Efficacy of flurbiprofen 8.75 mg spray in patients with sore throat due to an upper respiratory tract infection: A randomised controlled trial

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KEY MESSAGES
- Pharyngitis (sore throat) is usually caused by viral infections; therefore, antibiotics are generally not warranted.
- Flurbiprofen 8.75 mg spray (maximum five doses/day, for three days) provides effective symptomatic relief.

ABSTRACT
Background: Viral infections cause most cases of pharyngitis (sore throat); consequently, antibiotics are generally not warranted. However, a treatment targeting pain and inflammation, e.g. a topical non-steroidal anti-inflammatory spray, may be helpful for patients.

Objective: To evaluate the efficacy and safety of flurbiprofen 8.75 mg spray.

Methods: This randomised, double-blind, parallel group study was conducted at six community-based clinical research centres in Australia and two in New Zealand. Adults with sore throat due to upper respiratory tract infection (onset ≤ four days) took one dose of flurbiprofen (n = 249) or placebo spray (n = 256); after six hours, they could re-dose every three–six hours as required, for three days (max. five doses/day). The primary endpoint was the area under the change from baseline curve in throat soreness from zero–two hours (AUC0–2h). The change from baseline in other sore throat symptoms also assessed efficacy.

Results: The mean AUC0–2h for throat soreness was significantly greater with flurbiprofen spray (−1.82; 95% CI: −1.98 to 1.65) compared with placebo (−1.13; 95% CI: −1.27 to 0.99) (P < 0.0001). Significantly greater reductions from baseline were observed with flurbiprofen spray compared with placebo from the first time-points assessed (five minutes for throat soreness/difficulty swallowing, 20 minutes for sore throat pain intensity and 30 minutes for swollen throat) for up to six hours (P < 0.05 for all). There was no significant difference in adverse events between treatment groups during the three-day study.

Conclusion: Flurbiprofen spray provides rapid and long-lasting relief from sore throat symptoms, and is well-tolerated over three days.

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Flurbiprofen; non-steroidal anti-inflammatory; spray; pharyngitis; respiratory tract infections

Introduction
Pharyngitis is a self-limiting condition characterised by ‘inflammation of the oropharynx’, which may cause sore throat, malaise and fever.[1–3] Inflammatory mediators are thought to be responsible for sore throat, as demonstrated in studies where nasal or oropharyngeal challenge with Bradykinin and prostaglandins caused sore throat symptoms,[3–6] and stimulation of the pharyngeal mucosa with cold dry air increased inflammatory mediators and caused pain.[7] Most adult cases (~85–95%) are caused by viral upper respiratory tract infection (URTI),[1,2] although other causes include bacterial infections (including group A β-haemolytic streptococcus [GABHS], ~10% of cases) and non-infectious factors including smoking and air pollution.[2,3] URTI is a common reason for primary care consultations and as viruses cause most sore throats, antibiotics...
are not usually appropriate.[1,8] However, physicians continue to prescribe antibiotics inappropriately for sore throat and these prescribing practices contribute to the growing global problem of antibiotic resistance.[9,10]

Current treatment guidelines for sore throat advocate symptomatic relief, reserving antibiotics for bacterial infections (diagnosed by physical examination/culture) or if patients display ‘red-flag’ symptoms.[9,11–13] Antibiotics do not provide immediate or useful relief and have limited impact for bacterial sore throat (symptoms reduced by 16 hours over seven days of sore throat).[14,15] Antibiotics cause side-effects including diarrhea,[16,17] but further evidence suggests they may have more significant health impacts through their action on gut microbiota.[18–20] Patients presenting to primary care may, therefore, need reassurance that their condition is self-limiting, that antibiotics are not always needed, and treatment options are available for symptomatic relief.[13]

