et al. 1988a,b; Takabatake et al. 1986) [see section 5].

There are conflicting data concerning the effects of haemodialysis on roxatidine pharmacokinetics. Lameire and associates (1988a) reported that haemodialysis had no influence on roxatidine plasma concentrations in 3 patients who had received an oral dose of roxatidine acetate 150mg. Conversely, Aizawa et al. (1988) found that plasma roxatidine concentrations were markedly reduced in 3 patients after 4 hours' haemodialysis, and administration of roxatidine acetate 75mg to a small number of patients with chronic renal failure produced a mean roxatidine haemodialysis elimination rate of 35.7% (Hachisu & Yoshida 1991). Nevertheless, roxatidine acetate 75mg 3 times weekly appeared to be an effective regimen for peptic ulcer disease in patients undergoing haemodialysis 2 or 3 times per week (Hachisu & Yoshida 1991).

3. Therapeutic Efficacy

The therapeutic efficacy of oral roxatidine acetate has been investigated in patients with duodenal ulcer, gastric ulcer, and to a much lesser extent in patients with reflux oesophagitis, stomal ulcer, or those requiring prophylaxis for acid aspiration pneumonitis. Although a large amount of data has been obtained from noncomparative Japanese trials, an increasing number of double-blind studies have compared roxatidine acetate with the 'established' H2-receptor antagonists cimetidine and ranitidine. Additionally, recent large-scale trials have focused on the use of roxatidine acetate as maintenance therapy for the prevention of duodenal and gastric ulcer recurrence.

3.1 Duodenal Ulcer

3.1.1 Noncomparative and Dose-Ranging Studies

Roxatidine acetate 75mg twice daily has been administered in nonblind fashion to relatively small numbers of patients with duodenal ulcer. Six-week ulcer healing rates ranged from 73 to 93%, and 8-week rates from 87 to 95% (table II). Miyoshi and colleagues (1985e) found a dose-response relationship for endoscopic healing rates and documented rather low 6-week healing rates ranging from 50 to 73% after administration of roxatidine acetate 25 to 75mg twice daily. Hentschel and associates (1988) compared 2 dosage regimens of roxatidine acetate - 75mg twice daily and 150mg at bedtime - in double-blind fashion in over 300 outpatients with duodenal ulcer. Marked reductions in ulcer size were noted in both groups after 14 days' treatment, and respective 4-week ulcer healing rates were 89 and 88%. Gradual reductions in subjective assessments of day- and night-time epigastric pain, and a similar consumption of antacid tablets were documented for both groups; smoking did not influence ulcer healing rates.

3.1.2 Comparisons with Other H2-Receptor Antagonists

Both roxatidine acetate and cimetidine have shown endoscopic healing rates of about 75, 80 and 90% after 3, 4 and 6 weeks' administration, respectively, to patients with duodenal ulcer (fig. 3; table 3). Despite incomplete healing of some ulcers at the end of some trials, steady reductions in ulcer diameter and improvements in the subjective assessment of ulcer pain were noted during roxatidine acetate or cimetidine therapy. A gradual increase in the number of patients experiencing complete pain relief was also noted (Dammann et al. 1988b). Thus, roxatidine acetate and cimetidine have shown similar efficacy in the treatment of duodenal ulcer, and no statistically significant differences have been identified between the 2 agents.

Endoscopic ulcer healing rates of 60% after 2 weeks', 72 to 83% after 4 weeks', and 94% after 6 weeks' roxatidine acetate administration to patients with duodenal ulcer were documented; respective healing rates after ranitidine administration were 55%, 79 to 84%, and 89% (see table III). Ulcer healing rates and day- and night-time pain relief, calculated from life-table analyses (fig. 4), were not significantly different for the 2 agents. The mean daily consumption of antacid tablets was also similar in both groups (Hüttemann 1988).
Table II. Results of noncomparative and dose-ranging clinical trials in which roxatidine acetate was administered to patients with duodenal ulcer

