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MIDLANDS

TRENT MEDICINES INFORMATION SERVICE

QIPP Detail Aid Support Document

Providing support for quality in prescribing

TRIPTANS – choice of agent

KEY MESSAGES

- **There are few comparative studies between different agents. Oral sumatriptan (50mg or 100mg) has the most evidence of all the triptans and is a suitable first option for most people.**
- **With several triptans recently coming off patent and others soon to follow, all triptans should be prescribed generically. There are significant savings to be made by using generic products.**
- **If a dispersible triptan is required, generic zolmitriptan orodispersible 2.5 mg tablets are the preferred option as they are currently the only generic dispersible formulation available.**

WHAT IS THE PROBLEM?

- *The East Midlands spent over £3million on oral or intranasal triptans in 2011-12.*

The total spend on all triptans for the financial year 2011-12 was just over £3.6 million.
Just over £500,000 was spent on injectable sumatriptan, at an average cost per item of £97.72.
Sumatriptan was the most commonly prescribed triptan, followed by zolmitriptan, rizatriptan and naratriptan.

BNF Name	Total Items	Total Act Cost
Almotriptan	11,180	£247,161.34
Eletriptan	536	£18,167.25
Frovatriptan	5,405	£118,263.05
Naratriptan Hydrochloride	18,380	£614,552.88
Rizatriptan	23,347	£712,352.05
Sumatriptan Succinate	103,809	£1,114,463.79
Zolmitriptan	28,716	£779,374.37

- *Generic sumatriptan has the lowest acquisition cost. Even if half of all oral non-dispersible triptans had been prescribed as generic sumatriptan 100mg, over £750,000 would have been available for other health interventions.*

Using the difference in cost per item between each triptan and generic sumatriptan 100mg, the potential cost savings were calculated for each agent. Dispersible and non-oral agents were removed from the calculations.

BNF Name	Cost per item	Saving opportunity
Almotriptan	£20.90	£195,202.80
Eletriptan	£33.89	£16,321.20
Frovatriptan	£21.88	£99,668.20
Naratriptan Hydrochloride	£33.43	£551,216.20
Rizatriptan	£30.51	£156,235.72
Sumatriptan Succinate	£10.73	£172,258.56
Zolmitriptan	£27.14	£378,375.16
Total		£1,569,277.84

Half of this amount would be a saving of £784,639.

Date of Preparation: October 2012

- *A generic dispersible zolmitriptan tablet is now available. If all dispersible triptans were prescribed as zolmitriptan 2.5mg, a further £675,000 could be saved.*

Figures for dispersible tablets are as follows:

	Total Items	Total Act Cost	Cost/ item
Imigran Radis 100mg	529	£35,379.13	£66.88
Imigran Radis 50mg	626	£22,049.32	£35.22
Zolmitriptan orodispersible 2.5mg	5,559	£134,587.39	£24.21
Zolmitriptan orodispersible 5mg	2,286	£71,120.42	£31.11
Zomig Rapimelt 2.5mg	1,300	£30,538.11	£23.49
Zomig Rapimelt 5mg	408	£11,685.20	£28.64
Maxalt Melt 10mg (rizatriptan)	4,196	£126,243.93	£30.09
Rizatriptan oral lyophilisate 10mg	14,025	£412,238.96	£29.39
Total	28929	£843,842.46	

The cost per item for generic zolmitriptan orodispersible 2.5mg tablet, based on 8 tablets (the average number of tablets per prescription in 2011-12), would be £5.84. If all the dispersible tablets were prescribed as generic zolmitriptan 2.5mg, this would lead to a further potential saving of nearly £675,000.

- *Sumatriptan should always be prescribed generically; over £170,000 could have been saved simply by prescribing sumatriptan tablets generically.*

Although numbers of prescriptions are small, the cost per item for Imigran tablets, particularly the 100mg tablets which is the most expensive oral triptan on the market, makes it a significant spend.

BNF Name	Total Items	Total Act Cost	Cost/ item
Imigran 50mg tablets	1,751	£68,178.94	£38.94
Imigran 100mg tablets	1,655	£113,869.29	£68.80

WHAT IS THE EVIDENCE?

- *NICE Clinical Guidelines recommend an oral triptan (with the lowest acquisition cost) with a NSAID or paracetamol as first-line options for acute migraine. If this is consistently ineffective, they recommend trying one or more alternative oral triptans.*

The NICE Clinical Guideline on the management of headaches in adults and young people (September 2012) recommend that an oral triptan combined with a NSAID or paracetamol should be the first-line option for the management of migraine with or without aura. This is a change from other guidelines (BASH, AHA) which have recommended a simple analgesic first line. The NICE Guideline Development Group (GDG) recognised that the majority of patient will have tried these options before consulting their GP.

