

Table 14. Pharmacokinetic information on CYP inhibitor -Ca antagonist interactions and the description in the package insert.

|                         | Literature Information          |                         |              |  | Japan            |                          | USA               |                      | UK                                      |                      |                              |
|-------------------------|---------------------------------|-------------------------|--------------|--|------------------|--------------------------|-------------------|----------------------|---|----------------------|------------------------------|
|                         | Interaction with CYP inhibitors | AUC                     | Cmax         | Adverse effects/pharmacodynamics           | Reference        | Section of statement     | Quantitative data | Section of statement | Quantitative data                       | Section of statement |                              |
| <b>Dihydropyridines</b> |                                 |                         |              |  |                  |                          |                   |                      |   |                      |                              |
| Amlodipine              | Erythromycin                    | --                      | --           |  |                  | None                     |                   | None                 |   | Interaction          | No interaction <sup>Ⓟ</sup>  |
|                         | Itraconazole                    |                         |              |  |                  | None                     |                   | None                 |   | None                 |                              |
|                         | Cimetidine                      | No effect               | No effect    |  | (1) <sup>Ⓟ</sup> | None                     |                   | Special Studies      | No effect                               |                      | Special studies              |
| Felodipine              | Erythromycin                    | 2.5 fold                | 2.3 fold     | Palpitations, flushing, ankle edema        | (2) (3)          | Precautions              | --                | Precautions          | 2.5 fold (AUC and Cmax)                 | Interaction          | --                           |
|                         | Itraconazole                    | 6.3 fold                | 7.8 fold     | Increased heart rate, lower blood pressure | (4) (5)          | Precautions              | --                | Precautions          | AUC: 8 fold, Cmax: 6 fold               | Interaction          | --                           |
|                         | Cimetidine                      | 1.5 fold                | 1.5-1.6 fold |  | (6) (7)          | Precautions              | --                | Precautions          | 1.5 fold (AUC and Cmax)                 | Interaction          | -- <sup>Ⓟ</sup>              |
| Nicardipine             | Erythromycin                    |                         | --           |  |                  | None                     |                   | None                 |   | None                 |                              |
|                         | Itraconazole                    |                         | --           |  |                  | None                     |                   | None                 |   | None                 |                              |
|                         | Cimetidine                      |                         | --           |  |                  | Precautions              | --                | Precautions          | --                                      | Interaction          | -- <sup>Ⓟ</sup>              |
| Nifedipine              | Erythromycin                    |                         | --           |  | (8)              | Precautions <sup>Ⓟ</sup> | --                | None                 |   | Interaction          | -- <sup>Ⓟ</sup>              |
|                         | Itraconazole                    | 4.4 fold (trough level) | --           | Peripheral edema                           |                  | Precautions <sup>Ⓟ</sup> | --                | None                 |   | Interaction          | -- <sup>Ⓟ</sup>              |
|                         | Cimetidine                      | 1.6-2 fold              | 1.6-2.3 fold | Enhanced effect, increased HR              | (9)-(14)         | Precautions              | -- <sup>Ⓟ</sup>   | Precautions          | --                                      | Interaction          | -- <sup>Ⓟ</sup>              |
| Nisoldipine             | Erythromycin                    |                         | --           |  |                  | None                     |                   | None                 |   | None                 |                              |
|                         | Itraconazole                    |                         | --           |  |                  | None                     |                   | None                 |   | Contraindications    |                              |
|                         | Cimetidine                      | 1.3 fold                | 1.5 fold     | Not altered                                | (15) (16)        | Precautions              | -- <sup>Ⓟ</sup>   | Precautions          | 1.3-1.45 fold (AUC, Cmax), no PD effect | Interaction          | --                           |
| Isradipine              | Erythromycin                    |                         | --           |  |                  |                          |                   | None                 |   | Not designated       | Drugs alter activity of P450 |
|                         | Itraconazole                    |                         | --           |  |                  | NA                       |                   | None                 |   | Not designated       | Drugs alter activity of P450 |
|                         | Cimetidine                      |                         | --           |  |                  |                          |                   | Precautions          | AUC: 1.5 fold, Cmax: 1.36 fold          | Interaction          | 1.5 fold (BA)                |
| Nimodipine              | Erythromycin                    |                         | --           |  |                  |                          |                   | None                 |   | Interaction          | --                           |
|                         | Itraconazole                    |                         | --           |  |                  | NA                       |                   | None                 |   | Interaction          | --                           |
|                         | Cimetidine                      | 1.8 fold                | 1.5 fold     | No effect on PD                            | (17) (18)        | Precautions              |                   | Precautions          | AUC: 1.9 fold, Cmax: 1.5 fold           | Interaction          | --                           |
| Lacidipine              | Erythromycin                    |                         | --           |  |                  |                          |                   |                      |   | Interaction          | --                           |
|                         | Itraconazole                    |                         | --           |  |                  | NA                       |                   |                      | NA                                      | None                 | --                           |
|                         | Cimetidine                      |                         | --           |  |                  | NA                       |                   |                      | NA                                      | None                 | --                           |

| Drug          | Drug         | Effect             | Reference            | Contraindications                                | Contraindications                                      | Contraindications                           |
|---------------|--------------|--------------------|----------------------|--|--|---|
| Lercanidipine | Erythromycin | --                 |                      |  |  |   |
|               | Itraconazole | --                 | (19) <sup>d</sup>    |  |  |   |
|               | Cimetidine   | No effect          |                      |  |  | No significant modification in plasma level |
| Aranidipine   | Erythromycin | --                 |                      | Precautions                                      | NA   |   |
|               | Itraconazole | --                 |                      | Precautions                                      | NA   |   |
|               | Cimetidine   | --                 |                      | Precautions                                      | NA   |   |
| Azelidipine   | Erythromycin | --                 |                      | Precautions <sup>k)</sup>                        | NA   |   |
|               | Itraconazole | --                 |                      | Contraindications <sup>l)</sup><br>AUC: 2.8 fold | NA   |   |
|               | Cimetidine   | --                 |                      | Precautions                                      | NA   |   |
| Earnidipine   | Erythromycin | --                 |                      | Precautions <sup>k)</sup>                        | NA   |   |
|               | Itraconazole | --                 |                      | Precautions <sup>o)</sup>                        | NA   |   |
|               | Cimetidine   | --                 |                      | Precautions                                      | NA   |   |
| Benidipine    | Erythromycin | --                 |                      | None   | NA   |   |
|               | Itraconazole | --                 |                      | None   | NA   |   |
|               | Cimetidine   | --                 |                      | Precautions                                      | NA   |   |
| Cilnidipine   | Erythromycin | --                 |                      | None   | NA   |   |
|               | Itraconazole | --                 |                      | Precautions <sup>o)</sup>                        | NA   |   |
|               | Cimetidine   | --                 |                      | Precautions                                      | NA   |   |
| Efonidipine   | Erythromycin | --                 |                      | None   | NA   |   |
|               | Itraconazole | --                 |                      | None   | NA   |   |
|               | Cimetidine   | --                 |                      | Precautions                                      | NA   |   |
| Manidipine    | Erythromycin | --                 |                      | None   | NA   |   |
|               | Itraconazole | --                 |                      | None   | NA   |   |
|               | Cimetidine   | --                 |                      | Precautions                                      | NA   |   |
| Nilvadipine   | Erythromycin | --                 |                      | None   | NA   |   |
|               | Itraconazole | --                 |                      | Precautions                                      | NA   |   |
|               | Cimetidine   | --                 |                      | Precautions                                      | NA   |   |
| Nitrendipine  | Erythromycin | --                 |                      | None   | NA   |   |
|               | Itraconazole | --                 |                      | None   | NA   |   |
|               | Cimetidine   | 1.1-2.4 fold       |                      | Precautions                                      | NA   |   |
|               |              | 1.1-2.1 fold       | No effect on PD, ADR |  |  |   |
|               |              |                    | (20) (21)            |  |  |   |
| Others        |              |                    |                      |  |  |   |
| Verapamil     | Erythromycin | --                 |                      | None   | Clinically significant interactions have been reported | None  |
|               | Itraconazole | --                 |                      | Precautions                                      | Cytochrome inhibitors                                  | None  |
|               | Cimetidine   | No effect-1.4 fold | (22)-(26)            | None   | clearance of verapamil was either reduced or unchanged | Interaction                                 |
|               |              | No effect-1.4 fold |                      | Precautions                                      |  | --  |
| Diltiazem     | Erythromycin | --                 |                      | None   | None   | None  |
|               | Itraconazole | --                 |                      | None   | None   | None  |
|               | Cimetidine   | 1.5 fold           | (27)                 | Precautions                                      | AUC: 1.53 fold, Cmax: 1.58 fold                        | Interaction <sup>o)</sup>                   |
|               |              | 1.6 fold           |                      | Precautions                                      |  | --  |

