System organ class	Very common (≥ 1/10)	Common (≥1/100 to <1/10)	Uncommon (≥1/1,000 to <1/100)	Rare (≥1/10,000 to <1/1,000)	Very rare (< 1/10,000)
Blood and the lymphatic system disorders			Eosinophilia		
Nervous system disorders		Dizziness, headache, disturbance of taste	Vertigo somnolence, nervousness, insomnia,	Transient loss of consciousness, paraesthesia	Parosmia
Eye disorders			Blurred vision	Diplopia	
Cardiovascular disorders			Flush Palpitations	Atrial arrhythmia, hypotension, bradycardia	
Gastro-intestinal disorders	Diarrhoea	Nausea, vomiting, gastrointestinal pain, flatulence	Oral *Candida* infection, stomatitis anorexia, constipation, ,		Pseudomembranous colitis
Hepato-biliary disorders		Increase in liver enzymes (AST, ALT, alkaline phosphatase)	Hepatitis	Cholestatic jaundice	
Skin and subcutaneous tissue disorders			Rash, urticaria, pruritus	Eczema	Erythema multiforme
Musculoskeletal, connective tissue					Muscle cramps
Reproductive system disorders		Vaginal *Candida* infection			

Visual disturbances (<1%) associated with the use of Ketek, including blurred vision, difficulty focusing and diplopia, were mostly mild to moderate. They typically occurred within a few hours after the first or second dose, recurred upon subsequent dosing, lasted several hours and were fully reversible either during therapy or following the end of treatment. These events have not been associated with signs of ocular abnormality (see sections 4.4 and 4.7).
In clinical trials the effect on QTc was small (mean of approximately 1 msec). In comparative trials, similar effects to those observed with clarithromycin were seen with an on-therapy ΔQTc >30 msec in 7.6% and 7.0% of cases, respectively. No patient in either group developed a ΔQTc >60 msec. There were no reports of TdP or other serious ventricular arrhythmias or related syncope in the clinical program and no subgroups at risk were identified.

During post-marketing experience the following reactions have been reported (frequency unknown):
-Immune system disorders: Angioneurotic oedema, anaphylactic reactions including anaphylactic shock
-Cardiac disorders: QT/QTc interval prolongation
-Gastrointestinal disorders: Pancreatitis,
-Hepato-biliary disorders: Severe hepatitis and liver failure (see section 4.4)
-Nervous system disorders: Cases of rapid onset of exacerbation of myasthenia gravis have been reported (see sections 4.43 and 4.4).

4.9 Overdose

In the event of acute overdose the stomach should be emptied. The patients should be carefully observed and given symptomatic and supportive treatment. Adequate hydration should be maintained. Blood electrolytes (especially potassium) must be controlled. Due to the potential for the prolongation of the QT interval and increased risk of arrhythmia, ECG monitoring must take place

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: macrolides, lincosamides and streptogramins, ATC Code: J01FA15.

Telithromycin is a semisynthetic derivative of erythromycin A belonging to the ketolides, a class of antibacterial agents related to macrolides.

Mode of action

Telithromycin inhibits protein synthesis by acting at the ribosome level.

The affinity of telithromycin for the 50S bacterial subunit of ribosome is 10 fold higher than that of erythromycin A when the strain is susceptible to erythromycin A. Against erythromycin A resistant strains, due to an MLS_B mechanism of resistance, telithromycin shows a more than 20 fold affinity compared to erythromycin A in the 50S bacterial subunit.

Telithromycin interferes with the ribosome translation at the 23S ribosomal RNA level, where it interacts with domain V and II. Furthermore, telithromycin is able to block the formation of the 50S and 30S ribosomal subunits.

Breakpoints

The recommended MIC breakpoints for telithromycin, separating susceptible organisms from intermediately susceptible organisms and intermediately susceptible organisms from resistant organisms, are: susceptible ≤0.5 mg/l, resistant >2mg/l.

Antibacterial spectrum

The prevalence of resistance may vary geographically and with time for selected species and local information on resistance is desirable, particularly when treating severe infections. -As necessary, expert advice should be sought when the local prevalence of resistance is such that the utility of the agent in at least some types of infections is questionable.
This information provides only an approximate guidance on probabilities as to whether microorganisms will be susceptible to telithromycin.

