and the GIARA registries.

- LORHEN [3] is a regional registry of anti-TNF-treated patients in the Lombardy region. The main objectives are to monitor efficacy and safety under real-world and long-term treatment conditions.
- The GIARA registry (Gruppo Italiano Artrite Reumatoide Aggressiva) [4] was initiated in 1999 by the Italian Society of Rheumatology (SIR) to evaluate patients

with aggressive types of RA. The registry also receives funding from the pharmaceutical industry (Novartis). It comprises 1,218 patients from 94 participating centres.

- In addition to the above, MonitorNet [5] is a database established by SIR in January 2007 and funded by AIFA for the active long-term follow-up of patients with RA, PsA and AS treated with biologics.

5 Guidelines

There are no official national RA guidelines in Italy. The national patient organization (ANMAR) has published recommendations in addition to SIR's guidelines (Linee guida per la diagnosi precoce e la terapia dell'Artrite Reumatoide). The SIR guidelines are not binding but reflect common practice in Italy. Only one region – Puglia – has established guidelines.

6 Provision of care

Primary care in Italy is provided by GPs, paediatricians, and self-employed and independent physicians working alone under a government contract, who are paid a capitation fee based on the number of people (adults or children) on their list. They act as gatekeepers for access to secondary and specialist services, write pharmaceutical prescriptions and certifications, and visit patients at home if necessary. People may choose any physician they prefer, provided that the physician's list has not reached the maximum number of patients allowed (1,800 for GPs and 1,000 for paediatricians).

A co-payment by the patient is required as an additional source of financing and in an attempt to moderate the use of specialist ambulatory care. Tests for monitoring chronic conditions and treatment requested by people with low income are provided free of charge. Because waiting lists are long, co-payments high and the quality of services often unsatisfactory, especially in central and southern regions, many people seek care outside the NHS, especially if they have health insurance that covers the related costs. The exact role of the private insurance sector in Italy is not well known. In 1999, an estimated 30% of the population was covered by private insurance

The utilization of private services differs greatly by region. In 1999, private providers performed 19.7% of the specialist diagnostic procedures: 23.9% in central regions versus 16.5% in north-western Italy.

There are 47,000 GPs in Italy who provide the first contact for RA patients and 1,200 rheumatologists, whose training takes an additional 4 years after an MD degree. This

yields a ratio of one specialist per 49,700 members of the population or one per 41,300 of the adult population. However, not all of the rheumatologists treat RA patients, and half of the interviewees felt the number of rheumatologists was insufficient due to the length of the waiting lists and variability in service provision across regions.

7 Diagnosis

The diagnosis of RA is usually made by a rheumatologist (80%) following an initial screening and referral by a GP, but also by GPs themselves (20%). The initial diagnosis by the GP is critical as this will drive quick referral; respondents mentioned that misdiagnoses at the GP level are an issue in Italy.

According to all respondents, diagnosis is established between 6 weeks and 2 years after first onset of symptoms, with a mean estimate of around 1 year to 18 months after onset for most patients. The time to diagnosis depends on how quickly the patient is referred from the GP to a specialist and hence mainly on the expertise of the GP as the gatekeeper. It was mentioned that occasionally GPs apply a 'watch and wait' strategy to establish disease progression without referring the patient to the rheumatologist. It was also mentioned that patients may see a GP after RA has already started to progress.

Diagnosis is supported by a range of procedures supported by the EULAR recommendations: i.e. physical examination, blood tests, and rarely MRI and ultrasound and X-ray if there is substantial uncertainty around the diagnosis based on the other tests. These imagin techniques are used more rarely as there are budget restrictions on, and insufficient facilities for, the routine use of imaging processes in diagnosis. Although Italy has a high number of MRI scanners (9.8) per million of the population, facilities are not available throughout Italy and many patients have to travel for confirmatory diagnoses by imaging tests.

Most respondents in our study differentiate between patients with 'poor prognosis' and 'other patients' without systematically using explicit criteria. High titres of RF, high markers of inflammation (anti-CCP) and swelling of more than 10 joints were mentioned by one respondent and may underscore the rare use of imaging in the diagnostic workup.

8 DMARDs

In general, the largest barrier for treatment is the budget cap for hospital drugs, which is fixed nationally and then regionally. Hospital drugs in total cannot exceed 2.4% of global national health expenditure.

Treatment is initiated by rheumatologists immediately after a confirmed diagnosis. Steroids are recommended as symptomatic treatment, particularly in the first phase of the disease; however, once DMARDs are initiated steroids are tapered off or used at low doses. Anti-malarial medication is recommended as an adjunct to steroids for mild cases. However, for almost all patients (≥90%) the first treatment choice is MTX, as recommended by the SIR for moderate to severe cases and it is used mostly with NSAIDs and low-dose continuous steroids. MTX may also be combined with leflunomide, azathioprine or cyclosporine.

Treatment is changed immediately in the event of severe side effects, but patients are typically treated for 6 months to as long as 3 years before being switched to another treatment, usually due to insufficient treatment response.