-- No data  
NA: Not available

- a): As antibiotics - not stated.  
b): Cited company data (not published).  
c): No formal in vivo interaction studies have been performed.  
d): Asazole antifungals - stated.  
e): Also described the decrease in hepatic blood flow and increased gastric pH, leading to increased absorption.  
f): Antihypertensive effect may be potentiated.  
g): As strong inhibitors of CYP3A4 stated in interaction section.  
h): Provided ketoconazole data (15 fold in AUC, 8 fold in Cmax for S-lercanidipine).  
i): A review cited product information.  
j): Package insert stated that "these drugs increased blood concentration of other Ca blocker such as felodipine".  
k): As macrolide antibiotics -stated  
l): Also listed increased gastric pH, leading to increased absorption.  
m): Package insert stated that "cimetidine enhanced the effect of nifedipine".  
n): Stated that "may increase the drug effect, but there is no case report".  
o): As H2 antagonist - not stated.
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Table 15. Pharmacokinetic information on grapefruit juice-Ca antagonist interactions and the description in the package insert.

|                        | Literature Information |                    |   |           | Japan                |                                  | USA                  |  | UK                   |                       |
|------------------------|------------------------|--------------------|---|-----------|----------------------|----------------------------------|----------------------|--|----------------------|-----------------------|
|                        | AUC                    | Cmax               | Adverse effects/pharmacodynamics                      | Reference | Section of statement | Quantitative data                | Section of statement | Quantitative data                                      | Section of statement | Quantitative data     |
| <b>Dihydropyridine</b> |                        |                    |   |           |                      |                                  |                      |  |                      |                       |
| Amlodipine             | 1.1-1.2 fold           | 1.1-1.2 fold       | No significant differences in BP and HR               | (1) (2)   | None                 |                                  | Special Studies      | No significant effect                                  | Special Studies      | No significant effect |
| Felodipine             | 1.7-3.3 fold           | 2.4-4.0 fold       | Diastolic blood pressure lower, and heart rate higher | (3) -(11) | Precautions          | -                                | Precautions          | More than 2 fold increase in AUC and Cmax              | interaction          | -                     |
| Nicardipine            | 1.6 fold               | --                 | Higher heart rates                                    | (12)      | Precautions          | --                               | None                 |  | Interaction          | --                    |
| Nifedipine             | 2.0 fold               | 1.9 fold           | --  | (13)      | Precautions          | --                               | Precautions          | 2 fold increase in AUC and Cmax                        | Posology             | -- a)                 |
| Nisoldipine            | 2.0-4.1 fold           | 4.1-4.9 fold       | Decreased systolic and diastolic blood pressure       | (14) (15) | Precautions          | -- b)                            | Precautions          | AUC: 2 fold (up to 5 fold) Cmax: 3 fold (up to 7 fold) | Posology             | -- c)                 |
| Isradipine             | --                     | --                 | --  | --        |                      | NA                               |                      | NA   | Interaction          | --                    |
| Nimodipine             | 1.5 fold               | 1.2 fold           | More pronounced hemodynamic response                  | (16)      |                      | NA                               |                      | NA   | Interaction          | --                    |
| Lacidipine             | --                     | --                 | --  | --        |                      | NA                               |                      | NA   | Interaction          | --                    |
| Lercanidipine          | --                     | --                 | Pronounced antihypertensive effect d)                 | (17)      |                      | NA                               |                      | NA   | Contraindications    | --                    |
| Avanidipine            | --                     | --                 | --  | --        | Precautions          | -- e)                            |                      | NA   |                      | NA                    |
| Azelnidipine           | --                     | --                 | --  | --        | Precautions          | AUC: 3.3 fold, Cmax: 2.5 fold f) |                      | NA   |                      | NA                    |
| Barnidipine            | --                     | --                 | --  | --        | Precautions          | --                               |                      | NA   |                      | NA                    |
| Benidipine             | --                     | --                 | --  | --        | Precautions          | --                               |                      | NA   |                      | NA                    |
| Cilnidipine            | --                     | --                 | --  | --        | Precautions          | -- g)                            |                      | NA   |                      | NA                    |
| Efonidipine            | 1.7 fold               | 1.5 fold           | No difference in BP, HR and ADR                       | (18) h)   | Precautions          | AUC: 1.7 fold, Cmax: 1.5 fold    |                      | NA   |                      | NA                    |
| Manidipine             | --                     | --                 | --  | --        | Precautions          | --                               |                      | NA   |                      | NA                    |
| Nilvadipine            | --                     | --                 | --  | --        | Precautions          | -- i)                            |                      | NA   |                      | NA                    |
| Nitrendipine           | 2.3 fold               | 2.1 fold           | No significant effect                                 | (19)      | Precautions          | --                               |                      | NA   |                      | NA                    |
| <b>Others</b>          |                        |                    |   |           |                      |                                  |                      |  |                      |                       |
| Verapamil              | no effect-1.5 fold     | no effect-1.6 fold | Prolongation of PR                                    | (20)-(22) | Precautions          | --                               | Precautions          | --   | Contraindications    | --                    |
| Diltiazem              | No effect-1.2 fold     | No effect-1.2 fold | No significant differences                            | (23) (24) | None                 |                                  | None                 |  | None                 |                       |

--: No data

NA: Not available

a): Effect may last for at least three days after the last ingestion of grapefruit juice.

b): Start therapy after 4 days of cessation of regular grapefruit juice intake.

c): May potentiate the drug effects during the first 6-8 hours.

d): Cited product information.

e): Package insert stated that "grapefruit juice increased blood concentration of other Ca blocker such as nifedipine".

f): In house data

g): Package insert cited in house data without quantitative information.

h): Literature written in Japanese, and not cited in MEDLINE.

i): Stated that "may increase the drug effect, but there is no case report."