Commonly susceptible species

Aerobic Gram-positive bacteria

Staphylococcus aureus methicillin susceptible (MSSA)*

Lancefield group C and G (ß haemolytic) streptococci
Streptococcus agalactiae
Streptococcus pneumoniae *
Viridans group streptococci

Aerobic Gram- negative bacteria *Legionella pneumophila* *Moraxella catarrhalis**
Other *Chlamydophila pneumoniae** *Chlamydia psittaci* *Mycoplasma pneumoniae**
Species for which acquired resistance may be a problem Aerobic Gram-positive bacteria *Staphylococcus aureus* methicillin resistant (MRSA)+ *Streptococcus pyogenes** Aerobic Gram- negative bacteria *Haemophilus influenzae*$*$ *Haemophilus parainfluenzae*$$
Inherantly resistant organisms
Aerobic Gram- negative bacteria *Acinetobacter* *Enterobacteriaceae* *Pseudomonas*

* Clinical efficacy has been demonstrated for susceptible isolates in the approved clinical indications.
$ natural intermediate susceptibility
+Among MRSA the rate of MLSBc resistant strains is more than 80%, telithromycin is not active against MLS_Bc.

Resistance

Telithromycin does not induce MLS_B resistance in vitro to *Staphylococcus aureus*, *Streptococcus pneumoniae*, and *Streptococcus pyogenes*, an attribute related to its 3 keto function. Development of in vitro resistance to telithromycin due to spontaneous mutation is rare. The majority of MRSA are resistant to erythromycin A by a constitutive MLS_B mechanism.

In vitro results have shown that telithromycin is affected by the erythromycin ermB or mefA related resistance mechanisms but to lesser extent than erythromycin. While exposure to telithromycin did select for pneumococcal mutants with increased MICs, the MICs remained within the proposed susceptibility range.

For *Streptococcus pneumoniae*, there is no cross- or co-resistance between telithromycin and other antibacterial classes including erythromycin A and/or penicillin resistance-.

For *Streptococcus pyogenes*, cross-resistance occurs for high-level erythromycin A resistant strains.

Effect on oral and faecal flora

In a comparative study in healthy human volunteers, telithromycin 800 mg daily and clarithromycin 500 mg twice daily for 10 days showed a similar and reversible reduction of oral and faecal flora. However, in contrast to clarithromycin, no resistant strains of alpha streptococci emerged in saliva on treatment with telithromycin.

5.2 Pharmacokinetic properties

Absorption

Following oral administration, telithromycin is fairly rapidly absorbed. A mean maximum plasma concentration of about 2 mg/l is reached within 1-3 hour after dose with once-daily dosing of telithromycin 800 mg. The absolute bioavailability is about 57 % after a single dose of 800 mg. The rate and extent of absorption is unaffected by food intake, and thus Ketek tablets can be given without regard to food.

Mean steady-state trough plasma concentrations of between 0.04 and 0.07 mg/l are reached within 3 to 4 days with once-daily dosing of telithromycin 800 mg. At steady-state AUC is approximately 1.5 fold increased compared to the single dose.

Mean peak and trough plasma concentrations at steady state in patients were 2.9±1.6 mg/l (range 0.02-7.6 mg/l) and 0.2±0.2 mg/l (range 0.010 to 1.29 mg/l), during a therapeutic 800 mg once-daily dose regimen.

Distribution

The in vitro protein binding is approximately 60 % to 70 %. Telithromycin is widely distributed throughout the body. The volume of distribution is 2.9±1.0 l/kg. Rapid distribution of telithromycin into tissues results in significantly higher telithromycin concentrations in most target tissues than in plasma. The maximum total tissue concentration in epithelial lining fluid, alveolar macrophages, bronchial mucosa, tonsils and sinus tissue were 14.9±11.4 mg/l, 318.1±231 mg/l, 3.88±1.87 mg/kg, 3.95±0.53 mg/kg and 6.96±1.58 mg/kg, respectively. The total tissue concentration 24 h after dose in epithelial lining fluid, alveolar macrophages, bronchial mucosa, tonsils and sinus tissue were 0.84±0.65 mg/l, 162±96 mg/l, 0.78±0.39 mg/kg, 0.72±0.29 mg/kg and 1.58±1.68 mg/kg, respectively. The mean maximum white blood cell concentration of telithromycin was 83±25 mg/l.

