

Giuseppe Stirparo
Fabio Palazzo
Sergio De Filippis
Paolo Martelletti

Discrepancies between European countries and USA and Canada in the availability of triptans and in their licensed clinical properties

G. Stirparo (✉) • F. Palazzo
Institute for Research on Population and Social Policies,
Italian National Research Council,
Via Nizza 128, I-00198 Rome, Italy
e-mail: g.stirparo@irp.rm.cnr.it
Tel.: +39-06-49932866
Fax: +39-06-85834506

S. De Filippis • P. Martelletti
Headache Centre,
Sant'Andrea Hospital,
Department of Internal Medicine,
Second School of Medicine,
La Sapienza University, Rome, Italy

Abstract Triptans are presently a milestone in the treatment of migraine patients. Because of their effectiveness and safety, they have radically improved migraine treatment but their use has meant a substantial increase in spending for medicines. We compared available pharmaceutical forms, pack sizes, indications and dosages of triptans as listed in the summary of product characteristics of eight countries. We found that several differences exist between countries in the presentations of the triptans and in their licensing.

Key words Triptans • Indications

Introduction

Since the introduction, in early 1990s, of selective 5-HT_{1B/1D} agonists (triptans), the management of migraine has been radically improved because of the effectiveness, tolerability and safety of these drugs. Despite the high cost, the use of triptans has largely increased in recent years. Triptans have been referred to as “miracle” drugs. Before the introduction of triptans, pain medications worked by masking pain. Triptans, however, actually work at the level of the brain to stop the cause of pain. By raising the level of serotonin in the brain, triptans reduce the dilation of surrounding blood vessels, ending the source of the pain [1]. The first in this class of drugs was sumatriptan, which was followed by zolmitriptan, naratriptan, rizatriptan and almotriptan. These five different compounds are listed in the 2002 WHO-ATC list [2]. Although these drugs belong to the

same class and have many of the same characteristics, they also have differences. For these reasons we thought it was of interest to compare available triptans and their licensed clinical properties among European countries, the United States and Canada.

Materials and methods

We compared available pharmaceutical forms, pack sizes, indications and dosages of triptans as listed in the summary of product characteristics of eight countries (USA, Canada, UK, Germany, France, Italy, Sweden and Ireland). We studied 5 commercially available triptans:

- *Sumatriptan* is available in four forms: tablets, nasal spray, suppositories and auto-injectors for self-administration. Although the tablets are easier to use, the spray and injections

are better tolerated when the patient is nauseous. The spray is somewhat faster acting than the tablets, while the injections are the fastest acting of any of the formulations.

- *Zolmitriptan* is supplied in tablet and melt forms. It is generally well tolerated and is considered as effective as sumatriptan.
- *Naratriptan* is supplied only in tablet form.
- *Rizatriptan* is available in two types of tablets and in two types of melt.
- *Almotriptan*, the newest of the triptans currently available, is available in a 12.5-mg tablet.

Results

Among the eight countries considered, notable differences exist regarding the availability of the 5 major triptans and their pharmaceutical forms (Table 1). All four sumatriptan

formulations (tablets, injection, spray and suppositories) are available in Italy and Germany. Tablets and injection are available in the UK, injection and spray in France, spray and suppositories in Sweden, and tablets, injection and spray in both the US and Canada.

Sumatriptan tablets (25 mg) are available in the US only, 100-mg tablets are available in Italy, Germany and Canada, and 50-mg tablets are available in all countries investigated. The pack size for the 50-mg tablet ranges from 2 to 24 units in the UK, while it contains 4 units in Italy, 6 units in Germany and 9 units in the US and Canada.

Naratriptan is available in tablets of 1 mg only in the US, whereas the 2.5-mg form is available in the UK, Sweden and Germany. Zolmitriptan is obtainable in 2.5 and 5 mg tablets and melts. Rizatriptan is available in tablets and melts of 5 and 10 mg whereas almotriptan it is only available in 12.5-mg tablets in the UK.