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Table 16. Pharmacokinetic information on digoxin-Ca antagonist interactions and the description in the package insert.

|                        | Literature information: Change in digoxin  |  |               | Japan                |  | USA                  |  | UK                   |  |
|------------------------|--|--|---------------|----------------------|--|----------------------|--|----------------------|--|
|                        | PK   | PD   | Reference     | Section of statement | Quantitative data                          | Section of statement | Quantitative data  | Section of statement | Quantitative data                                      |
| <b>Dihydropyridine</b> |  |  |               |                      |  |                      |  |                      |  |
| Amlodipine             | Not significant (C <sub>ss</sub> )   | No change  | (1)           | None                 |  | Special studies      | Did not change serum digoxin levels or digoxin renal clearance                               | Special studies      | Did not change serum digoxin levels or renal clearance |
| Felodipine             | Unchanged (trough, 6 h), tend to increase (plasma), 1.2-1.5 fold (C <sub>max</sub> ), 1.4 fold (AUC) | No change  | (2)-(4)       | Precautions          | --   | Precautions          | The PK of digoxin was not significantly altered.   | Interaction          | No dosage adjustment is required                       |
| Nicardipine            | 1.07 fold (AUC) <sup>a)</sup> , 1.15 fold (plasma)   | --   | (5) (6)       | Precautions          | --   | Precautions          | Usually not alter the plasma digoxin   | interaction          | --   |
| Nifedipine             | 1.15 fold (AUC), 1.45 fold (plasma)  | --   | (7) (8)       | Precautions          | --   | Precautions          | -- b)  | Interaction          | --   |
| Nisoldipine            | 1.15 fold (trough), no effect (C <sub>ss</sub> )   | Systolic time intervals were significantly altered | (9) (10)      | Precautions          | --   | Precautions          | No significant interactions were found   | Interaction          | No interaction has been observed                       |
| Isradipine             | No effect (AUC, C <sub>ss</sub> ), 1.3 fold (C <sub>max</sub> )                                      |  | (11)          | NA                   |  | Precautions          | Did not affect clearance of digoxin  | Interaction          | Not modified   |
| Nimodipine             | No PK/PD interaction   |  | (12)          | NA                   |  | None                 |  | None                 |  |
| Lacidipine             | --   |  |               | NA                   |  |                      | NA   | Interaction          | No specific pharmacodynamic interaction                |
| Lercanidipine          | No effect <sup>a)</sup>  |  | (13)          | NA                   |  |                      | NA   | Interaction          | AUC: no effect, C <sub>max</sub> : 1.33 fold           |
| Aranidipine            | --   |  |               | Precautions          | --   |                      | NA   |                      | NA   |
| Azelidipine            | --   |  |               | Precautions          | AUC: 1.3 fold, C <sub>max</sub> : 1.5 fold |                      | NA   |                      | NA   |
| Barnidipine            | No effect (C <sub>ss</sub> )   | --   | (14)          | Precautions          | --   |                      | NA   |                      | NA   |
| Benidipine             | --   |  |               | Precautions          | --   |                      | NA   |                      | NA   |
| Cilnidipine            | --   |  |               | Precautions          | -- <sup>d)</sup>                           |                      | NA   |                      | NA   |
| Efonidipine            | --   |  |               | None                 | --   |                      | NA   |                      | NA   |
| Manidipine             | --   |  |               | Precautions          | -- <sup>d)</sup>                           |                      | NA   |                      | NA   |
| Nilvadipine            | No effect (plasma)   |  | (15)          | None                 |  |                      | NA   |                      | NA   |
| Nitrendipine           | 1.2 fold (AUC), 2.9 fold (plasma)  | Adverse effect                                     | (16) (17)     | Precautions          | --   |                      | NA   |                      | NA   |
| <b>Others</b>          |  |  |               |                      |  |                      |  |                      |  |
| Verapamil              | 1.5 fold (AUC), 1.4-1.8 fold (C <sub>ss</sub> ), 1.4 fold (C <sub>max</sub> ), 1.7 fold (plasma)     | Enhanced effect                                    | (8) (11) (18) | Precautions          | --   | Precautions          | 1.5-1.75 fold  | Interaction          | --   |
| Diltiazem              | 1.2 fold (AUC), no effect (AUC, C <sub>max</sub> , serum)  | --   | (19)-(21)     | Precautions          | --   | Warning              | Study 1: 1.2 fold (24 healthy male subjects) Study 2: no increase (12 patients, serum level) | Interaction          | Small increases (serum level)                          |

--: No data

NA: Not available

a): Not significant.

b): Isolated reports of patients with elevated digoxin levels.

c): A review cited in house data.

d): Package insert stated that "nifedipine increased plasma digoxin concentration."

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医療従事者に対するアンケート調査 (Fig 13-36)

Fig. 13 添付文書のどの部分をよく参考にしていますか(上位5つ)