Metabolism

Telithromycin is metabolized primarily by the liver. After oral administration, two-thirds of the dose is eliminated as metabolites and one-third unchanged. The main circulating compound in plasma is telithromycin. Its principal circulating metabolite represents approximately 13 % of telithromycin AUC, and has little antimicrobial activity compared with the parent medicinal product. Other metabolites were detected in plasma, urine and faeces and represent less or equal than 3 % of plasma AUC.

Telithromycin is metabolized both by CYP450 isoenzymes and non-CYP enzymes. The major CYP450 enzyme involved in the metabolism of telithromycin is CYP3A4. Telithromycin is an inhibitor of CYP3A4 and CYP2D6, but has no or limited effect on CYP1A, 2A6, 2B6, 2C8, 2C9, 2C19 and 2E1.

Elimination

After oral administration of radiolabelled telithromycin, 76 % of the radioactivity was recovered from faeces, and 17 % from the urine. Approximately one-third of telithromycin was eliminated unchanged; 20 % in faeces and 12 % in urine. Telithromycin displays moderate non-linear pharmacokinetics. The non-renal clearance is decreased as the dose is increased. The total clearance (mean ±SD) is approximately 58±5 l/h after an intravenous administration with renal clearance accounting for about 22 % of this. Telithromycin displays a tri-exponential decay from plasma, with a rapid distribution half-life of 0.17 h. The main elimination half-life of telithromycin is 2-3 h and the terminal, less important, half-life is about 10 h at the dose 800 mg once daily.

Special populations

-Renal impairment
In a multiple-dose study, 36 subjects with varying degrees of renal impairment, a 1.4-fold increase in $C_{max,ss}$, and a 2-fold increase in AUC $(0\text{-}24)_{ss}$ at 800 mg multiple doses in the severe renally impaired group (CLCR < 30 mL/min) compared to healthy volunteers were observed and a reduced dosage of Ketek is recommended (See Section 4.2.). Based on observed data, a 600 mg daily dose is approximately equivalent with the target exposure observed in healthy subjects. Based on simulation data, an alternating daily dosing regimen of 800 mg and 400 mg in patients with severe renal impairment can approximate the AUC (0-48h) in healthy subjects receiving 800 mg once daily.

The effect of dialysis on the elimination of telithromycin has not been assessed.

-Hepatic impairment
In a single-dose study (800 mg) in 12 patients and a multiple-dose study (800 mg) in 13 patients with mild to severe hepatic insufficiency (Child Pugh Class A, B and C), the C_{max}, AUC and $t_{1/2}$ of telithromycin were similar compared to those obtained in age- and sex-matched healthy subjects. In both studies, higher renal elimination was observed in the hepatically impaired patients. Due to limited experience in patients with decreased metabolic capacity of the liver, Ketek should be used with caution in patients with hepatic impairment (see also section 4.4).

-Elderly subjects
In subjects over 65 (median 75 years), the maximum plasma concentration and AUC of telithromycin were increased approximately 2 fold compared with those achieved in young healthy adults. These changes in pharmacokinetics do not necessitate dosage adjustment.

-Paediatric patients
The pharmacokinetics of telithromycin in paediatric population less than 12 years old have not yet been studied. Limited data, obtained in paediatric patients 13 to 17 years of age, showed that telithromycin concentrations in this age group were similar to the concentrations in patients 18 to 40 years of age.

-Gender
The pharmacokinetics of telithromycin are similar between males and females.

5.3 Preclinical safety data

Repeated dose toxicity studies of 1, 3 and 6 months duration with telithromycin conducted in rat, dog and monkey showed that the liver was the principal target for toxicity with elevations of liver enzymes, and histological evidence of damage. These effects showed a tendency to regress after cessation of treatment. Plasma exposures based on free fraction of active substance, at the no observed adverse effect levels ranged from 1.6 to 13 times the expected clinical exposure.