<table>
<thead>
<tr>
<th>Reference</th>
<th>No. of patients</th>
<th>Dosage (mg)</th>
<th>Endoscopic healing rate (%)&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>2 weeks</td>
</tr>
<tr>
<td><strong>Noncomparative trials</strong></td>
<td></td>
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<tr>
<td>Asaka et al. (1985)</td>
<td>15</td>
<td>75 bid</td>
<td></td>
</tr>
<tr>
<td>Fukuda et al. (1985)</td>
<td>9</td>
<td>75 bid</td>
<td></td>
</tr>
<tr>
<td>Sato et al. (1985)</td>
<td>19</td>
<td>75 bid</td>
<td></td>
</tr>
<tr>
<td>Takemoto et al. (1985)</td>
<td>41</td>
<td>75 bid</td>
<td></td>
</tr>
<tr>
<td>Tsuchiya et al. (1985)</td>
<td>32</td>
<td>75 bid</td>
<td></td>
</tr>
<tr>
<td><strong>Dose-ranging trials</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hentschel et al. (1988)</td>
<td>163</td>
<td>75 bid</td>
<td></td>
</tr>
<tr>
<td></td>
<td>170</td>
<td>150 nocte</td>
<td></td>
</tr>
<tr>
<td>Miyoshi et al. (1985a)</td>
<td>16</td>
<td>25 bid</td>
<td></td>
</tr>
<tr>
<td></td>
<td>22</td>
<td>50 bid</td>
<td></td>
</tr>
<tr>
<td></td>
<td>33</td>
<td>75 bid</td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup> Percentage of patients with ulcers healed.

Abbreviations: bid = twice daily; nocte = at bedtime.

Epidemiological evidence suggests that there is a link between peptic ulceration and cigarette smoking, and duodenal ulcer healing rates are known to be slower in smokers than nonsmokers (Hentschel et al. 1988; Hüttemann 1988). However, Hüttemann (1988), and Walt and associates (1991) found no significant differences in ulcer healing rates between smokers and nonsmokers treated with either roxatidine acetate or ranitidine.

3.2 Maintenance Therapy for the Prevention of Duodenal Ulcer Recurrence

About 80 to 90% of patients with duodenal ulcers healed by H<sub>2</sub>-receptor antagonists experience ulcer relapse within 1 to 2 years of stopping treatment. Additionally, for patients who receive H<sub>2</sub>-receptor antagonists as maintenance therapy, annual ulcer recurrence rates usually range from 15 to 44% (Brogden et al. 1982; European Cooperative Roxatidine Study Group 1991).

To date, only 2 trials have prospectively assessed the efficacy of roxatidine acetate as long term (6 to 12 months) maintenance therapy for the prevention of duodenal ulcer recurrence (Brunner 1988; European Cooperative Roxatidine Study Group 1991). In a multicentre noncomparative trial, a total of 105 patients with healed duodenal ulcers after short term treatment with roxatidine acetate 75mg twice daily, received 6 months’ maintenance treatment with roxatidine acetate 75mg every night. Ulcer relapse rates were 18% and 35% after 3 and 6 months, respectively. In contrast to the findings of short to medium term studies with roxatidine acetate in which smoking had no significant effect on ulcer healing (see Hentschel et al. 1988, for example), smoking was associated with a much greater relapse rate. After 6 months, smokers of more than 10 cigarettes per day had an ulcer relapse rate (18% of the total number of patients studied) twice that of nonsmokers (9%); the relapse rate was 8% for smokers of less than 10 cigarettes per day. Although reports of slight to moderate epigastric tenderness increased marginally during the study, there was no significant increase in the incidence of ulcer pain and indeed, most patients did not experience ulcer pain (Brunner 1988). In another multicentre, but randomised double-blind, trial 372 patients with healed duodenal ulcers received a similar roxatidine acetate maintenance
Fig. 3. Endoscopic ulcer healing rates after administration of roxatidine acetate or cimetidine for 3, 4 and 6 weeks to patients with duodenal ulcer; a = 330 patients; b = ulcers healed or markedly reduced in size; c = healing defined as complete epithelialisation of the ulcer crater. Abbreviations: bid = twice daily; qid = 4 times daily.

