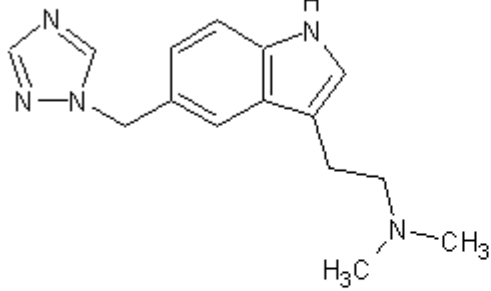


Drug In Focus February 2012: Rizatriptan

The following data is extracted from GenericsWeb Pipeline Patent Intelligence and is intended to give a brief outline of factors affecting the potential launch of generic equivalents of Merck's migraine treatment Rizatriptan (Maxalt®). Rizatriptan products had global sales of USD \$550m in 2010.

General information

Figure 1: General Information table for Rizatriptan

 <p>Molecular Structure</p>		<p>Chemical Name 3-[2-(dimethylamino)ethyl]-5-(1H-1,2,4-triazol-1-ylmethyl)indole</p>	
		<p>General Indications Treatment of acute migraine attacks</p>	
		<p>Innovator/Marketeer Merck (Maxalt, Maxalt Melt, Maxalt-MLT, Maxalt-RPD, Maxalt Smelt, Rizatan, Rizatan Smelt)</p>	
<p>Brand Product Attributes</p>			
Dosage Form	Route	Active Ingredient	Strengths
Tablets	Oral	Rizatriptan benzoate	5, 10 mg
Tablets	Orodispersible	Rizatriptan benzoate	5, 10 mg
Wafer	Orodispersible	Rizatriptan benzoate	5, 10 mg

INN Constraint Comment

Whilst patent protection for the Rizatriptan molecule expired in Canada in January 2012, protection extends to December 2012 in the US (see Figure 3); this date includes an additional 6 months paediatric extension on top of an original s156 extension. Noteworthy is that Orange book listed patent US5602162 appears to specifically disclaim the Rizatriptan molecule claimed in related issued patent US5298520, yet a paediatric extension extends expiry of the '162 patent to 2014. Reliance on 'face value' information contained in the Orange Book would therefore mislead the uninformed observer. Due to later authorisation of the product in Australia, the s70 extension on the molecule patent in this jurisdiction extends to June 2014. In Europe, many SPCs protecting the Rizatriptan molecule were granted with expiries in February 2013. Within the last few months however, Merck successfully complied with the agreed paediatric investigation plan (PIP) and has begun the process of applying for 6 month extensions to the terms of several SPCs, giving a potential expiry of August 2013.

Patent family US10448693A, the only additional key patent family identified for this INN, claims a freeze-dried unit bearing an identifying mark prepared in a container. Patents within this family are not considered to be a constraint to generic competition because the protected technology is likely to be circumvented.

Figure 2: Key Patent Indicator; the most significant patents protecting products containing Rizatriptan



Category	Priority Data	Patentee	Patent Scope	Cat	Flags
API	GB9102222A (01/02/1991)	Merck Sharp & Dohme [GB]	Rizatriptan molecule and its use in the treatment of migraine.		EXT, OB
Formulation: Freeze-dried; Process	US10448693A (01/10/1993)	Scherer Corp R P [US]	Fast-dissolving freeze-dried oral dosage form bearing an identifying mark formed within a blister pocket by a claimed process.		OB

Figure 3: Patent Family View priority application GB9102222A

Patent Country	Publication Number	Normal Expiry	Extension Number	Extension Expiry	Extension Subject	Data Excl. Expiry
AU	AU644939	31/01/2012		08/06/2014		08/06/2004
CA	CA2060139 CA2238140	28/01/2012 28/01/2012				16/07/2004
DE	EP0497512	24/01/2012	DE990007	11/02/2013	Rizatriptan Benzoate	11/02/2008
ES	EP0497512	24/01/2012	ES990033	11/02/2013	Rizatriptan Benzoate	11/02/2004
FR	EP0497512	24/01/2012	FR980037	11/02/2013	Rizatriptan	11/02/2008
GB	EP0497512	24/01/2012	GB980035P	10/08/2013	Rizatriptan (PED)	11/02/2008
US	US5298520 US5451588 US5602162 US5602163	28/01/2012 19/09/2012 11/02/2014 11/02/2014		29/12/2012		15/06/2015