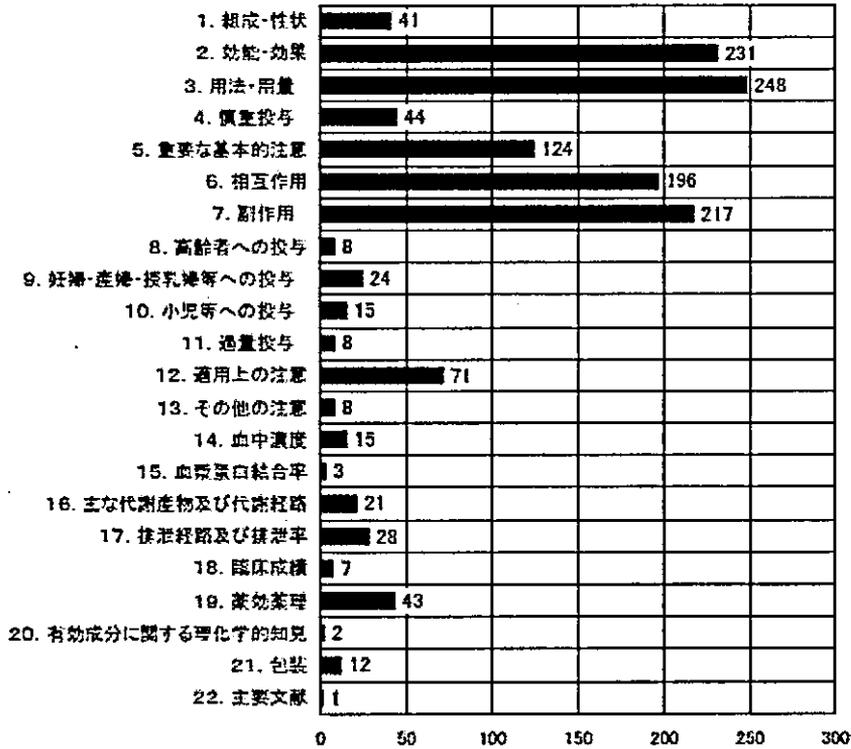


Fig. 14 添付文書情報は主としてどのように入手・管理していますか

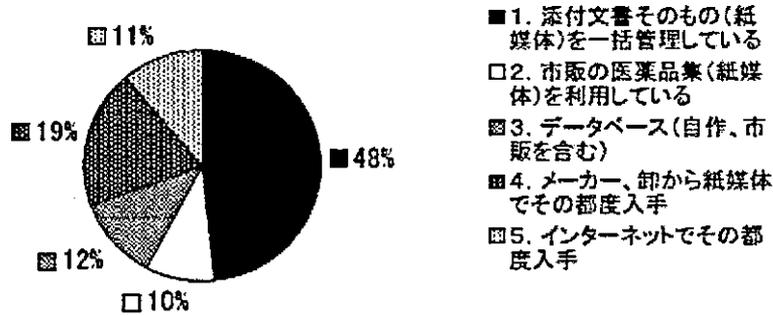


Fig. 15 インタビューフォームの情報は主にどのように入手していますか

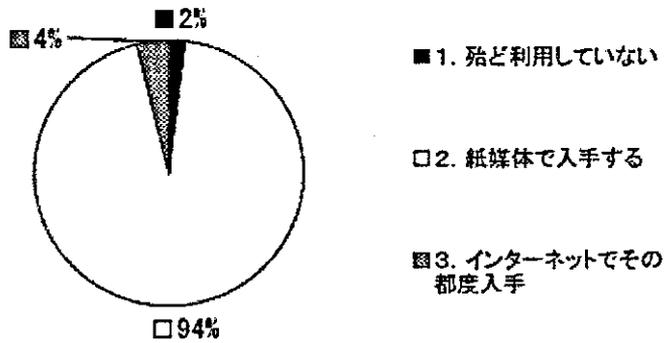


Fig. 16 使用上の注意の改訂時の変更理由及び根拠の記載の必要性

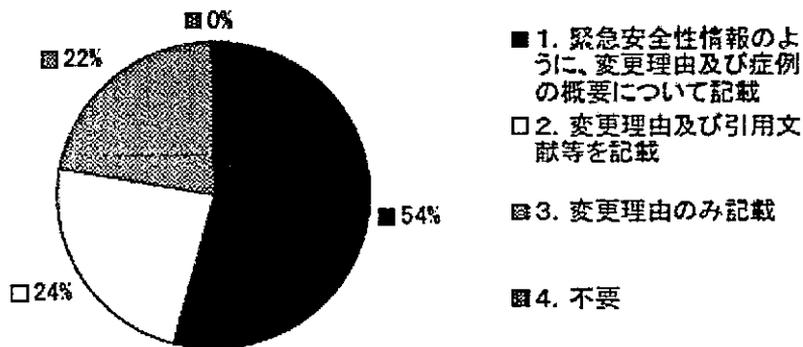


Fig. 17 現状の添付文書の相互作用欄に使用されている一覧表形式は使いやすいですか

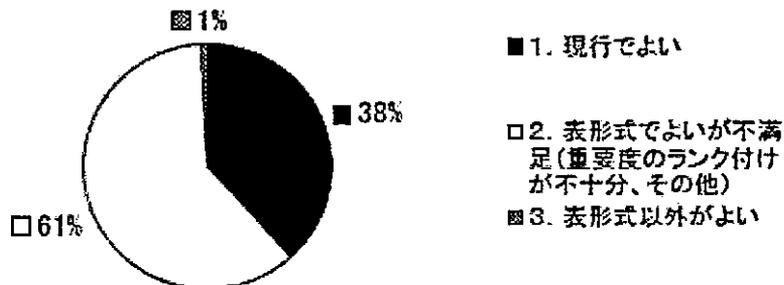


Fig. 18 添付文書の相互作用欄の記載順序について

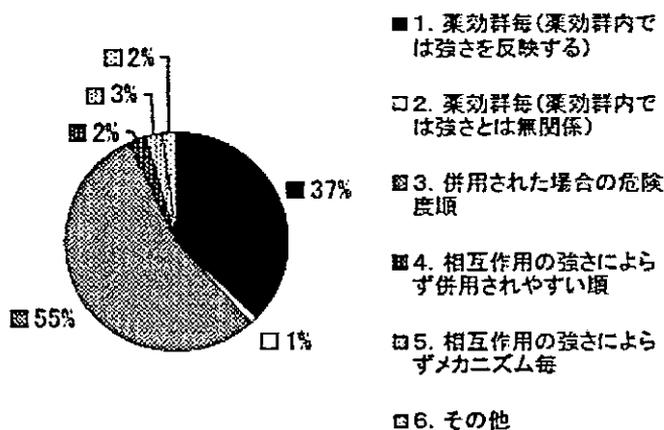


Fig. 19 クラスエフェクトと考えられる相互作用の記載方法について

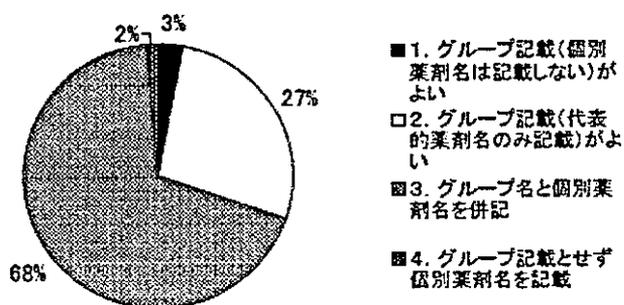


Fig. 20 臨床における有害事象の発生の十分な情報はないが、健常人の薬物動態試験で変動が大きい場合

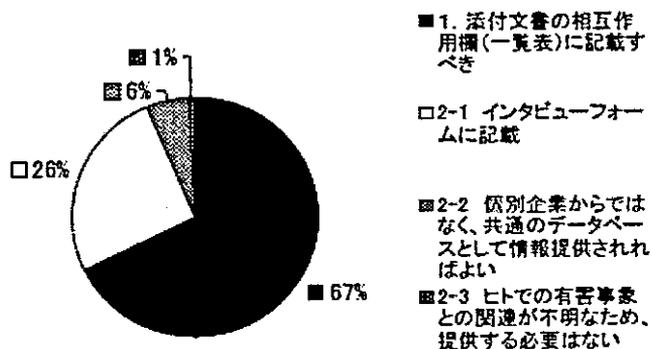


Fig. 21 臨床における有害事象の発生の十分な情報はないが、*in vitro* 試験で強い相互作用が認められた場合（臨床薬物動態試験はなく、有害事象は未知）