regimen or placebo for 12, rather than 6 months. Cumulative recurrence rates were significantly (p = 0.0001) lower in roxatidine acetate vs placebo recipients throughout the study: 13 vs 40%, 30 vs 60%, and 35 vs 66% after 4, 9 and 12 months, respectively (fig. 5). Of patients experiencing ulcer relapse, this was asymptomatic in 26% of roxatidine acetate and 16% of placebo recipients. Although smoking and alcohol consumption had no influence on ulcer recurrence rate, this may have been because relatively small numbers of roxatidine acetate-treated patients actually smoked or drank (European Cooperative Roxatidine Study Group 1991).

Thus, roxatidine acetate 75 mg administered every night would seem to be an effective regimen for the prevention of duodenal ulcer recurrence. Large-scale comparative trials with 'traditional' H₂-receptor antagonists such as cimetidine and ranitidine would be useful to confirm the efficacy of roxatidine acetate in this indication.

3.3 Gastric Ulcer

3.3.1 Noncomparative and Dose-Ranging Studies

Several noncomparative trials have assessed the efficacy of roxatidine acetate 75 mg administered twice daily to relatively small numbers of patients with gastric ulcer (table IV). Four-week endoscopic ulcer healing rates ranged from 35 to 59%, and 8-week healing rates ranged from 77 to 96%.

The efficacy of 3 roxatidine acetate dosage regimens (25, 50 and 75 mg twice daily) was assessed in a small-scale, nonblind trial in 68 patients with gastric ulcer (Miyoshi et al. 1985e). Ulcer healing rates after 8 weeks' therapy tended to be greater with 100 and 150 mg, compared with 50 mg daily doses (78 and 77% vs 69%, respectively). Healing rates after 4 weeks had been very similar (39 and 41% vs 38%, respectively). Although such data indicate no real therapeutic advantage of 150 over 50 mg/d, a clearer dose-response relationship was identified in patients with duodenal ulcer (Miyoshi et al. 1985e; see section 3.1.1). A larger study compared the efficacy of roxatidine acetate 75 mg twice daily with that of 150 mg once daily in a total of 343 patients with gastric ulcer under a double-blind protocol, and demonstrated similar ulcer healing rates after 4 (54 vs 57%) and 8 (84 vs 86%) weeks (Rösch 1988). Gradual reductions in day- and nighttime epigastric pain were also noted during the 8-week treatment period: mean pain score was reduced from 2.07 to 0.2 with a 75 mg twice daily regimen, and from 2.06 to 0.36 with a 150 mg once daily schedule. In terms of ulcer healing rates, pain relief, and concomitant use of antacid tablets, there were no significant differences between the 2 groups. Smoking status and alcohol consumption had no significant influence on ulcer healing rates in either treatment group.
3.3.2 Comparisons with Other H₂-Receptor Antagonists

Roxatidine acetate and cimetidine produced similar ulcer healing rates of approximately 80% after 8 weeks' administration to patients with gastric ulcer (see table III). Although some ulcers remained unhealed after 8 weeks, reductions in ulcer size were noted during treatment with no significant difference between the 2 groups. There was also a steady increase in the number of patients experiencing a complete and permanent relief of ulcer pain during therapy, again with no significant difference between the 2 regimens (Dammann et al. 1988b). Epigastric pain has also disappeared significantly more often in roxatidine acetate vs cimetidine recipients during the first week of treatment (Miyoshi et al. 1985b). Thus, in terms of efficacy, no significant differences between roxatidine acetate and cimetidine have been documented.

Similar statistically significant reductions in mean ulcer diameter, and similar ulcer healing rates were noted in both roxatidine acetate and ranitidine recipients after 4 and 8 weeks' treatment (table III). Smoking had no significant influence on ulcer healing rates in either treatment group, and no significant difference in the concomitant use of antacid tablets was noted between the 2 regimens. Significant increases occurred in the number of patients experiencing complete relief of day- and night-time epigastric pain (Judmaier 1988). Overall, no significant differences were identified between roxatidine acetate and ranitidine in this study, suggesting that the 2 agents have similar efficacy in the treatment of patients with gastric ulcer.