Figure 4: Marketing Authorisations for products containing Rizatriptan Key Countries

Amongst the US approvals, tentative FDA approvals have been identified for generic Rizatriptan Sodium, awarded to Cipla, Mylan, Sandoz AND Teva. In the UK, Generic authorisations awarded to Actavis, Aspire, Generics UK, Glenmark, Jenson, Sandoz, Teva and Winthrop is indicative of the likely competition Rizatriptan will face across Europe upon SPC expiry.

Country	Innovator	Other (Generics)
UK	3	18
Australia	8	0
Canada	4	5
USA	4	5 (Tentative)

Figure 5: Top Patent Applicants

This chart shows a representation of patentees who have filed the most patent families for this INN. Note the prominence of relevant applications filed by manufacturers of competing triptans, Pfizer (Eletriptan) and Glaxo (Naratriptan, Sumatriptan) whose scope overlaps with Rizatriptan; as well as the diversity of applicants represented by the significant portion outside the top five.

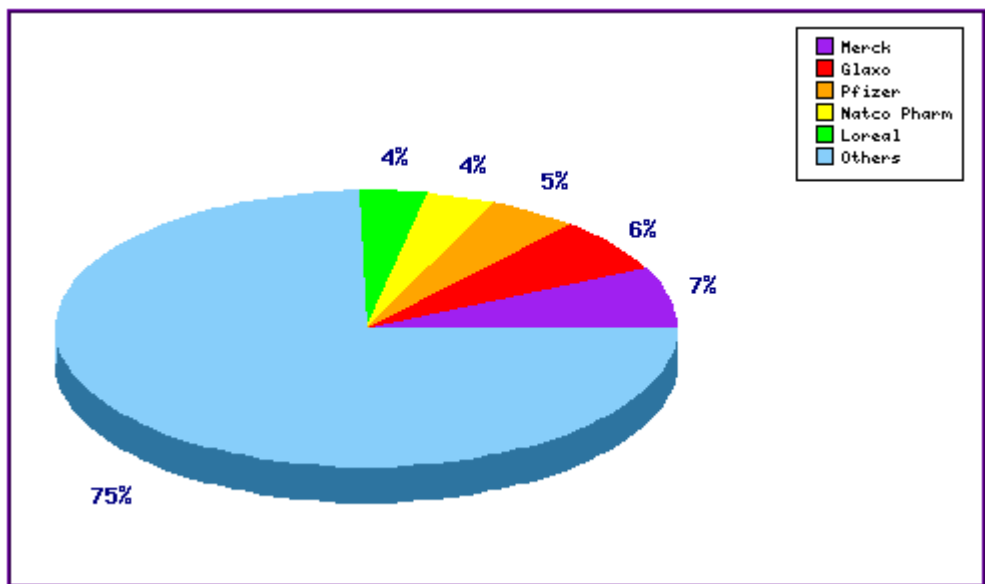


Figure 6: Patent Filing Trend

This chart represents the timing of the earliest priority filing date for each patent family identified for this molecule as well as the type of claims found in the applications. Note the strong responsive patenting by generic companies post-launch, particularly in the area of formulations.