Flurbiprofen, a non-steroidal anti-inflammatory drug (NSAID), targets inflammation, a key cause of sore throat symptoms.[3,21] Previous studies have demonstrated the efficacy of flurbiprofen lozenge and granule formulations (8.75 mg per dose) for symptomatic relief of sore throat.[22–24] Recently, an innovative spray formulation containing 8.75 mg of flurbiprofen per dose has been developed for sore throat symptom relief. The spray formulation offers advantages such as rapid delivery to the affected area and is convenient to use.[25] Here we present the first efficacy and safety study of flurbiprofen spray in patients with sore throat due to URTI. The methods used were based on the validated Sore Throat Pain Model, which has been used for studies of flurbiprofen 8.75 mg lozenge.[23,24,26,27]

Methods

Study design

This randomised (1:1), double-blind, placebo-controlled, parallel group, multiple-dose study was performed at six community-based clinical research centres in Australia and two in New Zealand from 1 June to 28 September 2012. The centres were selected because of previous clinical trial experience and having strong primary care practice links. All but one of the principal investigators was a general practitioner. The study was conducted according to the Declaration of Helsinki (EU Directive 2001/20/EC), and complied with the International Conference on Harmonisation Good Clinical Practice and regulatory requirements (Australian New Zealand Clinical Trials Registry: ACTRN12612000457842). The study was approved by the Bellberry Human Research Ethics Committee on 19 April 2012 (approval number 2012-03-706) and the Uniting Care Health Human Research Ethics Committee on 4 May 2012 (approval number 1209). All patients provided written informed consent.

Study population

Adult patients who either presented to their general practice or community pharmacy, or responded to advertisements, were evaluated for sore throat (onset ≤ four days) due to URTI. Patients were included if they had subjective and objective findings of sore throat, including baseline scores of ≥ six on the Throat Soreness Scale (TSS); ≥50 mm on the Difficulty Swallowing Scale (DSS); ≥33 mm on the Swollen Throat Scale (SwoTS) (Table 1) and ≥ five points on the Tonsillo-Pharyngitis Assessment (TPA), an index of seven physician-assessed objective features of pharyngitis.[23,24]

Patients were ineligible if they had any evidence of mouth breathing, severe coughing, any allergy and/or intolerance to the study drug, formulation ingredients or hypersensitivity to paracetamol. Standard warnings and contraindications for NSAIDs were used to assess patient eligibility.

Study medications

Using a computer-produced, blocked randomisation schedule (produced by an independent statistician using SAS V9.2), patients were randomised to receive flurbiprofen 8.75 mg cherry mint flavoured spray or placebo spray without added flavour or odour. Patients were allocated a unique subject number, and the study drug was randomised to this sequence. Both sprays were matched for appearance and were packaged in identical 20 mL bottles labelled with ‘either flurbiprofen or placebo spray’. The patients and the investigator were blinded to the study medication, and were not informed the active product was flavoured. Patients took one dose (three sprays) and were instructed not to re-dose for six hours, after which they could re-dose every three–six hours, as required, up to five doses/day for three days. Rescue medication (two paracetamol 500 mg tablets) was supplied if required, up to four times/day for three days. Study medications were provided by Reckitt Benckiser (Hull, UK).

Study assessments

All study assessments and timings completed by the patients are detailed in Table 1.

Patients completed the first three hours of assessments under supervision then left the centre with trial
Table 1. Study assessments and timings