Table 1 Available formulations of triptans in 8 countries. Values are number of units per package

Triptan	Italy	UK	France	Sweden	Germany	Ireland	USA	Canada
Sumatriptan								
Tablet								
25 mg	–	–	–	–	–	–	9	–
50 mg	4	2, 3, 6, 12, 18, 24	2, 6	2, 6, 18	6	2, 6	9	9
100 mg	4	2, 3, 6, 12		2, 6, 18	3, 6	–		9
Injection								
6 mg	2	–	1, 2	2, 3	2	–	2	2
Spray								
5 mg	–	–	–	–	–	–	6	6
10 mg	–	–	1, 2	2, 6	2	–	–	–
20 mg	2	1, 2, 4, 6, 12, 18	1, 2, 6	2, 6, 18	2, 6	–	6	6
Suppository								
25 mg	2	–	–	2, 6, 18	6	–	–	–
Naratriptan								
Tablet								
1 mg	–	–	–	–	–	–	9	–
2.5 mg		2, 4, 6, 12	–	2, 6, 18	2, 6	–	9	–
Zolmitriptan								
Tablet								
2.5 mg	3	3, 6, 12, 18	2, 6, 18	3, 6, 18	–	–	6	–
5 mg	–	–	–	3, 6, 18	–	–	3	–
Melt								
2.5 mg	2	2, 6	–	2, 6, 12	–	–	6	–
5 mg	–	–	–	–	–	–	3	–
Rizatriptan								
Tablet								
5 mg	3	6	–	2, 6, 18	3, 6	–	6	–
10 mg	3	3, 6	–	2, 6, 18	3, 6	–	6	–
Melt								
5 mg	–	–	–	2, 6, 18	3, 6	–	6	–
10 mg	3	3, 6	–	2, 6, 18	3, 6	–	6	–
Almotriptan								
Tablet								
12.5 mg	–	3, 4, 6, 9	–	–	–	–	–	–

Table 2 Licensed posologies for 5 triptans in 8 countries

Sumatriptan spray	
10–40 mg	France, USA, Canada
20–40 mg	Germany, Ireland, Italy, Sweden, UK
Sumatriptan tablets	
25–200 mg	Usa, Canada
50–200 mg	France, Germany, Ireland, Sweden, Italy, UK
Sumatriptan injection	
6–12 mg	France, Germany, Ireland, Italy, Usa, Canada
Naratriptan tablets	
1–2.5 mg	USA
2.5–2.5 mg	Germany, Sweden, UK
2.5–5 mg	France
Zolmitriptan tablets	
1.25–10 mg	USA
2.5–10 mg	France, Germany, Italy, Sweden
2.5–15 mg	UK
Rizatriptan tablets	
10–20 mg	Germany, Italy, Sweden, UK
5–30 mg	USA
Almotriptan tablets	
12.5–25 mg	UK

The differences in triptan availability for the eight countries are also reflected in the licensed dosages (Table 2). For sumatriptan spray, in most of the European countries the approved attack dosage is 20 mg whereas in France the licensed attack dosage is 10 mg, the same as in the US and

Canada. The maximal daily dosage is 40 mg in all countries investigated, including France, US and Canada.

For the oral form, the maximal daily dosage is 200 mg in all eight countries. The attack dose is 50 mg in all European countries, while it is 25 mg in the US and Canada. For the injection formulation, the minimum and maximum licensed posologies are 6 and 12 mg, respectively.

The attack dose for naratriptan is 2.5 mg in European countries while it is 1 mg in the US.

The attack dose for zolmitriptan is 2.5 mg in all European countries while it is 1.25 mg in the US. The maximal daily dose is 10 mg in the US and in all the European countries but the UK (where it is 15 mg). For rizatriptan, the attack dose is 5 mg in US (half of the European dosage), but the maximal daily dosage is 30 mg as compared with 20 mg in European countries. Finally, almotriptan is available in 12.5-mg tablets (minimum) and 25-mg tablets (maximum) in the UK.

Discussion

There are differences between the different countries in the presentations of triptans and in their licensed indications and dosages. The differences between European countries and US and Canada are not always in the same directions and thus a more important role of the scientific community is necessary in better harmonizing the utilization of this important therapeutic class.

References

1. <http://headaches.about.com>
2. – (2000) WHO Collaborating Centre for Drug Statistics Methodology. ATC code 2002, WHO-CC, Oslo