Phospholipidosis (intracellular phospholipid accumulation) affecting a number of organs and tissues (e.g., liver, kidney, lung, thymus, spleen, gall bladder, mesenteric lymph nodes, GI-tract) has been observed in rats and dogs administered telithromycin at repeated doses of 150 mg/kg/day or more for 1 month and 20 mg/kg/day or more for 3-6 months. This administration corresponds to free active substance systemic exposure levels of at least 9 times the expected levels in human after 1 month and less than the expected level in humans after 6 months, respectively. There was evidence of reversibility upon cessation of treatment. The significance of these findings for humans is unknown.

In similarity to some macrolides, telithromycin caused a prolongation of Qtc interval- in dogs and on action potential duration in rabbit Purkinje fibers in vitro. Effects were evident at plasma levels of free drug 8 to 13 times the expected clinical level. Hypokalaemia and quinidine had additive/supra-additive effects in vitro while potentiation was evident with sotalol. Telithromycin, but not its major human metabolites, had inhibitory activity on HERG and Kv1.5 channels.

Reproduction toxicity studies showed reduced gamete maturation in rat and adverse effects on fertilization. At high doses embryotoxicity was apparent and an increase in incomplete ossification and in skeletal anomalies was seen. Studies in rats and rabbits were inconclusive with respect to potential for teratogenicity, there was equivocal evidence of adverse effects on foetal development at high doses.

Telithromycin, and its principal human metabolites, were negative in tests on genotoxic potential *in vitro* and *in vivo*. No carcinogenicity studies have been conducted with telithromycin.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core:

Microcrystalline cellulose
Povidone K25
Croscarmellose sodium
Magnesium stearate

Tablet coating:

Talc
Macrogol 8000
Hypromellose 6 cp
Titanium dioxide E171
Yellow iron oxide E172
Red iron oxide E172

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

No special precautions for storage.

6.5 Nature and contents of container

Two tablets are contained in each blister cavity.

Available as packs of 10, 14, 20 and 100 tablets.
Opaque PVC/Aluminium blisters

Available as pack of 5 x 2 tablets.
Opaque PVC/Aluminium perforated unit dose blisters.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7. MARKETING AUTHORISATION HOLDER

Aventis Pharma S.A.
20, Avenue Raymond Aron
F-92160 ANTONY
France

8. MARKETING AUTHORISATION NUMBERS

EU/1/01/191/001-005

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first ~~authorizaton~~ authorisation: 9 July 2001
Date of first renewal: 9 July 2006

10. DATE OF REVISION OF THE TEXT

P52

PACKAGE LEAFLET

This PL was approved by the CHMP on 22 March 2007 and is pending for endorsement by the European Commission

PACKAGE LEAFLET: INFORMATION FOR THE USER

Ketek 400 mg film-coated tablets
Telithromycin

Read all of this leaflet carefully before you start taking this medicine.
- Keep this leaflet. You may need to read it again.
- If you have further questions, ask your doctor or your pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. WHAT KETEK IS AND WHAT IT IS USED FOR

Ketek belongs to one of a group of medicines called ketolides, a new class of antibiotics related to macrolides. Antibiotics stop the growth of bacteria which cause infections.

Ketek is used in adults and adolescents of 12 years and older to treat infections due to bacteria against which the medicine is active. In adolescents of 12 years and older, Ketek can be used to treat: infections of the throat. In adults, Ketek can be used to treat infections of the throat, infections of the sinuses, chest infections in patients with long standing breathing difficulties and pneumonia.

2. BEFORE YOU TAKE KETEK

Do not take Ketek:

- if you suffer from myasthenia gravis, a rare disease which causes muscle weakness.
- if you are allergic (hypersensitive) to telithromycin, to any of the macrolide antibiotics or to any of the other ingredients of Ketek. If in doubt, talk to your doctor or pharmacist.
  if you have had a hepatitis and/or jaundice while taking Ketek in the past.
- if you are taking certain medicinal products to control the blood level of cholesterol or other lipids.
- if you or someone in your family are known to have an abnormality of electrocardiogram (ECG) called "long QT syndrome".
- while taking other medicines containing any of the following active substances:
  - ergotamine or dihydroergotamine (tablets or inhaler for migraine)
  - terfenadine or astemizole (allergic problems)
  - cisapride (digestive problems)
  - pimozide (psychiatric problems)

-if you have severely impaired renal function and/or severely impaired hepatic function, do not take Ketek while taking other medicines containing any of the following active substances:
- ketoconazole (anti fungal treatment)
- a medicine called protease inhibitor (HIV treatment)

Refer also to section "Taking other medicines".