Table III. Results of large-scale, double-blind trials which assessed the efficacy of roxatidine acetate in relation to other H₂-receptor antagonists in patients with peptic ulcer disease

<table>
<thead>
<tr>
<th>Reference</th>
<th>No. of pts</th>
<th>Dosage (mg)</th>
<th>Endoscopic ulcer healing rates (% of patients)</th>
<th>Relative efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>2 wks 3 wks 4 wks 6 wks 8 wks</td>
<td></td>
</tr>
<tr>
<td>Duodenal ulcer</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cimetidine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dammann et al. (1988b)</td>
<td>248</td>
<td>ROX: 150 nocte</td>
<td>81</td>
<td>82</td>
</tr>
<tr>
<td></td>
<td>a</td>
<td>CIM: 800 nocte</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inoue (1988)</td>
<td>156</td>
<td>ROX: 75 bid</td>
<td>75</td>
<td>92</td>
</tr>
<tr>
<td></td>
<td>174</td>
<td>RAN: 200 qid</td>
<td>74</td>
<td>93</td>
</tr>
<tr>
<td>Ranitidine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hüttemann (1988)</td>
<td>169</td>
<td>ROX: 75 bid</td>
<td>72</td>
<td>94</td>
</tr>
<tr>
<td></td>
<td>93</td>
<td>RAN 150 bid</td>
<td>79</td>
<td>89</td>
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<tr>
<td>Walt et al. (1991)</td>
<td>99</td>
<td>ROX: 150 nocte</td>
<td>60</td>
<td>83</td>
</tr>
<tr>
<td></td>
<td>97</td>
<td>RAN: 300 nocet</td>
<td>55</td>
<td>84</td>
</tr>
<tr>
<td>Gastric ulcer</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Cimetidine</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Inoue (1988)</td>
<td>181</td>
<td>ROX: 75 bid</td>
<td>37</td>
<td>82</td>
</tr>
<tr>
<td></td>
<td>183</td>
<td>RAN: 200 qid</td>
<td>42</td>
<td>80</td>
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<tr>
<td>Ranitidine</td>
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<tr>
<td>Judmaier (1988)</td>
<td>181</td>
<td>ROX: 75 bid</td>
<td>60</td>
<td>86</td>
</tr>
<tr>
<td></td>
<td>93</td>
<td>RAN: 150 bid</td>
<td>66</td>
<td>88</td>
</tr>
</tbody>
</table>

a Data not provided.

Abbreviations: ROX = roxatidine acetate; CIM = cimetidine; RAN = ranitidine; nocte = every night; bid = twice daily; qid = 4 times daily; = signifies equivalent to.
Daytime

Estimated survival function

Roxatidine
Ranitidine

Night-time

Estimated survival function

Days of treatment

0.0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1.0

0 5 10 15 20 25 30 35 40 45

Fig. 4. Day- and night-time pain relief, based on life-table analyses, for patients with duodenal ulcers who received roxatidine acetate 75mg twice daily (n = 169) or ranitidine 150mg twice daily (n = 93); each point indicates the percentage of patients with complete or continued pain relief at the respective time (after Hüttemann 1988).

3.4 Maintenance Therapy for the Prevention of Gastric Ulcer Recurrence

In a noncomparative, multicentre trial, 78 patients with gastric ulcers healed by the twice daily administration of roxatidine acetate 75mg, received roxatidine acetate 75mg at night for 6 months. The 6-month ulcer recurrence rate was 35% (25/71 patients). There was no significant increase in the incidence of epigastric pain during the trial period and no correlation was seen between the ulcer relapse rate and pain recurrence (Börsch 1988). Another multicentre, but double-blind placebo-controlled, trial assessed the efficacy of 12 months' maintenance therapy with roxatidine acetate 75mg at night in 269 patients with healed gastric ulcer. Cumulative ulcer recurrence rates after 4, 9 and 12 months were 11 vs 39%, 28 vs 60% and 32 vs 71%, respectively, for roxatidine acetate vs placebo recipients (fig. 5). In agreement with the work of Börsch (1988), smoking and alcohol consumption appeared to have no significant influence on the rate of ulcer recurrence (European Coop- erative Roxatidine Study Group 1991).