9 Biologics

Use of biologics is discouraged in first-line treatment and thus is typically prescribed after use of two or three DMARDs. Within an academic setting prescription of biologics is more frequent.

Overall, an estimated 7% of patients receive biologics. There is a high unmet need due to prescription restrictions for biologics, with one respondent estimating that only 17% of patients in need of biologics actually receive them. In line with regional guidelines anti-TNFs are the first treatment option after small molecule DMARDs. Typically, biologics are used in patients with severe RA or who fail to sufficiently respond to DMARDs after 3 months or in patients with special needs (such as those whose profession is based on manual dexterity and strength). Efficacy considerations drive the choice of drug, with priority given to drugs with more clinical data and experience.

- First line: Adalimumab (Humira) and etanercept (Enbrel) are the most frequently used biologics. Infliximab (Remicade) is less frequently used as a first-line option. Efficacy, costs and long-term experience are the main reasons given by interviewees for these choices.
- Second line: Abatacept, rituximab and anakinra are mentioned as subsequent options depending on patient response to the first-line agent, due to the different mechanism of action for these drugs. Switching is mainly motivated by efficacy considerations.
- Further (post-second-line) options were not prioritised by the respondents.

It was estimated that there are 200 infusion facilities at national level. This capacity was seen as sufficient in principle for adequate management with biologics, but the uneven

geographic distribution of facilities results in additional waiting time, travel and costs for patients receiving treatment.

10 Treatment consistency with EULAR recommendations

The consistency with which the diagnosis and treatment of RA in Italy follows key EULAR recommendations is shown below (Table 1) for information gathered from desk research and from the interview panel.

Table 1. Consistency of Italian RA practice with EULAR recommendations

		National practice consistent with EULAR recommendations		
	EULAR recommendation	**Desk research**	**Interviews**	**Comments**
Diagnosis	Patient presenting with arthritis is referred to and seen by a rheumatologist ideally within 6 weeks of symptomatic onset	No	No	May take 6–72 weeks Diagnosis may be established by GP
	Clinical examination for detecting arthritis includes ultrasound, power Doppler, and MRI	Yes	No	
	Diagnosis requires at least the following laboratory tests: complete blood cell count, urinary analysis, transaminases, and antinuclear antibodies	Yes	Yes	
	Measurement of the following factors for patients presenting with early arthritis: number of swollen and tender joints, ESR and CRP, level of RF and anti-CCP antibodies, and radiographic erosions bodies	No	Yes	Not mentioned specifically by guidelines
Treatment	Patients developing persistent/erosive arthritis should initiate DMARDs as early as possible	Yes	Yes	Not mentioned specifically by guidelines
	Use of patient information and education programmes about coping with pain and disability and maintaining work	No	No	Patients are mostly informed by patient associations (such as ANMAR) and the national healthcare system. No programme is employed
	NSAIDs are considered in symptomatic patients	Yes	Yes	
	Systematic glucocorticoids to reduce pain and swelling are considered as a (mainly temporary) adjunct to DMARD treatment	Yes	Yes	
	Among DMARDs, MTX is considered the anchor drug and should be used first in patients at risk of developing persistent disease	Yes	Yes	

		National practice consistent with EULAR recommendations		
	EULAR recommendation	**Desk research**	**Interviews**	**Comments**
	The main goal of DMARD treatment is to achieve remission. Regular monitoring of disease activity and adverse events guide decisions on the choice or change of DMARDs and/or biologics used	Yes	Yes	
	Non-pharmaceutical interventions, such as dynamic exercises, occupational therapy and hydrotherapy, are applied as treatment adjuncts	No	50% Yes 50% No	Not mentioned specifically by guidelines Depends on the case and the treating physician. There are rheumatologists who are keen on treatments that are non-pharmaceutical in nature and others that do not consider them
Monitoring	Disease monitoring includes tender and swollen joint counts, ESR and CRP assessment at 1 to 3 months	No	Yes	
	Structural damage is assessed by X-ray every 6 to 12 months. Functional assessment is used to complement disease activity and structural damage	No	60% Yes 40% No	The first assessment is done after 6—12 months from diagnosis. Afterwards, only if it is needed (normally every 24 months)

Note: The specific wording of the recommendations has been shortened in some instances for editorial reasons

11 Sources

In addition to the references listed in the text the following sources were used in compiling Italian details in this monograph.

Epidemiology

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Registries

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Delivery of care

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Guidelines

- http://www.reumatologia.it/obj/File/LG_AR_2004_v02.pdf

Medical Treatment

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12 References

1. L'Istituto Nazionale di Statistica (ISTAT). Compendio statistico Italiano 2008. Last modified May 2009. *Available at:* http://www.istat.it/dati/catalogo/20090721_00/testointegrale20090721.pdf (Accessed 02 Oct 2009).

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4. Marchesoni A, Govoni M, Valentini G, et al. The Italian registry of aggressive rheumatoid arthritis -- the GIARA project. *J Rheumatol* 2007; **34**:2374-2381.

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