| Assessment | Scale ratings | 0–360 minutes after first dose | 360 minutes after first dose to end of Day 3 | Follow-up* |
|------------|---------------|--------------------------------|--------------------------------------------|------------|
|            |               | Pre-first dose | 5, 10, 15, 20, 30, 45, 60, 75, 90, 105, 120, 150, 180, 240, 300, 360 | Pre-dose and two hours post-each dose (± 15 minutes) | End of Day 1 (± 15 minutes) | End of Day 2 | End of Day 3 | Final visit |
| Demographics/medical history | X | | | | | | | |
| Throat soreness on the TSS† | 11-point ordinal subjective scale: 0 = not sore to 10 = very sore | X | X | X | X | X | X | X |
| Difficulty swallowing on the DSS‡ | 100-mm VAS: 0 = not difficult to 100 = very difficult | X | X | X | X | X | X | X |
| Swollen throat on the SwoTS‡ | 100-mm VAS: 0 = not swollen to 100 = very swollen | X | X | (from 30 minutes) | X | X | X | X | X |
| Sore throat pain intensity on the STPIS† | 100-mm VAS: 0 = no pain to 100 = severe pain | X | (from 20 minutes) | X | X | X | X | X |
| Sore throat relief on the Sore Throat Relief Scale | 7-point categorical scale: no, slight, mild, moderate, considerable, almost complete and complete relief | X | (from 20 minutes) | X | X | X | X | X |
| Throat pain on the TPS | 4-point categorical scale: no, mild, moderate and severe pain | X | X (120, 180 and 360 minutes) | X | X | X | X | X |
| GLOBAL | 5-point categorical scale: poor, fair, good, very good, excellent | X (180 minutes) | X | | | | | |
| SATIS | 7-point categorical scale: extremely dissatisfied, very dissatisfied, dissatisfied, somewhat satisfied, satisfied, very satisfied, extremely satisfied | X (180 minutes) | X | | | | | |
| CLIN | 5-point categorical scale: poor, fair, good, very good, excellent | X (180 minutes) | | | | | | |
| Spray usage | X | X | | | | | | |
| AEs | X | X | X | X | X | X | X | |

AE: adverse event; CLIN: practitioner clinical assessment of drug efficacy; DSS: Difficulty Swallowing Scale; GLOBAL: patient global evaluation of the study medication; SATIS: patient satisfaction scale; STPIS: Sore Throat Pain Intensity Scale; SwoTS: Swollen Throat Scale; TPS: Throat Pain Scale; TSS: Throat Soreness Scale; VAS: visual analogue scale.

*Follow-up was completed 1–4 days after Day 3.

†For the symptom assessments, patients were asked to swallow then complete the rating scales within 90 seconds at each time-point.
medication, rescue medication and patient diaries. Patients attended a follow-up visit within seven days to hand in their patient diary. Adverse events (AEs) were recorded throughout the study.

Sample size

To determine the study sample size, data were extrapolated from a study of flurbiprofen 8.75 mg granules.[22] Assuming the same variability and similar efficacy of the spray, 244 patients per group were required to provide at least 90% power to demonstrate a difference between the treatments at the 5% significance level.

Primary and secondary endpoints

The primary endpoint was the area under the change from baseline curve in severity of throat soreness, from zero–two hours post-first dose (AUC0–2h). The main secondary endpoints were AUC in severity of throat soreness over three and six hours (AUC0–3h and AUC0–6h) and AUC over two, three and six hours for difficulty swallowing (DSS AUC0–2h, DSS AUC0–3h and DSS AUC0–6h) and swollen throat (SwoTS AUC0–2h, SwoTS AUC0–3h and SwoTS AUC0–6h). The summed pain intensity difference (SPID) over two, three and six hours (STPIS SPID0–2h, STPIS SPID0–3h and STPIS SPID0–6h) and total sum of pain relief ratings over two, three and six hours (TOTPAR0–2h, TOTPAR0–3h, and TOTPAR0–6h) were also evaluated. All AUC and SPID endpoints were calculated using the trapezoidal rule. The last recorded score was carried forward for any missing assessments up to six hours. For ease of interpretation, the AUC or SPID values obtained were divided by the total hours the scale was assessed.

Other secondary endpoints included change from baseline in severity of throat soreness, sore throat pain intensity, difficulty swallowing and swollen throat as well as sore throat relief up to six hours, at the end of Day 1, at 24 hours (±15 minutes) post-first dose and at the end of Days 2 and 3. The percentage of patients who reported ’moderate sore throat relief’ (maintained for at least 30 minutes) was also assessed. Differences between the treatment groups for GLOBAL, SATIS, CLIN, spray usage and rescue medication consumption were evaluated.

Statistical analyses

For the primary efficacy endpoint, least square means were compared using analysis of covariance (ANCOVA) with baseline severity of throat soreness as a covariate and factors for treatment group and centre. Throat soreness, sore throat pain intensity, difficulty swallowing and swollen throat were analysed using the same ANCOVA model, with the relevant baseline value as the covariate. TOTPAR, overall spray usage and rescue medication consumption were analysed using the same method with baseline severity of throat soreness as a covariate. Two-sided statistical tests were performed with significance determined at the 5% significance level using SAS V9.2.