3.5 Other Therapeutic Uses

3.5.1 Reflux Oesophagitis

Data from noncomparative trials involving small numbers of patients suggest that roxatidine acetate 75mg administered twice daily may be effective in the treatment of reflux oesophagitis. Eight-week endoscopic healing rates ranged from 53 to 60%, and 83 to 97% of all subjective and objective

Fig. 5. Cumulative ulcer recurrence rates after 4, 9 and 12 months' administration of placebo or roxatidine acetate 75mg every night to a total of 641 patients with healed peptic ulcers; at all times, roxatidine acetate vs placebo recipients had significantly lower (p = 0.0001) ulcer recurrence rates (after Brandstatter et al. 1991).
Table IV. Results of noncomparative and dose-ranging clinical trials in which roxatidine acetate was administered to patients with gastric ulcer

<table>
<thead>
<tr>
<th>Reference</th>
<th>No. of patients</th>
<th>Dosage (mg)</th>
<th>Endoscopic healing rate (%)&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
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<td>4 weeks</td>
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<td>Noncomparative trials</td>
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<td>Asaka et al. (1985)</td>
<td>34</td>
<td>75 bid</td>
<td></td>
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<tr>
<td>Fukuda et al. (1985)</td>
<td>14</td>
<td>75 bid</td>
<td></td>
</tr>
<tr>
<td>Harada et al. (1990)</td>
<td>22&lt;sup&gt;b&lt;/sup&gt;</td>
<td>75 od</td>
<td></td>
</tr>
<tr>
<td>Mizuochi et al. (1985)</td>
<td>16</td>
<td>75 bid</td>
<td></td>
</tr>
<tr>
<td>Sato et al. (1985)</td>
<td>23</td>
<td>75 bid</td>
<td></td>
</tr>
<tr>
<td>Takemoto et al. (1985)</td>
<td>62</td>
<td>75 bid</td>
<td></td>
</tr>
<tr>
<td>Tsuchiya et al. (1985)</td>
<td>33</td>
<td>75 bid</td>
<td></td>
</tr>
<tr>
<td>Dose-ranging trials</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Miyoshi et al. (1985)e</td>
<td>18</td>
<td>25 bid</td>
<td>38</td>
</tr>
<tr>
<td></td>
<td>19</td>
<td>50 bid</td>
<td>39</td>
</tr>
<tr>
<td></td>
<td>31</td>
<td>75 bid</td>
<td>41</td>
</tr>
<tr>
<td>Rösch (1988)</td>
<td>172</td>
<td>75 bid</td>
<td>54</td>
</tr>
<tr>
<td></td>
<td>171</td>
<td>150 nocte</td>
<td>57</td>
</tr>
</tbody>
</table>

<sup>a</sup> Percentage of patients with ulcers healed.
<sup>b</sup> Patients received concomitant therapy with aldiox (aluminium dihydroxyallantoinate) 0.8 g/day.

Abbreviations: od = once daily; bid = twice daily; nocte = at bedtime.

symptoms (e.g. dysphagia, epigastralgia and heartburn) disappeared within 4 weeks of starting therapy (Inoue 1988; Kishi 1986; Sekiguchi et al. 1985). Additionally, in a double-blind trial, roxatidine acetate 150mg administered at night (n = 20), and 75mg administered twice daily (n = 22) produced 8-week endoscopic healing rates of 56 and 60%, respectively. After 12 weeks, respective healing rates were 75 and 81% (Sekiguchi et al. 1990). Thus, initial data suggest that roxatidine acetate may be an effective agent in the treatment of reflux oesophagitis, although these preliminary findings require confirmation in longer-term studies.