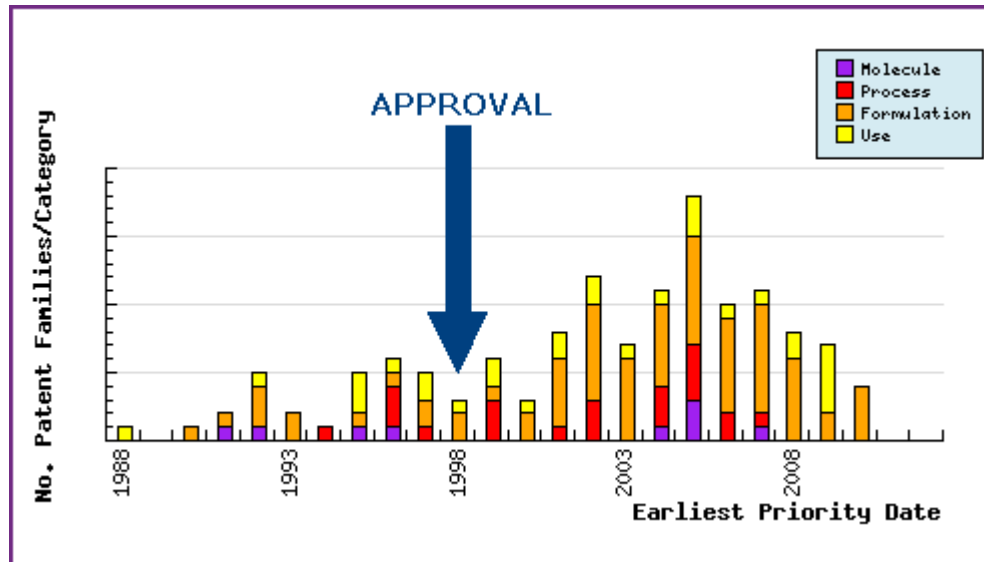
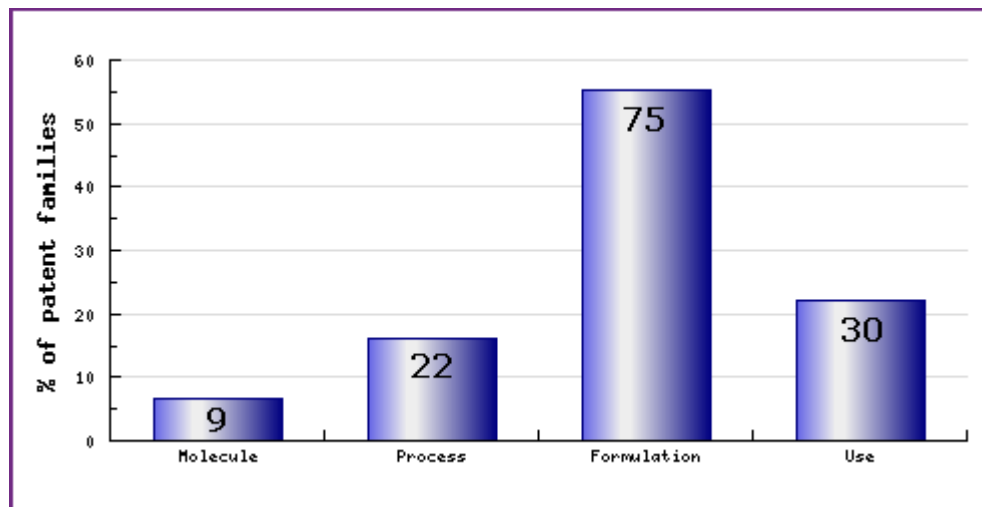


Figure 7: Patent Category Distribution

The types, number and relative distribution of patents that have been filed for Rizatriptan obtained via a comprehensive patent search (Pipeline Developer report). Note the dominance of formulation and use patent families. In addition to a wide range of oral formulations, several other administration-specific formulations have also been identified, including transdermal, nasal, buccal and inhalable formulations. The use patent families identified relate to a wide range of indications in addition to the currently approved migraine indication.



In summary, the API patent remains in force in most major territories, representing a barrier to generic competition. The number of generics available in Canada, many being authorised just two days after Canadian molecule patent expiry, the significant number of marketing authorisation holders identified in Germany and the UK and tentative ANDA approvals

observed in the US is indicative of the interest shown by generic companies for Rizatriptan generics. Merck quite reasonably anticipates that sales in the US and Europe will decline significantly following corresponding patent expiry

Please visit www.genericsweb.com to find out more about Pipeline Patent Intelligence and how it can assist your generic drug development. Register to receive our monthly newsletter INNsight, and a GenericsWeb staff member will call you to discuss your needs.

GenericsWeb - February 2012

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