Take special care with Ketek:
- if you have had certain heart problems such as coronary heart disease, ventricular arrhythmias, bradycardia or if you have had certain abnormal blood tests due to medical conditions such as hypokalaemia, hypomagnesaemia.
- if you develop severe or prolonged or bloody diarrhoea during or after taking Ketek tablets, consult your doctor immediately since it may be necessary to interrupt the treatment. This may be a sign of bowel inflammation (*pseudomembranous colitis*) which can occur following treatment with antibiotics.
- ~~if you suffer from myasthenia gravis, a rare disease which causes muscle weakness.~~
- ~~if you experience any worsening of your symptoms of myasthenia gravis during treatment with Ketek, you should interrupt treatment with Ketek and immediately seek medical attention.~~
- if you have liver disease.
- if you experience visual disturbances (blurred vision, difficulty in focusing, double vision)
- if you experience transient loss of consciousness (fainting).
- Ketek tablets are not recommended for use in children and adolescents less than 12 years old.

Refer also to sections "Do not take Ketek"~~ and~~, "Taking other medicines" and "Driving and using machines".

Taking other medicines
Please tell your doctor if you are taking or have recently taken any other medecines, including medicines obtained without a prescription, as some of them could have an interaction with Ketek.

You should not use Ketek with medicines containing ergotamine or dihydroergotamine tablets or ergotamine inhalers for migraine, terfenadine or astemizole for allergic problems, cisapride for digestive problems and pimozide for psychiatric problems. You should not use Ketek if you are taking certain medicinal products to control the blood level of cholesterol or other lipids, like simvastatin. Refer also to section "Do not take Ketek".

It is particularly important for your doctor to know if you are taking medicines containing phenytoin, and carbamazepine (for epilepsy), rifampicin (antibiotic), phenobarbital or St John's wort, medicines like tacrolimus, cyclosporin and sirolimus (for organ transplantation), or metoprolol (against heart disorder) or the anti HIV medicine ritonavir.

Taking Ketek with food and drink
Ketek may be taken with or without food.

Pregnancy and Breast-feeding
If you are pregnant do not take Ketek tablets as the safety of Ketek in pregnancy is insufficiently established. If you are breast-feeding do not take Ketek tablets.

Driving and using machines
Limit driving or other hazardous activities while taking Ketek. If you have vision problems or faint while taking Ketek, do not drive, operate heavy machinery, or engage in dangerous activities.
Taking Ketek tablets may cause side effects such as visual disturbances, which may reduce the capacity to carry out certain tasks. Rare cases of transient loss of consciousness (fainting), which may be preceded by vagal symptoms (malaise, gastrointestinal distress), have been reported. These symptoms may appear as early as after the first dose of Ketek.~~ You should be aware of the potential effect of these symptoms on your ability to drive or operate machinery~~

3. HOW TO TAKE KETEK

Your doctor will tell you how many Ketek tablets to take, at what time and for how long.

The usual duration of treatment is 5 days for infections of the throat, infections of the sinuses, chest infections in patients with long standing breathing difficulties and 7 to 10 days for pneumonia.

The recommended dose of Ketek for adults and children of 12 years and older is two tablets of 400 mg once daily (800 mg once daily).
If you have severe renal insufficiency you should take alternating daily doses of 800 mg (two tablets of 400 mg) and 400 mg (one tablet of 400 mg), starting with the 800 mg dose.

Swallow the tablets whole with a glass of water.
It is best to take tablets at the same time each day. If possible take the tablets before going to bed, to reduce the potential impact of visual disturbances and loss of consciousness.

If you take more Ketek than you should
If you accidentally take one tablet too many, nothing is likely to happen. If you accidentally take several tablets too many, contact your doctor or pharmacist. If possible, take your tablets or the box with you to show the doctor or pharmacist.