3.5.2 Prophylaxis of Acid Aspiration Pneumonitis

Acid aspiration pneumonitis is one of the most dangerous complications of general anaesthesia (Kawanishi et al. 1986). Perioperative reflux and subsequent aspiration of gastric juice has been associated with a relatively high mortality rate of 20 to 70% for patients with aspirated gastric juice volume greater than 25ml and pH less than 2.5 (Yokoi et al. 1985). Treatment with H<sub>2</sub>-receptor antagonists such as roxatidine acetate is aimed at increasing gastric pH and decreasing the volume of gastric juice.

In nonblind studies, 1 or 2 doses of roxatidine acetate 75mg have been administered to patients awaiting surgery (i.e. before induction of anaesthesia) [Kawanishi et al. 1986; Yokoi et al. 1985]. The volume and acidity of gastric contents was significantly reduced immediately after induction (Yokoi et al. 1985) and during the perioperative period (Kawanishi et al. 1986), compared with control patients who did not receive roxatidine acetate. Compared with placebo, roxatidine acetate 75mg, administered the evening before and 2 hours before surgery, significantly (p < 0.05) reduced the volume of gastric juice (the volume exceeded 25ml in 4.5% of roxatidine acetate vs 33.3% of placebo recipients) and increased its pH (at extubation no roxatidine acetate vs 31% of placebo recipients had an intragastric pH < 2.5) [Tanaka et al. 1985]. Similar results were reported by Tryba et al. (1988) with roxatidine acetate 150mg administered as a single
dose the evening before surgery. These initial studies indicate that roxatidine acetate 150mg, administered as a single or divided dose before the induction of anaesthesia, reduced the risk of acid aspiration pneumonitis by decreasing the volume of gastric juice and increasing its pH.

3.5.3 Stomal Ulcer

Stomal ulcer may occur in the remaining duodenum or stomach after duodenal or gastric resection for the treatment of peptic ulcer disease. H2-Receptor antagonists may be effective agents for treating stomal ulcers. For example, twice daily administration of roxatidine acetate 75mg to patients with stomal ulcer produced a 4-week endoscopic healing rate of 56% (Fukutomi 1985) and an 8-week healing rate of approximately 80% (Fukutomi 1985; Inoue 1988). Eight-week ulcer healing rates were greater in out- (91%) than in-patients (67%) and epigastric pain had disappeared in 95% of patients after 3 weeks' treatment (Fukutomi 1985).

4. Tolerability

Worldwide tolerability data from a total of 1885 patients show that the most common adverse events during roxatidine acetate therapy are hypersensitivity reactions of the skin [rash (0.37%)] and gastrointestinal tract [diarrhoea (0.58%), constipation (0.37%) and nausea (0.32%)], and CNS effects [headache (0.69%), asthenia (0.42%) and dizziness (0.27%); see fig. 6]. Additionally, in completed trials involving roxatidine acetate recipients, only 1 patient has experienced a serious (as defined by FDA criteria) and possibly drug-related adverse event: confusion (Dammann et al. 1988b).

Japanese nonblind, noncomparative and comparative trials, which involved a total of 1623 patients, revealed an overall incidence of 1.7% for adverse reactions produced by roxatidine acetate (Inoue 1988). 28 patients experienced 30 adverse events, which usually resolved after stopping treatment. The major reactions were skin rashes, constipation and CNS effects (Inoue 1988). Although changes in AST and ALT levels, and eosinophil counts occurred in some patients, these were not considered clinically significant (Inoue 1988).