The intent-to-treat (ITT) population was used to evaluate the efficacy results and consisted of all patients who took study medication, and had at least one post-baseline assessment recorded. The safety population was used to evaluate the safety data and the demographic and baseline characteristics, and included all patients who took study medication.

Results

Study population

In total, 573 patients were screened, and 505 enrolled (flurbiprofen spray n = 249, placebo spray n = 256; Figure 1). Both treatment groups were well matched for baseline demographics and clinical characteristics (Table 2). Seven patients withdrew (five receiving flurbiprofen and two receiving placebo) (Figure 1).

Primary endpoint – single dose

The AUC0–2h for throat soreness was significantly greater with flurbiprofen spray compared with placebo (P < 0.0001, Table 3).
Secondary endpoints – single dose

The AUC0–3h and AUC0–6h for throat soreness were significantly greater with flurbiprofen spray compared with placebo ($P < 0.0001$, Table 3). Similar results were observed in favour of flurbiprofen spray for all endpoints (DSS AUC, SwoTS AUC, STPIS SPID and TOTPAR) at two, three and six hours ($P < 0.0001$ for all).

The change from baseline in severity of throat soreness was significantly greater with flurbiprofen spray compared with placebo from five minutes (first time-point), and at each subsequent time-point until six hours ($P < 0.01$ for all). Similarly, difficulty swallowing was significant from five minutes ($P < 0.05$), sore throat pain intensity from 20 minutes ($P < 0.01$), swollen throat from 30 minutes ($P < 0.001$) and sore

### Table 2. Patient demographics and baseline characteristics.

|                      | Flurbiprofen 8.75 mg spray ($n = 249$) | Placebo spray ($n = 256$) | Overall ($n = 505$) |
|----------------------|--------------------------------------|---------------------------|---------------------|
| Age (years) Mean ± SD| 25.5 (9.9)                           | 25.7 (10.3)               | 25.6 (10.1)         |
| Range                | 18–67                                | 18–73                     | 18–73               |
| Gender, n (%) Female | 104 (41.8)                           | 118 (46.1)                | 222 (44.0)          |
| Male                 | 145 (58.2)                           | 138 (53.9)                | 283 (56.0)          |
| Race, n (%) Caucasian| 209 (83.9)                           | 212 (82.8)                | 421 (83.4)          |
| Asian                | 31 (12.4)                            | 31 (12.1)                 | 62 (12.3)           |
| Afro-Caribbean       | 2 (0.8)                              | 1 (0.4)                   | 3 (0.6)             |
| Other                | 7 (2.8)                              | 12 (4.7)                  | 19 (3.8)            |
| TPA score Mean ± SD  | 7.76 (2.167)                         | 7.71 (2.212)              | 7.73 (2.188)        |
| Median               | 7                                    | 7                         | 7                   |
| Baseline pain TPS, n (%) Moderate pain | 199 (79.9) | 219 (89.6) | 418 (82.8) |
| Severe pain          | 29 (11.7)                            | 16 (6.3)                  | 45 (8.9)            |
| Baseline throat soreness Mean ± SD | 6.93 (0.895) | 6.99 (0.838) | 6.96 (0.866) |
| Median               | 7                                    | 7                         | 7                   |
| Minimum              | 5.0                                  | 5.0                       | 5.0                 |
| Maximum              | 10.0                                 | 10.0                      | 10.0                |
| Baseline STPIS (mm) Mean ± SD | 67.75 (11.021) | 69.11 (9.972) | 68.44 (10.514) |
| Median               | 68.0                                 | 70.0                      | 69.0                |
| Minimum              | 6.0                                  | 38.0                      | 6.0                 |
| Maximum              | 98.0                                 | 100.0                     | 100.0               |
| Baseline DSS (mm) Mean ± SD | 68.60 (10.911) | 69.66 (10.214) | 69.14 (10.566) |
| Median               | 68.0                                 | 70.0                      | 69.0                |
| Minimum              | 45.0                                 | 44.0                      | 44.0                |
| Maximum              | 98.8                                 | 95.0                      | 98.8                |
| Baseline SwoTS (mm) Mean ± SD | 66.53 (13.625) | 67.62 (11.793) | 67.09 (12.728) |
| Median               | 67.0                                 | 68.0                      | 68.0                |
| Minimum              | 33.0                                 | 33.0                      | 33.0                |
| Maximum              | 98.0                                 | 100.0                     | 100.0               |