If you forget to take Ketek
If you forget to take a dose, take it as soon as possible. However, if it is nearly time for your next dose skip the missed dose and take the next tablet at the usual time.

If you stop taking Ketek
Take the complete course of tablets prescribed by your doctor, even if you begin to feel better before you have finished them all. If you stop taking the tablets too soon, the infection may return, or your condition may get worse.
If you stop taking the tablets too soon you may also create a bacterial resistance to the medicine.
If you feel you are suffering from a side effect, tell a doctor immediately to get advice before taking the next dose.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS

Like all medicines Ketek can cause side effects, although not everybody gets them. Most of them are mild and transient, but very rare cases of serious adverse liver reactions and liver failure, including fatal cases, have been reported. So, if any of the following happens, stop taking Ketek and tell your doctor immediately:

- Allergic or skin reactions such as face swelling, general allergic reactions including allergic shock, or serious skin conditions associated with red spots, blisters.
- Severe, persistent or bloody diarrhoea associated with abdominal pain or fever, which can be a sign of serious bowel inflammation which may occur very rarely following treatment with antibiotics.
- Signs and symptoms of hepatitis (liver disease) such as yellowing of skin and eyes, dark urine, itching, loss of appetite or abdominal pain.
- Worsening of a condition called myasthenia gravis, a rare disease which causes muscle weakness. ~~Reports have included death and life-threatening breathing trouble that happens fast in myasthenia gravis patients~~.

The above serious side effects are uncommon (1 out of 1000 to less than 1 out of 100), rare (1 out of 10,000 to less than 1 out of 1000 patients) or very rare (less than 1/10,000 patients including isolated report), but may require urgent medical attention.

The other side effects listed below are given with an estimation of the frequency with which they may occur.

The most common side effect (10 or more out of 100 patients) which may occur with Ketek is diarrhoea, usually mild and temporary.

Other side effects which may commonly (1 to 10 out of 100 patients) occur with Ketek are:
Nausea, vomiting, abdominal pain, flatulence (excess wind), dizziness, headaches, disturbance of taste, vaginal *Candida* infection (fungal infection associated with local itching, burning and white discharge), increase in liver enzymes (detected by blood test).

Uncommon or rare side effects (1 out of 10,000 to less than 1 out of 100 patients) which may occur with Ketek are:
Constipation, anorexia (loss of appetite), stomatitis (inflammation in themouth), oral *Candida* infection (fungal infection), hepatitis, rash, urticaria (hives), pruritus (itching), eczema, somnolence, insomnia, nervousness, vertigo, paraesthesia (tingling of the hands or feet), , visual disturbances (blurred vision, difficulty in focusing, double vision), , flushes, transient loss of consciousness (fainting), arrhythmia, bradycardia or palpitations (changes in heart rate or in ECG), hypotension (low blood pressure), eosinophilia (increase of certain white blood cells, detected by blood test).
Very rare side effects(less than 1 out of 10,000 patients) which may occur with Ketek are :
Disturbance of smell, muscle cramps.

Additional side effects which may occur with Ketek are:
abnormality of electrocardiogram (ECG) called prolongation of QT interval and inflamed pancreas (pancreatitis).
During post-marketing experience, liver failure has been reported (frequency unknown).

If any of these undesirable effects are troublesome, severe, or do not wear off as treatment goes on, tell your doctor.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE KETEK

Keep out of the reach and sight of children.

Do not use Ketek after the expiry date which is stated on the pack.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION

What Ketek contains

- The active substance is telithromycin
- The other ingredients are microcrystalline cellulose, povidone K25, croscarmellose sodium, magnesium stearate in the tablet core as well as talc, macrogol 8000 , hypromellose 6 cp, titanium dioxide E171, yellow iron oxide E172, red iron oxide E172 in the film-coating.

What Ketek looks like and contents of the pack

Ketek 400 mg tablets are light orange, oblong, biconvex, film-coated tablet imprinted with "H3647" on one side and "400" on the other.