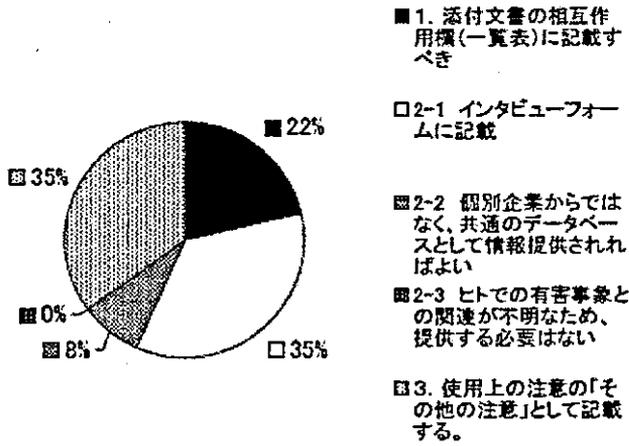


Fig. 22 臨床における有害事象の発生の十分な情報はないが、動物試験等で重大な有害事象(薬物動態、薬理作用含む)が生じる場合

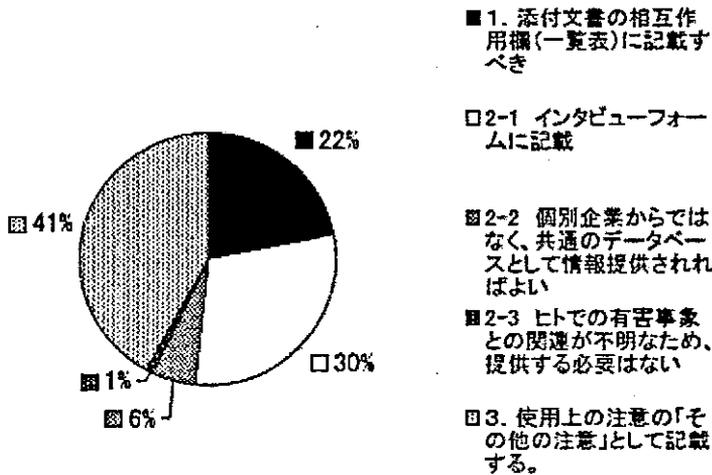


Fig. 23 臨床における有害事象の発生の十分な情報はないが、類薬で臨床上の相互作用が知られている場合

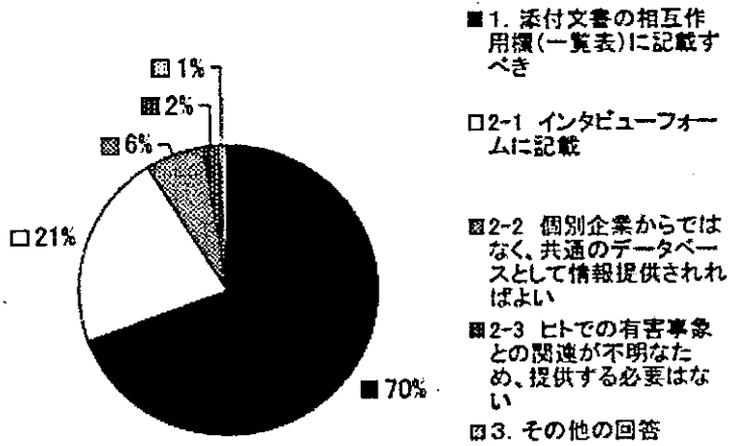


Fig. 24 臨床薬物動態データ(AUC, Cmax)の記載方法 (相互作用欄)