The GDG reviewed triptans as a class, and did not appraise the evidence comparing different triptans to each other. They considered that different triptans were equally effective and thus concluded that it is cost effective to try a less costly triptan first.

The GDG considered that efficacy of triptans can vary between individuals; their consensus opinion was that failure to respond to a particular triptan may not be indicative that another triptan will also not work. It may be worth considering an alternative triptan if there's no response to the first one.

Response should not be judged on one migraine attack alone- the GDG considered that people should be encouraged to use triptan for at least three attacks before considering an alternative triptan.

- *Sumatriptan has more evidence from randomised controlled trials to support its use than any other triptan. There are few comparative studies between agents. A systematic review in 2001 found that, compared with sumatriptan 100mg:*
  Rizatriptan 5mg was similar; 10mg showed better effectiveness and consistency with similar tolerability;
  Eletriptan 20mg was less effective with similar tolerability; 40mg was similar; 80mg showed better effectiveness, similar consistency, but lower tolerability;
  Zolmitriptan 2·5mg and 5mg were similar;
  Almotriptan 12·5mg showed similar effectiveness at 2 hours but other results were better;
  Naratriptan 2·5mg was less effective but better tolerated;

There a few comparative studies between oral triptans.

A systematic review, published in the Lancet in 2001, reviewed 53 clinical trials involving 24,089 patients. They compared sumatriptan 100mg with other triptans in assessing their safety and effectiveness. Overall, 59% of patients given sumatriptan 100mg reported an improvement from moderate or severe pain to mild or no pain, 2 hours after the dose had been taken and 29% of patients were pain-free at 2 hours. Overall, 67% of patients had a consistent response in at least two of three treated attacks.
The following table is taken from the paper:

*Comparison of the main efficacy and tolerability measures for the oral triptans versus 100 mg sumatriptan.**

	Initial 2h relief	**Sustained pain free**	**Consistency**	**Tolerability**
Sumatriptan 25mg	-	=/-	-	+
Sumatriptan 50mg	=	=	=/-	=
Zolmitriptan 2.5mg	=	=	=	=
Zolmitriptan 5mg	=	=	=	=
Naratriptan 2.5mg	-	-	-	++
Rizatriptan 5mg	=	=	=	=
Rizatriptan 10mg	+	+	+(+)	=
Eletriptan 20mg	-	-	-	=
Eletriptan 40mg	=/+	=/+	=	=
Eletriptan 80mg	+(+)	+	=	-
Almotriptan 12.5mg	=	+	+	++

= indicates no difference when compared with sumatriptan 100 mg
+ indicates better when compared with sumatriptan 100 mg
- indicates inferior when compared with sumatriptan 100 mg

The SIGN guideline on the diagnosis and management of headache in adults (2008) identified three systematic reviews; the large review and meta-analysis discussed above, a systematic review compared efficacy and tolerability of triptans with placebo and a systematic review of RCTs examined efficacy and tolerability of frovatriptan compared with placebo.
The following are the main results from the three systematic reviews:

Response at two hours

Compared with 100mg sumatriptan, 10mg of rizatriptan and 80mg of eletriptan showed a greater proportion of patients with initial two hour relief.

Sustained pain-free at two hours

Compared with sumatriptan 100mg, 80mg eletriptan, 12.5mg almotriptan, and 10mg rizatiptan showed higher sustained pain-free rates at two hours post-dose.
Rizatriptan 10mg (number needed to treat (NNT)=3.1) showed higher pain-free rates at two hours than sumatriptan 50mg (NNT=4.0), sumatriptan 100mg (NNT=4.3) and naratriptan 2.5 mg (NNT=9.2).

Recurrence rates 2-24 hours

Comparison of headache recurrence rates for different triptans is problematic. Less potent, slower acting triptans which only relieve milder headaches tend to show lower recurrence rates because mild headaches may be less likely to recur. Compared with sumatriptan 100mg (30%, 95% CI 27-33), recurrence rates were lower for 40-80mg eletriptan and higher for 5 and 10mg rizatriptan. The risk of headache recurrence within 24 hours was reduced by frovatriptan, (RR 0.74, 95% CI 0.59-0.93, p=0.009) but this apparent benefit needs to be assessed in the light of confounding by headache severity.

Sustained pain-free rates

Compared with sumatriptan 100mg (rate =20%, 95% CI 18-21), sustained pain-free rates were higher for 10mg rizatriptan, 80mg eletriptan and 12.5mg almotriptan and lower for 20mg eletripan.