Ketek tablets are presented in blister packs. Two tablets are contained in each blister cavity.
They are available in packs of 10, 5x2, 14, 20 and 100 tablets. Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

The marketing authorisation holder of Ketek is:
Aventis Pharma S.A.
20 Avenue Raymond Aron
F-92160 ANTONY
France

The manufacturer of Ketek is:
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I-67019 Scoppito (L'Aquila), Italy

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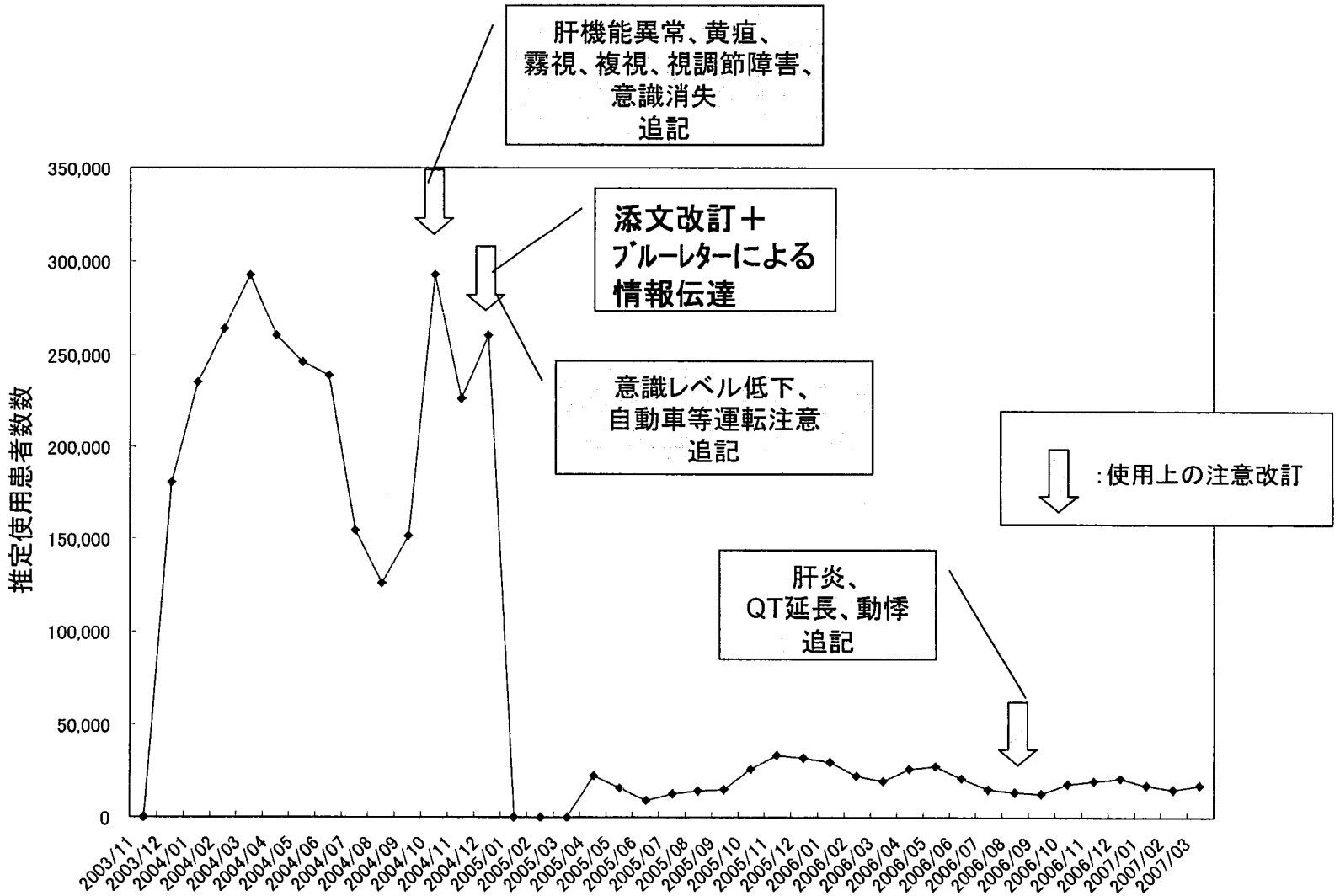

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