DSS: Difficulty Swallowing Scale; TPA: Tonsillo-Pharyngitis Assessment; TPS: Throat Pain Scale; SD: standard deviation; STPIS: Sore Throat Pain Intensity Scale; SwoTS: Swollen Throat Scale.

### Table 3. Area under the change from baseline curve from zero–two hours (AUC0–2h), zero–three hours (AUC0–3h) and zero–six hours (AUC0–6h) for throat soreness (measured on an 11-point scale where 0 = not sore and 10 = very sore; ITT population).

|                      | Flurbiprofen 8.75 mg spray spray ($n = 249$) | Placebo spray ($n = 256$) | Overall ($n = 505$) |
|----------------------|--------------------------------------------|---------------------------|---------------------|
| AUC0–2h Mean (SD)    | −1.82 (1.350)                              | −1.13 (1.142)             |                    |
| Min, max             | −5.38, 0.42                                | −5.92, 0.98               |                    |
| 95% CI               | −1.98, −1.65                               | −1.27, −0.99              |                    |
| LS mean              | −1.81                                     | −1.12                     |                    |
| Difference between LS means (95% CI)−0.70 (−0.91, −0.48) |                  |                          |
| $P$-value            | <0.0001                                    |                          |                    |
| AUC0–3h Mean (SD)    | −2.01 (1.405)                              | −1.31 (1.233)             |                    |
| Min, max             | −6.67, 0.61                                | −7.08, 0.99               |                    |
| 95% CI               | −2.19, 1.84                                | −1.46, 1.16               |                    |
| LS mean              | −2.02                                     | −1.30                     |                    |
| Difference between LS means (95% CI)−0.72 (−0.94, 0.49) |                  |                          |
| $P$-value            | <0.0001                                    |                          |                    |
| AUC0–6h Mean (SD)    | −2.14 (1.551)                              | −1.50 (1.385)             |                    |
| Min, max             | −7.55, 1.06                                | −8.54, 0.55               |                    |
| 95% CI               | −2.34, −1.95                               | −1.67, −1.33              |                    |
| LS mean              | −2.16                                     | −1.50                     |                    |
| Difference between LS means (95% CI)−0.66 (−0.91, −0.41) |                  |                          |
| $P$-value            | <0.0001                                    |                          |                    |

AUC: area under the change from baseline curve; CI: confidence interval; ITT: intent-to-treat; LS: least square; SD: standard deviation. For ease of interpretation, the AUC values obtained were divided by the total hours the scale was assessed for reporting purposes.

### Secondary endpoints – single dose

The AUC0–3h and AUC0–6h for throat soreness were significantly greater with flurbiprofen spray compared with placebo ($P < 0.0001$, Table 3). Similar results were observed in favour of flurbiprofen spray for all endpoints (DSS AUC, SwoTS AUC, STPIS SPID and TOTPAR) at two, three and six hours ($P < 0.0001$ for all).

The change from baseline in severity of throat soreness was significantly greater with flurbiprofen spray compared with placebo from five minutes (first time-point), and at each subsequent time-point until six hours ($P < 0.01$ for all). Similarly, difficulty swallowing was significant from five minutes ($P < 0.05$), sore throat pain intensity from 20 minutes ($P < 0.01$), swollen throat from 30 minutes ($P < 0.001$) and sore
throat relief from 20 minutes ($P < 0.0001$; all first time-points), for up to six hours.

At two, three and six hours, and the final visit, fewer patients reported their throat pain as ‘moderate-to-severe’ with flurbiprofen spray compared with placebo ($P < 0.01$ for two, three and six hours; $P = 0.319$ for final visit). During the six hours post-first dose, 137/249 (55.0%) of patients reported at least 30 minutes of moderate sore throat relief with flurbiprofen spray compared with 89/256 (34.8%) receiving placebo ($P < 0.001$).