Consistency

Triptans produced a response to headache at two hours in at least one of three treated attacks in 79-89% of patients, compared with around 50% in placebo, two of three treated attacks in 47-72% of patients, compared with 17-33% in placebo and three of three treated attacks in 16-47% of patients compared with up to 9% in placebo. Triptan use led to freedom from pain at two hours in 51-59% of patients, compared with 18% in placebo. Sustained pain-free response in two of three treated attacks was achieved in 14-42% of patients compared with 3-13% with placebo and three of three treated attacks in 1-17% of patients compared with <2% with placebo.
Compared with placebo, the highest consistency rates were for 100mg sumatriptan and 12.5mg almotriptan.

Adverse event rates

100mg sumatriptan had a mean placebo subtracted rate of any adverse events of 13% (95% CI 8-18). Rates for other triptans overlap, except for lower values for 2.5mg naratriptan and 12.5mg almotriptan; these rates also do not differ from placebo.

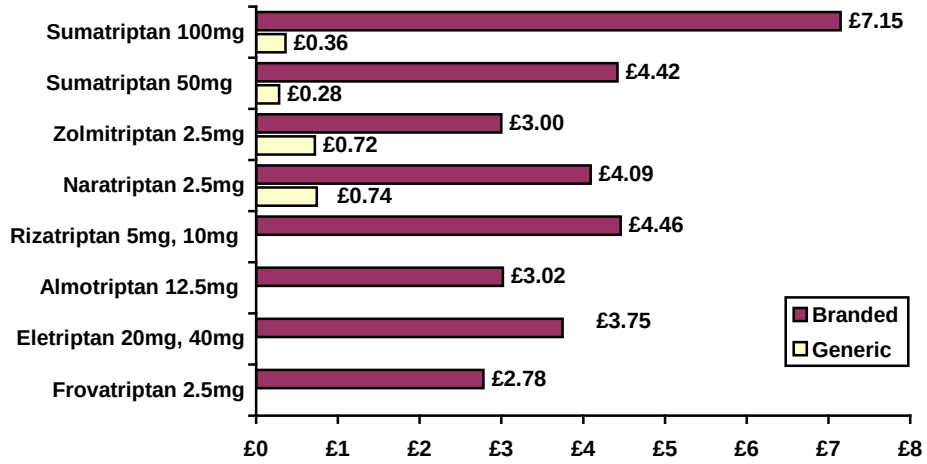
- *NICE recommend that an anti-emetic be considered in addition to other acute treatment for migraine even in the absence of nausea and vomiting. If vomiting restricts oral treatment despite an anti-emetic, consider a non-oral formulation e.g. zolmitriptan nasal spray. Sumatriptan nasal spray is not useful if vomiting precludes oral therapy as it is absorbed mostly through the GI tract; whereas about 30% of intranasal zolmitriptan is absorbed through the nasal mucosa.*

The addition of an antiemetic is based on the NICE GDG informal consensus. The decision to add an antiemetic is likely to depend on patient preference and experience of benefit without anti-emetic. The GDG noted that anti-emetics may have an effect on migraine itself and can be a useful adjunct even if the patient does not have significant nausea and vomiting.

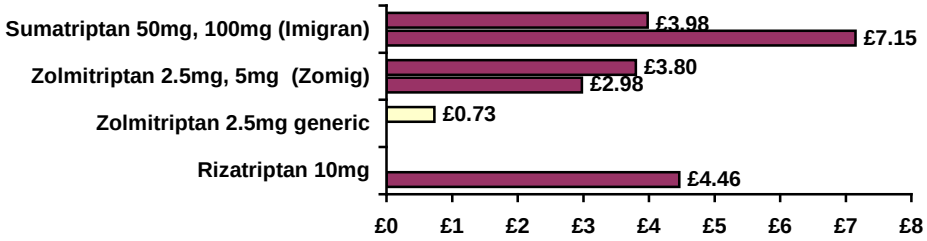
The British Association for the Study of Headaches (BASH) guidelines, updated in 2010, notes that sumatriptan nasal spray is not useful if vomiting precludes oral therapy since its bioavailability depends largely on ingestion.

WHAT ARE THE COSTS?
Costs per dose

Oral tablets



Dispersible tablets



Costs per dose. Taken from Drug Tariff/ MIMS October 2012

References:

1. NICE Clinical Guideline 150 2012 Headaches: Diagnosis and management of headaches in young people and adults Available from www.nice.org.uk
2. Ferrari MD, Roon KI, Lipton RB, Goadsby PJ. Oral triptans (serotonin 5-HT1B/1D agonists) in acute migraine treatment: a meta-analysis of 53 trials Lancet, 2001; 358(9294): 1674
3. SIGN Clinical Guideline 107 Diagnosis and management of headache in adults November 2008 Available from www.sign.ac.uk
4. BASH (2010) Guidelines for all healthcare professionals in the diagnosis and management of migraine, tension-type, cluster and medication-overuse headache. British Association for the Study of Headache. Available from www.bash.org.uk

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