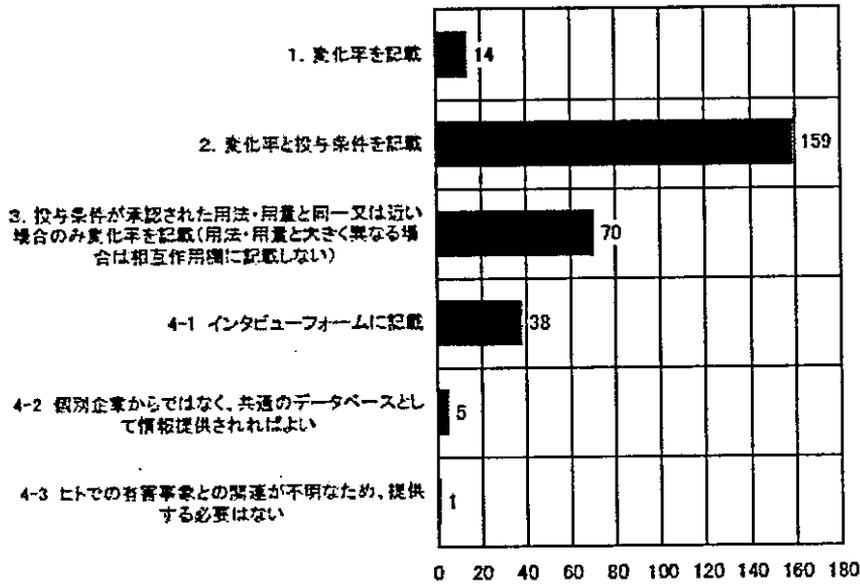


Fig. 25 食品類（嗜好品、サプリメント、健康食品等を含む）との相互作用

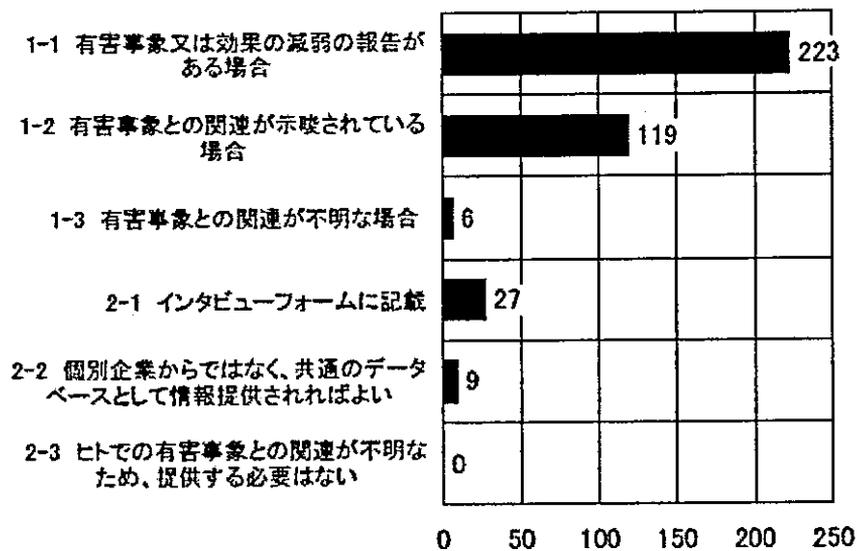


Fig. 26 食品成分に薬剤との薬理的な相互作用の可能性が示されている場合

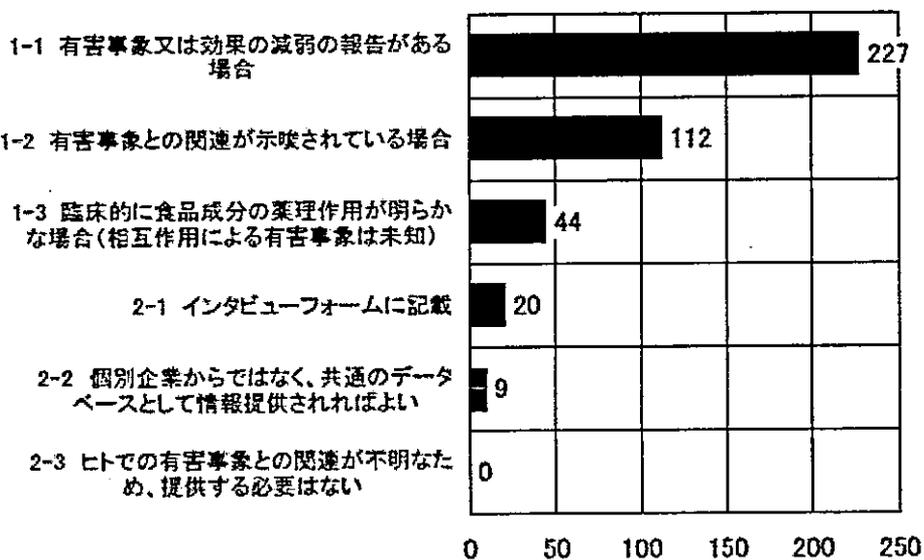


Fig. 27 食品類と薬剤を併用した場合の有害事象報告があるが作用メカニズムが不明な場合

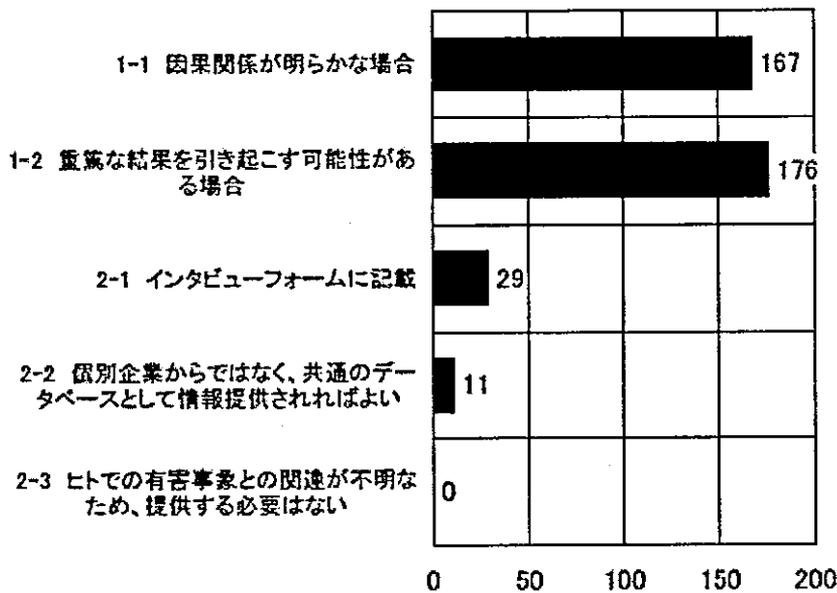


Fig. 28 国内では殆ど使用されていないか、摂取方法が大きく異なる食品類との併用で有害事象報告がある場合

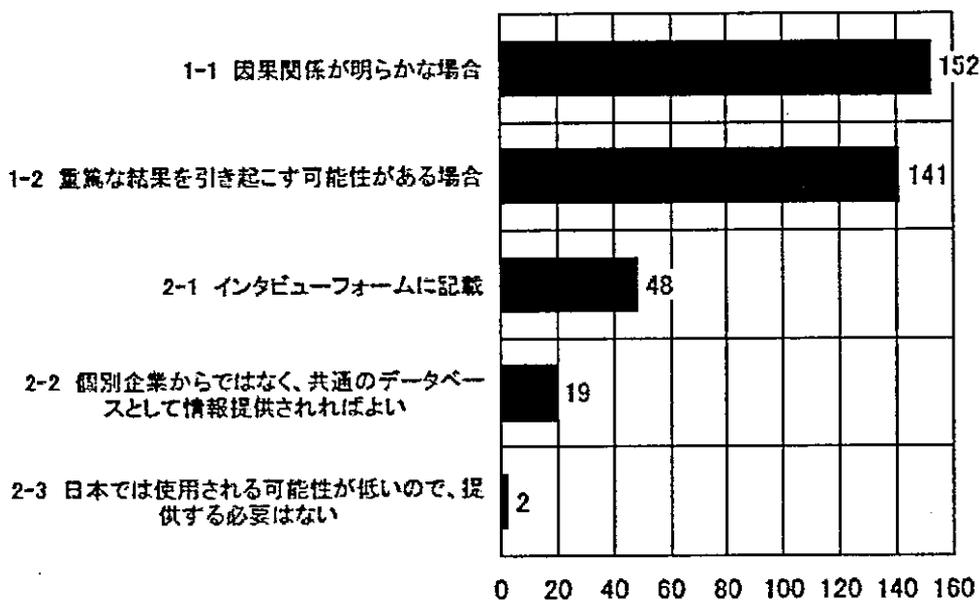


Fig. 29 相互作用の項での分子種の記載方法（相互作用に関与する薬物代謝・輸送分子種が判明している場合）

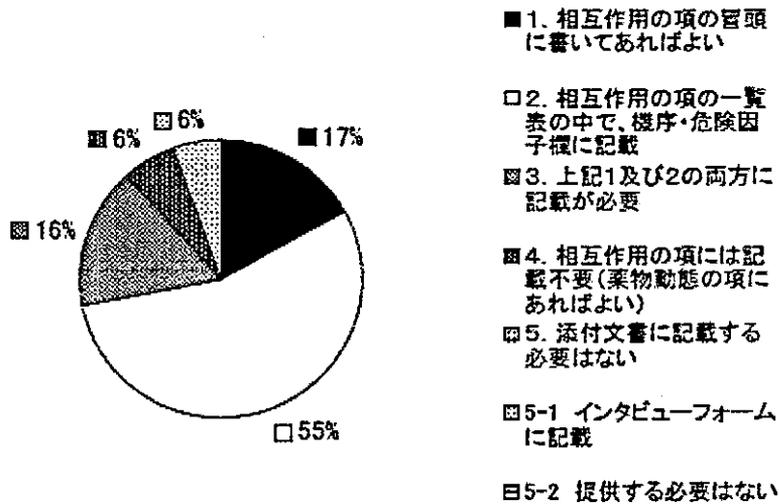


Fig. 30 後発医薬品の相互作用欄の記載について

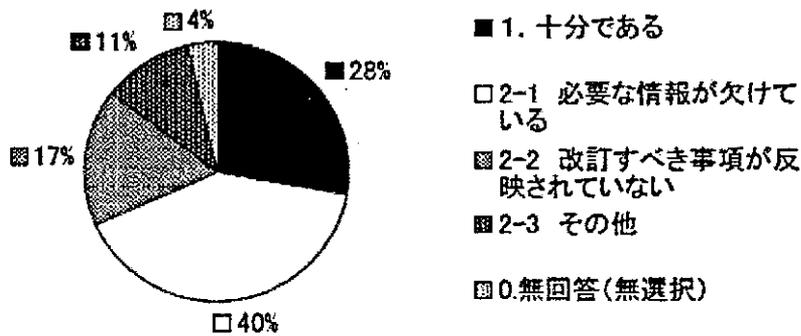


Fig. 31 添付文書の記載順序について

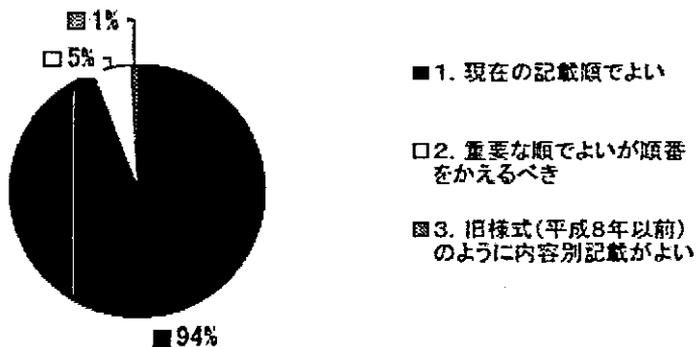


Fig. 32 添付文書の重要事項のハイライトの作成について

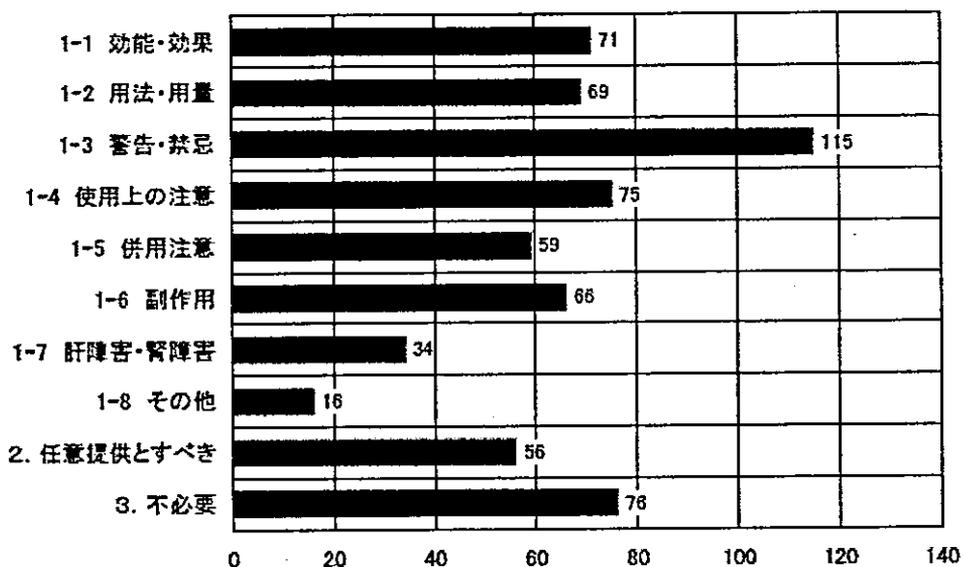


Fig. 33 処方箋の確認の際、どのような場合に医師への照会・助言を行いますか

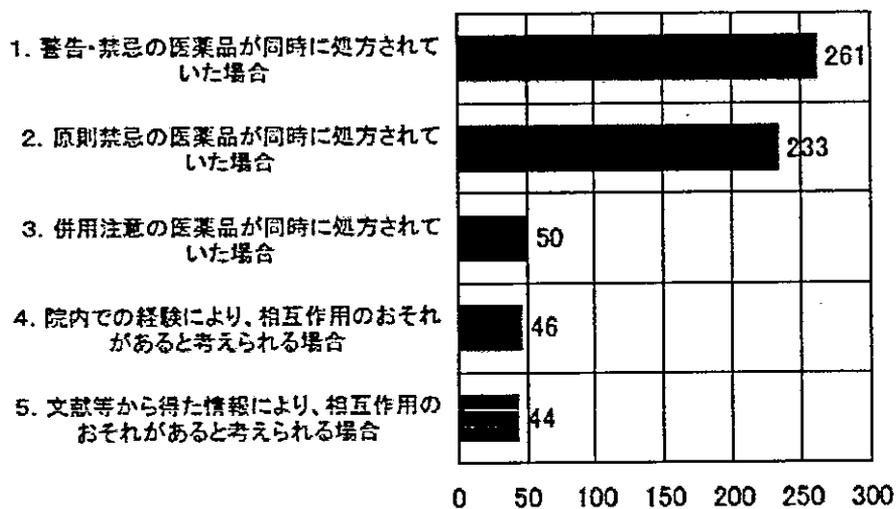


Fig. 34 添付文書に「患者向けの薬剤交付時の注意」を設ける必要がある相互作用情報

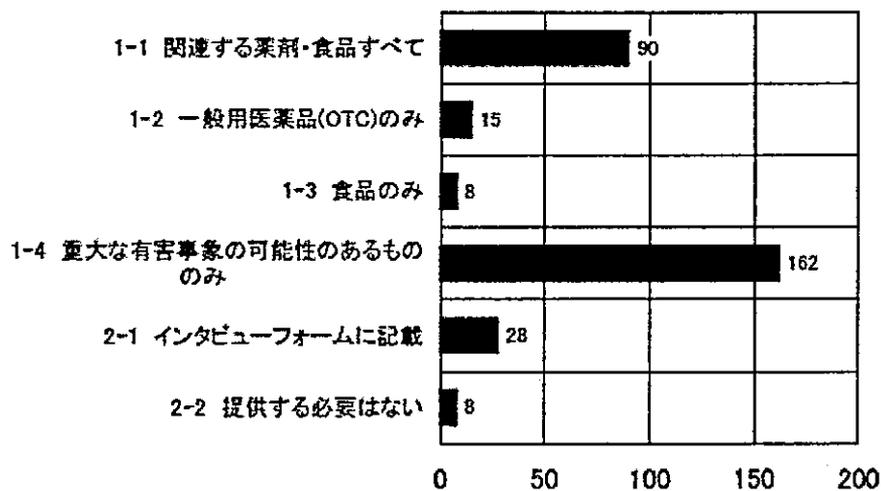


Fig. 35 添付文書（薬物動態欄）に記載すべき事項

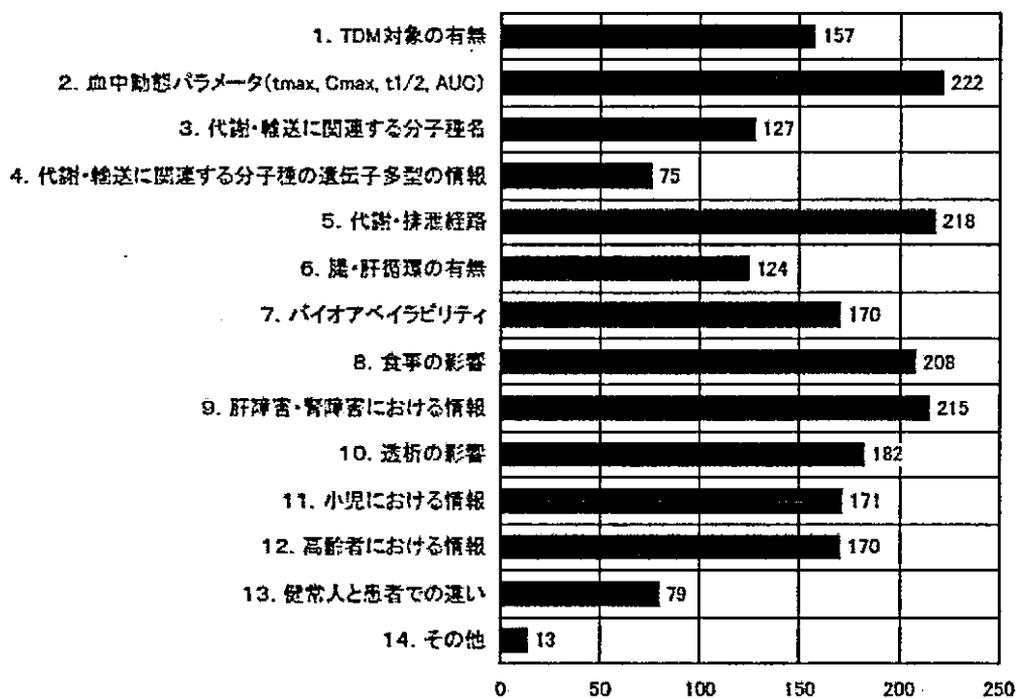
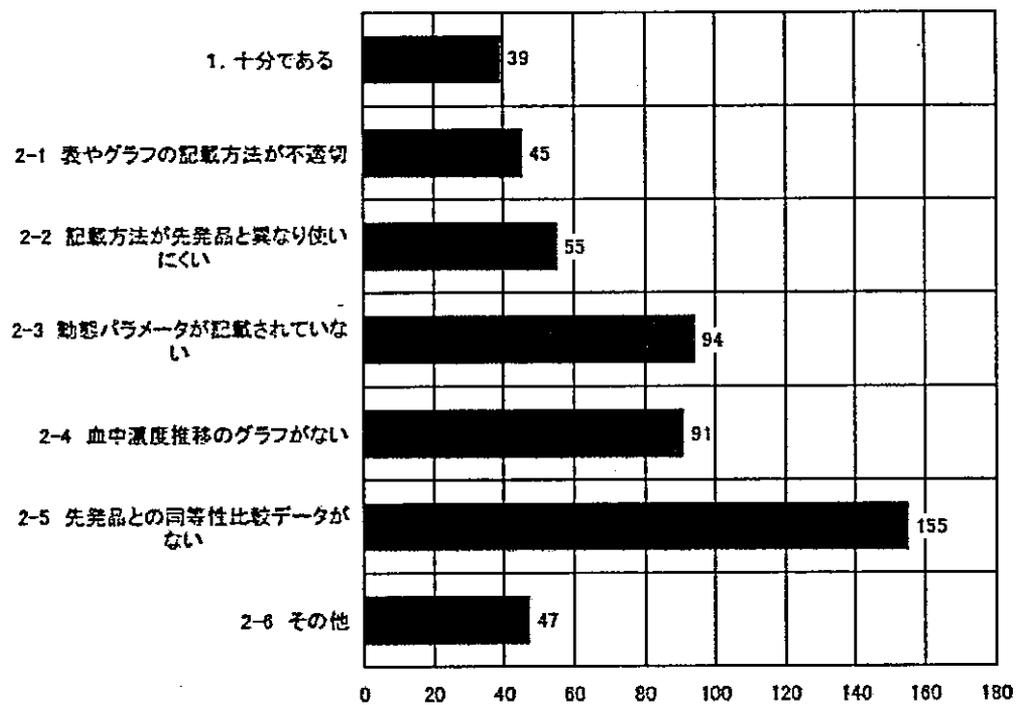


Fig. 36 後発医薬品の薬物動態欄の記載について



**Table 17-1**

シンバスタチンの添付文書：2004年2月改訂（第12版）：販売開始1991年12月