**Secondary endpoints – multiple dose effects**

Compared with placebo, flurbiprofen spray provided a greater reduction in the change from baseline in the severity of throat soreness, difficulty swallowing, swollen throat and sore throat pain intensity, and significantly greater sore throat relief with flurbiprofen spray compared with 89/256 (34.8%) receiving placebo ($P < 0.001$).

**Overall treatment rating**

At the end of Day 3, for the GLOBAL evaluation, more patients rated flurbiprofen spray as fair or above (207/238 [87.0%]) compared with placebo (175/251 [69.7%]; $P < 0.0001$) and more patients rated flurbiprofen spray as good or above (153/238 [64.3%]) compared with placebo (125/251 [49.8%]; $P < 0.05$).

At the end of Day 3, for the CLIN evaluation, more practitioners rated flurbiprofen spray as fair or above (199/243 [81.9%]) compared with placebo (159/253 [62.8%; $P < 0.0001$) and more rated flurbiprofen spray as good or above (135/243 [55.6%]) compared with placebo (113/253 [44.7%]; $P < 0.05$).

**Spray usage**

Overall spray usage was similar between the treatment groups: 1.21 doses (95% CI: 1.12–1.29) and 1.15 doses (95% CI: 1.08–1.22) during Day 1 and 4.47 doses (95% CI: 4.08–4.87) and 4.10 doses (95% CI 3.73–4.46) over the three-day period for flurbiprofen and placebo, respectively.

**Rescue medication consumption**

Rescue medication consumption was similar between the treatment groups: 2.18 doses (95% CI: 1.95–2.42) and 2.38 doses (95% CI: 2.10–2.65) during Day 1 and 5.76 doses (95% CI: 4.66–6.86) and 5.65 doses (95% CI: 4.69–6.62) over the three-day period for flurbiprofen spray and placebo, respectively.

**Safety**

More patients receiving flurbiprofen spray reported AEs compared with placebo following a single dose (flurbiprofen spray 6.8%, placebo 3.1%), which approached statistical significance ($P = 0.055$) and during the overall three-day treatment period (flurbiprofen spray 12.4%, placebo 8.2%; $P = 0.119$). Most AEs were mild (Table 4).

**Discussion**

**Main findings**

This study evaluated the efficacy and safety of flurbiprofen spray in patients with sore throat due to URTI. Flurbiprofen spray rapidly reduced symptoms and provided significantly more relief for up to six hours compared with placebo, and over three days. Sore throat usually resolves within three–seven days[15] therefore, patients may require treatment for several days, particularly in the first few, when symptoms are most severe. At study end (before unblinding), both patients and the investigator rated flurbiprofen spray more favourably than placebo.

| Table 4. Treatment-emergent adverse events. |
|---------------------------------------------|
| Flurbiprofen 8.75 mg spray (n = 249)*        | Placebo spray (n = 256)†                       | All patients (n = 505) |
|---------------------------------------------|------------------------------------------------|------------------------|
| | Headache, n (%)                           | 7 (2.8)                                        | 6 (2.3)                | 13 (2.6)                         |
| | Throat irritation, n (%)                  | 6 (2.4)                                        | 2 (0.8)                | 8 (1.6)                          |
| | Abdominal discomfort, n (%)               | 1 (0.4)                                        | 1 (0.4)                | 2 (0.4)                          |
| | Dyspepsia, n (%)                          | 1 (0.4)                                        | 1 (0.4)                | 2 (0.4)                          |
| | Chest discomfort, n (%)                   | 1 (0.4)                                        | 1 (0.4)                | 2 (0.4)                          |
| | Ulcer, n (%)                              | 1 (0.4)                                        | 1 (0.4)                | 2 (0.4)                          |
| | Seasonal allergy, n (%)                   | 1 (0.4)                                        | 0 (0.0)                | 1 (0.2)                          |
| | Alcohol poisoning, n (%)                  | 1 (0.4)                                        | 0 (0.0)                | 1 (0.2)                          |
| | Back pain, n (%)                          | 0 (0.0)                                        | 1 (0.4)                | 1 (0.2)                          |
| | Rash, n (%)                               | 0 (0.0)                                        | 1 (0.4)                | 1 (0.2)                          |
| No adverse events were assessed as definitely related to the study medication. |

*In the flurbiprofen spray group, 8/249 (3.2%) of patients reported AEs that were probably related to the study medication and 9/249 (3.6%) reported AEs possibly related to the study medication.