In short term studies monitored by the manufacturer, 66/1603 (4.1%) patients experienced adverse reactions considered at least possibly related to the drug (Dammann et al. 1988b). Again, the major reactions were skin rashes, gastrointestinal symptoms (constipation, diarrhoea, nausea, vomiting, dysphagia, rectal disorder) and CNS effects (headache, vertigo, asthenia, dizziness, insomnia, nervousness, sensory disturbances, malaise). Treatment was stopped in 12 patients (0.7%) because of adverse effects. Other events considered at least possibly related to roxatidine acetate therapy included angina pectoris, tachycardia, oedema, reduced libido, impotence and hyperlipaemia. Like cimetidine and ranitidine, roxatidine acetate has been associated with raised serum cholesterol levels in approximately 3% of recipients. This may be explained by increases in dietary cholesterol resulting from relief of ulcer pain and subsequent increases in appetite (Dammann et al. 1988b).

Roxatidine acetate, unlike cimetidine, has no antiandrogenic activity (see section 1.6) and no effect on hepatic drug metabolism (section 1.7). Thus, roxatidine acetate may be expected to have a better tolerability and safety profile than cimetidine. However, in terms of rare serious adverse effects, such as hepatitis, cholestasis, leucopenia and agranulocytosis, more extensive clinical experience with roxatidine acetate is required before definitive statements about tolerability and safety, relative to other H2-receptor antagonists, can be made (Dammann et al. 1988b).

5. Dosage and Administration

The recommended oral dosage of roxatidine acetate in the treatment of peptic ulcer disease is 75mg in the morning and evening, or 150mg in the evening for 8 weeks. If endoscopy reveals ulcer healing, then the duration of treatment may be reduced. The absence of gastric cancer should be confirmed before treatment with roxatidine acetate is started. In several world markets, roxatidine acetate 75mg every evening is approved for the pre-
vention of duodenal and gastric ulcer recurrence. Roxatidine acetate elimination is reduced in patients with renal dysfunction. Thus, in patients with a creatinine clearance (CLCR) of 20 to 50 ml/min, the roxatidine acetate dosage should be reduced to 75mg once daily; in patients with CLCR < 20 ml/min the dosage should be reduced to 75mg once every 2 days.

6. Place of Roxatidine Acetate in Therapy

The aetiology of duodenal and gastric ulcer remains unclear and, as such, treatment of the underlying causes has not been possible. Drug treatment has been aimed at relieving symptoms and healing ulcers by interaction with gastric acid secretion, defensive factors which protect the gastrointestinal mucosa, and/or mucosal repair. Histamine H2-receptor antagonists suppress gastric acid secretion, and since their development these agents have revolutionised treatment of peptic ulcer disease. The therapeutic success of cimetidine and ranitidine has led to development of several other H2-receptor antagonists, including roxatidine acetate.

Although clinical experience with roxatidine acetate has been relatively limited, the drug has shown similar efficacy to the established histamine H2-receptor antagonists cimetidine and ranitidine in terms of healing duodenal and gastric ulcers. However, the efficacy of roxatidine acetate has yet to be evaluated against that of omeprazole, a specific inhibitor of H+/K+-ATPase with potent antisecretory properties.

Indications from large-scale studies are that roxatidine acetate, like other drugs in its class, prevents ulcer relapse when given as maintenance therapy. Large-scale comparative trials with "established" H2-receptor antagonists (e.g. cimetidine and ranitidine) would be useful to further demonstrate the efficacy of roxatidine acetate in the prevention of peptic ulcer recurrence.

Too few patients with reflux oesophagitis or stomal ulcer have been treated with roxatidine acetate to allow any conclusions to be drawn, but since initial results have been encouraging and other H2-receptor antagonists have shown efficacy in these indications, further investigation seems warranted. Treatment with roxatidine acetate prior to surgery may reduce the risk of pulmonary acid aspiration, one of the major complications of general anaesthesia.

Roxatidine acetate has been well tolerated in clinical trials. Unlike cimetidine, it has no antiandrogenic activity and has no influence on the hepatic metabolism of other drugs. Thus, roxati-
dine acetate is effective in the management of duodenal or gastric ulcer without some of the pharmacological actions that lead to unwanted effects associated with cimetidine. Wider clinical experience may also establish a role for roxatidine acetate in the treatment of other disorders of gastric acid secretion such as reflux oesophagitis and pulmonary acid aspiration.

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