**【使用上の注意】 3.相互作用**

本剤は、主に肝代謝酵素チトクロームP450 3A4 (CYP3A4)により代謝される。

**【併用禁忌】（併用しないこと）**

| 薬剤名等                                    | 臨床症状・措置方法                  | 機序・危険因子                        |
|---|----------------------------|--------------------------------|
| イトラコナゾール：<br>イトリゾール<br>ミコナゾール：<br>フロリード | 急激な腎機能悪化を伴う横紋筋融解症があらわれやすい。 | これらの薬剤はCYP3A4を阻害し、本剤の代謝が抑制される。 |

**【併用注意】（併用に注意すること）**

| 薬剤名等  | 臨床症状・措置方法  | 機序・危険因子  |
|---|--|--|
| シクロスポリン   | 急激な腎機能悪化を伴う横紋筋融解症があらわれやすい。<br>併用を必要とする場合には、本剤の投与量は10mg/日を超えないこと。〔自覚症状（筋肉痛，脱力感）の発現，CK（CPK）上昇，血中及び尿中ミオグロビン上昇並びに血清クレアチニン上昇等の腎機能の悪化を認めた場合は直ちに投与を中止すること。〕 | これらの薬剤はCYP3A4を阻害し、併用により本剤の代謝が抑制されるおそれがある。<br>腎障害のある患者には特に注意すること。 |
| エリスロマイシン<br>クラリスロマイシン<br>HIV プロテアーゼ阻害剤：<br>リトナビル等 | 急激な腎機能悪化を伴う横紋筋融解症があらわれやすい。<br>〔自覚症状（筋肉痛，脱力感）の発現，CK（CPK）上昇，血中及び尿中ミオグロビン上昇並びに血清クレアチニン上昇等の腎機能の悪化を認めた場合は直ちに投与を中止すること。〕                                   |  |

**9.その他の注意**

シンバスタチン投与中に非常に大量のグレープフルーツジュースを摂取した場合（1.14 L/日以上），シンバスタチンおよびその活性代謝物の血清中濃度が増加したとの報告がある。

Table 17-2

## シンバスタチンの添付文書改訂案

## 【使用上の注意】3.相互作用

本剤は、主に薬物代謝酵素チトクロームP450 3A4 (CYP3A4)により代謝される。