† In the placebo spray group, 9/256 (3.5%) reported AEs possibly related to the study medication.
**Strengths and limitations**

This was the first efficacy and safety study of a new flurbiprofen spray formulation; therefore, although the results are promising, flurbiprofen spray is only one potential option for pain relief in patients with acute sore throat, and should be recommended only if appropriate. The study was conducted on an established drug formulation, over a short period, and the study design was robust and used well-validated methodologies.[23,24,26,27] Patients in both groups took a similar number of doses over three days, enabling a fairer comparison between treatments. However, patients were recruited from different sources (general practice, community pharmacy or advertisements) and may have had a diverse range of symptoms although this would more accurately represent the patient population. Another limitation was that the placebo was not matched, as it was flavourless and odourless. However, treatments were provided in identical packaging, and sufficient steps were taken to ensure both patients and investigator were blinded to the study medication, and were not informed the active product was flavoured. A review of the potential issues with blinding in this study concluded that only a series of unlikely events would have led to the blinding being broken. For example, an issue would have only occurred if a member of the study site staff had consulted documentation describing the study drug, or if they had tasted or smelt the products and then informed the patient of their opinion. The mild cherry and mint flavour was not considered detectable by anyone dosing the patients and, as the study was a parallel design, patients would not have tried both products. Also, at the time of the study, the flurbiprofen spray was not marketed in Australia and New Zealand and was, therefore, unfamiliar to patients. Therefore, sufficient steps were taken to ensure the blinding was complete and that there was no bias towards either treatment. The removal of the flavour from the placebo spray also meant that comparisons between the treatments were against the whole product and sensorial benefits of the flavour were assessed.

**Comparison with existing literature**

Previous studies have also been conducted using flurbiprofen granules, which significantly reduced throat soreness for up to five hours compared with placebo ($P < 0.05$) and flurbiprofen lozenge, which significantly reduced sore throat pain intensity, difficulty swallowing and swollen throat for up to four hours compared with placebo ($P < 0.05$ for all).[22,23] In this study, flurbiprofen spray provided at least 30 minutes of at least moderate relief in a higher proportion of patients, and previously patient perception of at least moderate relief from acute pain has been shown to be clinically important.[28]

Many patients visit physicians with sore throat and in a questionnaire-based study in Belgium, the top two reasons for visiting a doctor were to establish the cause (85.5%) and seek pain relief (84.5%); hopes for an antibiotic only ranked 11th out of 13 items (37.6%).[1,8,29] Therefore, patients who seek advice may be looking for symptomatic relief, instead of antibiotics.

**Implications**

The healthcare setting in Australia and New Zealand is similar to that in Europe, and healthcare provision for ailments such as sore throat is provided by the local pharmacy, as well as the physician who plays an important role in consultations for URTI. As such, the results of this study are likely to be generalisable to European populations.

The long-lasting relief provided by flurbiprofen spray may mean that patients would not need to regularly re-dose and could resume normal activities quickly. The reduction in functional symptoms (difficulty swallowing and swollen throat) would also be of benefit to patients and could be attributed to flurbiprofen’s anti-inflammatory action. As sore throat is self-limiting and in most cases does not require antibiotics, patients may just need advice on self-managing their symptoms.[13] Active dialogue with patients will enable physicians to advise on self-management when appropriate, the expected course of their sore throat, and what symptoms may warrant a return visit.[13]

**Conclusion**

This study showed that flurbiprofen 8.75 mg spray provides relief for up to six hours, from a range of sore throat symptoms and is well-tolerated over three days.

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**Declaration of interest**

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