## 【併用禁忌】（併用しないこと）

| 薬剤名等                                    | 臨床症状・措置方法                  | 機序・危険因子  |
|---|----------------------------|--|
| イトラコナゾール：<br>イトリゾール<br>ミコナゾール：<br>フロリード | 急激な腎機能悪化を伴う横紋筋融解症があらわれやすい。 | 肝CYP3A4の阻害により、血中濃度(AUC)の増加することが報告されている(イトラコナゾール: 10-19倍) |

## 【併用注意】（併用に注意すること）

| 薬剤名等  | 臨床症状・措置方法  | 機序・危険因子  |
|---|--|--|
| シクロスポリン   | 急激な腎機能悪化を伴う横紋筋融解症があらわれやすい。併用を必要とする場合には、本剤の投与量は10mg/日を超えないこと。〔自覚症状（筋肉痛、脱力感）の発現、CK（CPK）上昇、血中及び尿中ミオグロビン上昇並びに血清クレアチニン上昇等の腎機能の悪化を認めた場合は直ちに投与を中止すること。〕 | シクロスポリンが本剤の肝への取り込みを抑制し、血中濃度の増加すること(AUC: 3-8倍)が報告されている。腎障害のある患者には特に注意すること。                                |
| エリスロマイシン<br>クラリスロマイシン<br>ジルチアゼム<br>ベパミル<br>HIV プロテアーゼ阻害剤：<br>リトナビル等 |  | 肝CYP3A4の阻害により、血中濃度(AUC)の増加することが報告されている(エリスロマイシン: 6倍、ジルチアゼム: 5倍、ベパミル: 5倍、HIVプロテアーゼ阻害剤: 5-31倍)。危険因子: 腎障害患者 |
| グレープフルーツジュース  |  | 小腸CYP3A4の阻害により、血中濃度の増加すること(AUC: 3.6-16倍)が報告されている。  |
| ジゴキシン   | 併用する場合は、ジゴキシンの血中濃度のモニターを十分に行うこと。   | 本剤によるジゴキシンのP-糖たん白質の抑制で、ジゴキシンの血中濃度の増加すること(AUC: 1.2倍)が報告されている。   |

## 9. その他の注意

~~シンバスタチン投与中に非常に大量のグレープフルーツジュースを摂取した場合（1.14L/日以上）、シンバスタチンおよびその活性代謝物の血清中濃度が増加したとの報告がある。~~